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Effect of the COVID-19 pandemic on anxiety among children with cystic fibrosis and their mothers

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Abstract

Background: We aimed to evaluate anxiety among children with cystic fibrosis (CF) and their mothers related to the COVID-19 pandemic.

Methods: A total of 45 patients with CF and their mothers were enrolled in the study together with 90 age-matched healthy children and their mothers as a control group. The State and Trait Anxiety Inventory (STAI) was administered by teleconference with children aged 13–18 years old and their mothers. The STAI for children was administered with children aged 9–12 years. Results were compared with age-matched healthy children and their mothers. The relationship between anxiety scores of children with CF and their mothers was evaluated by comparing with clinical data of children with CF. At the conclusion of the teleconference, mothers were asked whether their anxiety had changed as a result of the interview.

Results: It was found that healthy children aged 13–18 years had higher state anxiety scores than age-matched children with CF. Mothers of children with CF had higher trait anxiety scores, especially those of children aged 0–12 years, than mothers of healthy children ($p<0.05$). For mothers of children with CF, state anxiety scores were higher among those whose children had chronic *Pseudomonas* infection ($p<0.05$). Most mothers of children with CF stated that their anxiety decreased following the interview.

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Conclusion: The COVID-19 pandemic may increase anxiety among mothers of children with CF as well those with healthy children. However, COVID-19 had no effect on the anxiety of children with CF. Informing parents of children with CF about COVID-19 by teleconference may decrease anxiety.

Introduction

Cystic fibrosis (CF) is a chronic, life-shortening disease with multisystemic involvement. The respiratory system is affected in most patients with CF, with chronic pulmonary infections that lead to respiratory failure being the main cause of death for these patients[1,2]. Major causes of morbidity and mortality are respiratory complications[3], and chronic illnesses can cause a number of psychological problems and distress among children and their parents[4-6]. Many studies have shown that depression and anxiety rates are elevated among children with CF and their parents[7-10]. It has been shown that general family functions, depression, and anxiety symptoms show a strong relationship with health outcomes among patients with CF[11,12]. Anxiety and depressive symptoms are associated with poorer quality of life, low lung function, reduced physical functioning, and severity of chest symptoms[9]. Parental anxiety and depression increase the risk of depression and anxiety also in the child and negatively affect the treatment compliance and health outcomes[13]. Determination and treatment of parental mental health problems such as depression and anxiety might improve the child's adherence to treatment[14]. Therefore, routine annual screening of depression and anxiety is recommended for patients with CF and their families[15].

1 Coronavirus disease 2019 (COVID-19) is a newly emerging disease that has become a global public health issue. The etiological agent responsible for this disease is severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).

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The disease first appeared in the Hubei province of China, and whilst it follows human-to-human transmission, the pathway for this virus to establish human infection remains a mystery[16]. Mild fever, dry cough, nasal congestion, sore throat, headache, muscle pain, and malaise are observed among milder patients, with some patients being asymptomatic. Moderate-to-severe patients experience respiratory symptoms such as dyspnea, shortness of breath, and tachypnea, which can result in severe pneumonia and acute respiratory distress syndrome leading to mortality[17]. The mortality risk was found to be increased among patients with underlying diseases, secondary infections, and elevated inflammatory indicators[18]. In the initial stage of COVID-19 infection in China, a cross-sectional study was conducted for evaluating immediate psychological responses and associated factors in general population which indicated that one third of subjects had moderate-to-severe anxiety; moreover, female gender, student status, specific physical symptoms (such as muscle pain, dizziness, and coryza), poor self-reported health status and having a chronic ilness were significantly associated with adverse psychological effect as a result of the outbreak (such as higher levels of stress, anxiety, and depression)[19]. 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[20].

Viral respiratory infections take a more severe course among patients with CF than among the general population and negatively affect lung function. During the 2009 influenza pandemic, the H1N1 virus caused significant morbidity among patients with CF, and in a subgroup with severe lung disease, H1N1 infection was associated with respiratory impairment, mechanical ventilation, and even death[21,22].

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Therefore, there is a strong probability that COVID-19 may cause anxiety among children with CF and their families.

We aimed to evaluate anxiety experienced by children with CF and their mothers following COVID-19 being declared a global pandemic by the World Health Organization (WHO). We also aimed to compare the results to age-matched healthy children and their mothers about how intensity of anxiety elevations may differ between the two groups. And to compare the anxiety levels of children and mothers according to the children's gender and age groups. As clinical severity of CF may affect the anxiety status of patients and their parents we investigated the relation between the anxieties of both the children and their mothers and clinical findings of children with CF. Another aim of this study was the evaluation of the effect of the provided information about COVID-19 by their own doctors to parents of children with CF.

Material and Methods

The study included all children aged 0–18 years with CF and their mothers who were patients at the pediatric pulmonology department. Totally 48 patients who have been followed regularly in pediatric pulmonology department were called by phone. Two patients could not be reached and one patient declined to participate in the study. A total of 45 patients with CF and their mothers were included in the study group and 90 healthy age-matched children and their mothers were placed in a control group. Healthy children did not come to hospitals except emergency situations because of transmission risk of COVID-19 during the study period. Children in control group were recruited through snowball sampling. Children of medical system workers were not included the study due to the fact that they might have more knowledge and higher anxiety about COVID-19 because of the high risk of viral

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transmission risk in the hospitals. Because of the risk of contamination from the SARS-CoV-2 virus and the prohibition on travel and activities, participants were asked to respond to questions and scales by teleconference (audio with video) between 15–20 April, 2020. The doctors who examine them regularly in the pediatric pulmonology department conducted the interviews. The interviews were done separately with the child and parent. After the child's age and gender and the mothers' age and education level were recorded first scales related to anxiety and then a questionnaire about COVID-19 were administered. After these, mothers were informed about COVID-19 in terms of spread of SARS-CoV-2, protection methods, hand sanitization and wearing masks, symptoms and signs of COVID-19 and things to do in case of illness according to the advices in WHO website[23]. Since self-reported symptoms could be effected, participants informed about the aim of the study after applying the anxiety scales and then questionnaire about COVID-19 was applied and mothers were informed about COVID-19.

Questions were prepared by the authors using the WHO website about COVID-19 advice for public: myth busters[24] to measure mothers' knowledge about the disease with true or false answers. Questions consisted of issues about the viability of SARS-CoV-2 on surfaces, methods of contamination, treatment for COVID-19, mortality risk among children, risk factors for infection, and comorbid diseases. The number of correct answers were recorded.

Clinical information was also recorded from hospital files for the study, as follows: patient's age and gender; number of hospital admissions and hospitalization episodes in the last year; presence of chronic *Pseudomonas* infection; and clinical severity of patient. Chronic *Pseudomonas* infection was defined as when more than 50% of months, when samples had been taken, were *P. aeruginosa* culture positive[25].

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Mean follow-up duration which was defined as the time period between the time of the diagnosis of CF and the last control time in the clinic was noted. Results for pulmonary function tests (PFT) were recorded for patients who could perform in the last control, and forced vital capacity (FVC), forced expiratory volume (FEV), FEV in 1 s (FEV1), and forced expiratory flow (FEF25–75) spirometry tests were recorded as predicted percentages. In addition, the FEV1/FVC ratio was recorded and assessed based on age, gender, and height, and the modified Shwachman-Kulczycki Score (mSKS) was used to determine the clinical severity of the disease. Scores were provided for four sections: general activity, findings from physical examination, nutritional status, and radiological findings. Each parameter was scored from 5 (severely impaired) to 25 (normal), which resulted in a total score categorized as excellent (86–100), good (71–85), mild (56–70), moderate (41–55), and severe (<40)[26,27]. Clinical severity of CF was rated by the same pediatric pulmonologist. Scales related to anxiety were applied by teleconference with children aged over 9 years with CF and their mothers. Patients with CF and their mothers were identified as the 'study group'.

A 'control group' consisted of age-matched healthy children and their mothers who had also been enrolled in the study. Anxiety scales were applied by teleconference to children older than nine years, and all mothers.

Anxiety scales were not applied to participants younger than nine years of age. The State-Trait Anxiety Inventory for Children (STAI-C) is an anxiety measurement tool for evaluating the state and traits of anxiety among children aged 9–12 years. It contains two separate scales to measure the concepts of state and trait anxiety. The state scale, which is a measure of temporary anxiety states, consists of 20 items asking children how they feel at the present time. The trait scale consists of 20 items that ask

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children how they feel in general. This measures relatively stable individual differences in anxiety trends. Items are rated on a 3-point scale with responses: hardly ever, sometimes, and often[28-30]. Higher scores indicate a higher level of anxiety. Validation and reliability study of the Turkish version was performed by Özusta[30].

For children aged 13–18 years (and all mothers), the State-Trait Anxiety Inventory (STAI) was used. This is used to measure the presence and severity of existing anxiety symptoms and general anxiety tendencies. The test-retest reliability coefficients in the initial development ranged from 0.31 to 0.86 with intervals ranging from 1 hour to 104 days[31]. Validation and reliability study of the Turkish version was performed by Oner and Le Compte[32]. There are two sub-scales within this scale. First, the state-anxiety inventory (consisting of 20 items) evaluates the current state of anxiety and asks how participants feel “right now” using items that measure subjective anxiety, tension, nervousness, anxiety, and activation/arousal. The responses of the state-anxiety scale evaluate the "present" intensity of current emotions: 1) not at all, 2) somewhat, 3) moderately so, and 4) very much so. The trait-anxiety scale (also consisting of 20 items) evaluates relatively stable aspects of “anxiety tendency,” including general calmness, trust, and security situations. The responses of the trait-anxiety scale evaluate the “in general” frequency of emotions: 1) almost never, 2) sometimes, 3) often, and 4) almost always[31,32]. Higher scores indicate a higher level of anxiety.

Since the COVID-19 pandemic is a newly emerging situation, the current anxiety of children was measured using the STAI and STAI-C state scales and general anxiety was measured using the trait scale of STAI and STAI-C.

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At the end of the teleconference, after informing the mothers about COVID-19 they were asked whether their anxiety had changed as a result of the interview. Answers were noted as decreased, increased, or not changed.

All data collected from mothers and children were compared between the study and control groups. In the study group, the relation between anxiety results of children and mothers was compared with the number of hospital admissions and hospitalization episodes in the last year, the presence of chronic *Pseudomonas* infection, mean follow-up duration, PFT results, and mSKS for all CF patients.

Data analysis was performed using the Statistical Package for Social Sciences (SPSS) v.22.0. Continuous variables were presented as mean ± standard deviation (SD), median, and minimum and maximum levels, while categorical variables were presented as rate and percentage values. Mann-Whitney U, independent t-test, Chi-Square, and Spearman correlation tests were conducted for the analysis. A p value of less than 0.05 was considered statistically significant.

This study was approved by Ethical Committee of Medicine Faculty (Date: 13/04/2020, number: 266).

Results

All mothers were primary caregivers for their children. The average time of interview by teleconference was 20 min. In the study group, 25 patients were aged 0–8 years (14 male and 11 female); 14 patients were aged 9–12 years (6 male and 8 female); and 6 were aged 13–18 years (3 male and 3 female). In the control group, 46 patients were aged 0–8 years (20 male and 26 female); 22 patients were aged 9–12 years (14 male and 8 female); and 22 patients were aged 13–18 years (12 male and 10

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female). None of the children or their mothers of family members had COVID-19 before or during the study period in either group. No statistical difference was identified in terms of the age (99.0 [63.3-139.5] vs 106.7 [53.0-159.1] months) and gender of the children (22 [48.9] vs 44 [48.9] female) and the mothers' age (34.0 [31.0-41.5] vs 38 [32.0-44.0] years) between both groups ($p > 0.05$), however mothers in control group had a higher education level ($p<0.001$), as shown in Table 1.

The mean follow-up duration was 78.0 ± 48.7 months, with 12 patients having been hospitalized in the last year. The mean mSKS for patients was 75.2 ± 13.8, with 4 having had chronic *Pseudomonas* infection in the last year. Clinical data for patients with CF are presented in Table 2.

Neither state not trait anxiety scores differed by gender for 9–12 year olds and 13–18 year olds in both study and control groups ($p > 0.05$). Anxiety scores for children according to age group were compared between the study and control groups. It was found that state anxiety scores for children aged 13–18 years in the control group were higher than for the age-matched children with CF (29.0 [27.8-32.3] vs 41.5 [35.5-46.3]; $p = 0.003$). No correlation was observed between state and trait anxiety scores and hospital admission, hospitalization in the last year, clinical scores, and follow up duration in children with CF. Anxiety scores for children are presented in Table 3.

When the results for mothers' anxiety were evaluated, trait anxiety in the study group was significantly higher than in the control group (41.7 ± 8.9 vs 36.2 ± 8.3; $p = 0.001$). There was a positive correlation between state and trait anxiety scores for mothers of children with CF ($r = 0.590$, $p < 0.001$). The percentage of questions answered correctly concerning knowledge about COVID-19 was higher for mothers in

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the control group (64.3 [57.1-78.6] vs 78.6 [71.4-85.7]; p = 0.001). Trait anxiety scores were higher for mothers in the study group (whose children were aged 0–8 years and 9–12 years) than those with children of the same age in the control group (41 [35-47] vs 36 [30.8-42]; p = 0.030; 43.5 [40.8-47.3] vs 33 [29.5-39]; p = 0.002). However, there were no significant differences between mothers in the study and control groups when comparing state and trait anxiety scores according to the children's age groups (p > 0.05). Comparisons of anxiety status between mothers in both groups and according to their children's age are shown in Table 4.

There was no significant correlation between mother's state and trait anxiety scores and their children's mSKS, follow-up duration, hospital admission and duration of hospitalization episode in the last year, and PFT results in the study group. Only 4 patients had chronic *Pseudomonas* infection, and mothers' state anxiety score (58.5 ± 7.3) was higher for children with CF with chronic *Pseudomonas* infection than mothers of children with CF without chronic *Pseudomonas* infection (47.3 ± 10.3) (p = 0.042).

There was a moderate, positive correlation between mothers' state anxiety scores and trait anxiety scores for 9–12 year-old children (r = 0.625; p = 0.017) in the study group. The percentage of questions answered correctly concerning knowledge about COVID-19 was negatively correlated with mothers' trait anxiety scores (r = -0.323; p = 0.031) in the study group.

At the end of the teleconference, mothers were asked whether their level of anxiety had changed as a result of taking part in the interview. Among mothers in the study group, 84% reported a decrease in anxiety, while 6.7% reported an increase, and 8.9% reported no change. Among mothers in the control group, 34.4% reported a

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decrease in anxiety, while 12.2% reported an increase, and 53.3% reported no change. Mothers' anxiety in the study group decreased significantly compared with mothers in the control group ($p = 0.000$).

Discussion

The burden and effects of COVID-19 are felt all around the world, and this is likely to cause fear and anxiety. In our study, trait anxiety for mothers of children with CF was found to be especially high for those with younger children; however, children with CF had no elevated anxiety scores compared with healthy children in the control group. It was also found that the teleconference with mothers of children with CF made them feel less anxious about the COVID-19 pandemic.

Many studies have shown that patients with CF have higher levels of anxiety compared with healthy controls[33,34]. Anxiety symptoms were found to be more frequent among the adolescent population and adults compared with the general population, with a prevalence of 11%–33%[9]. Among patients with CF in the 7–14 year-age group, anxiety was reported as the most prevalent diagnosis[35]. However, in our study, healthy children aged 13–18 years had higher state anxiety scores, and girls demonstrated higher anxiety levels than boys. Similar to the findings of a study on children and adolescents with non-CF bronchiectasis, state anxiety was found to be higher in the healthy control group[36]. Since children with CF experience constant disease anxiety, their scores may be increased during the COVID-19 pandemic. However, more pronounced anxiety among healthy children may be because these children have not encountered the fear of disease before. Facing the risk of experiencing a serious health problem for the first time may increase their fear and anxiety. Perhaps CF could be protective in some way as these children have already

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faced stressful experiences and perhaps have developed more adaptive coping strategies to manage future crisis than the general population. Management of CF requires a complex, time-consuming treatment regimen with several medications, chest physiotherapy, pulmonary exacerbations, frequent hospital visits, and hospitalization episodes. Caregivers of children with CF demonstrate a high prevalence of anxiety symptoms[37]. Mothers of children with CF in our study had higher trait anxiety scores compatible with the literature. Parents' anxiety demonstrates a strong correlation with health outcomes among patients with CF[10]. Elevated rates of anxiety symptoms have been found to be negatively correlated with quality of life among parents of children with CF, notably elevated levels of depressive symptoms[10,37]. These are all known to affect the health outcomes of children with CF. In our study, mothers of children with CF aged 0–12 years had higher trait anxiety scores than mothers of healthy children in the same age group. However, there were no differences among mothers of children aged 13–18 years. Mean mSKS and PFT results were higher among our patients with CF, which may help them to feel good in terms of their disease. In a study with adolescent children with CF, caregivers' anxiety scores were associated with adolescents' scores, and lower anxiety symptoms were found among adolescent patients who had adapted quite well to their illness[38]. These could be compatible with our results.

In our study there was a moderate, positive correlation between the state anxiety scores of the mothers and trait anxiety scores of the 9–12 year-old children. Compatible with our results, it was demonstrated that elevated anxiety levels of mothers lead to an increase which is also more likely to be elevated among teens[15].

Pseudomonas aeruginosa is associated with an increased rate of decline in FEV1, a failure to recover baseline lung function after a pulmonary exacerbation, and

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shortened survival[39]. Chronic *Pseudomonas* infection was found to be related with anxiety among patients with bronchiectasis unrelated to CF[40,41]. Furthermore, *Pseudomonas aeruginosa* infection was shown to be significantly associated with higher caregiver burden[41]. There is evidence that parents of children with CF may be very anxious about the acquisition of *Pseudomonas aeruginosa*[42,43]. Mothers of children with CF who have chronic *Pseudomonas* infection had higher state anxiety scores in our study. Knowing the destructive results of *Pseudomonas* infection and having experienced a pulmonary exacerbation may have increased the state anxiety of these particular mothers.

At the end of the teleconference, most mothers of children with CF stated that their anxiety decreased after the interview. As CF is a lifelong, chronic disease, good cooperation occurs between the families and children's doctors over the years. Talking to a familiar doctor about this new situation and obtaining information may have offered the mothers some relief. It should be recommended to families of children with chronic diseases to provide an interview with their doctor to obtain correct information in such sudden and emerging situations. During this period, people may be afraid of going to hospital, due to a fear of COVID-19 infection; thus, communication with patients and their families by teleconference may help to decrease their anxiety about any additional probable worse effects of COVID-19 for patients with CF.

This was a timely study for understanding how mental health of patients with CF and their parents are changing during a crisis like this pandemic. This data can help to guide future psychosocial screening and intervention provided to children with chronic illness and their families during these times. However, we had some limitations. Sample size was small and only 20 children could fill the anxiety

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inventory because of age limitation of anxiety scales and subgroup analyses (such as age and gender) were performed in fewer subjects. Also it is difficult to interpret the results because age group allocations were not matched across groups.

In conclusion, caregivers of children with CF are already anxious about the disease and emerging pandemics such for COVID-19 may increase their anxiety. During this period, providing information about COVID-19 to parents of children with CF by their own doctors may have a positive effect on families, especially those who have younger children and children with chronic *Pseudomonas* infection. Longitudinal and larger studies may provide more information to guide future psychosocial screening and intervention given to children with a chronic illness and their families during a crisis like this pandemic. **References**

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Tables

Table 1. Comparison of age and gender of children and mothers' age and education level between two groups.

	Study Group (n=45)	**Control Group (n=90)**	**P**
Age of children, month			0.845*

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Median (IRQ)	99.0 (63.3-139.5)	106.7 (53.0-159.1)	
Gender, n(%)			1.00**
Female	22 (48.9)	44 (48.9)	
Male	23 (51.1)	46 (51.1)	
Age of mothers (year)	34.0 (31.0-41.5)	38 (32.0-44.0)	0.083*
Education level of mothers n(%)			
Primary school	13 (28.9)	4 (4.4)	<0.001**
Middle school	7 (15.6)	0 (0)	
High school	13 (28.9)	21 (23.3)	
University	11 (24.4)	53 (58.9)	
Post graduate	1 (2.2)	12 (13.3)	

**Mann-Whitney U test **Chi-Square test*

Table 2. Clinical data of children with CF.

n=45	n %
Mean follow-up duration, month	
mean±sd	78.0 ± 48.7
Hospital admission in the last year	
mean±sd	5.2 ± 3.3
Number of hospitalization in the last year	
None	33 73.3
1	8 17.8
2	4 8.9

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Total hospitalization duration, day	
mean±sd	13.1 ± 6.9
mSKS*	
mean±sd	75.2 ± 13.8
Chronic Pseudomonas infection	4 8.9
Pulmonary function test, mean±sd	
FEV1 %	74.8 ± 25
FVC %	74.8 ± 24.6
MEF25-75 %	72.1 ± 31.5
FEV1/FVC	97.1 ± 9.8

* modified Shwachman-Kulczycki Score

Table 3. Comparison of anxiety status of children in two groups.

	State anxiety		**Trait anxiety**	
	Study gr. Control gr.	**P**	**Study gr. Control gr.**	**P**
9-12 years	n=12 n=21		n=12 n=21	
mean±sd	28.4 ± 5.2 29.4 ± 4.1	0.547*	35.2 ± 7.6 31.9 ± 5.7	0.172*
Girl	n=7 n=8	0.222**	n=7 n=8	0.684**
Median (IRQ)	27(25-30) 30(28.2-34.7)	0.921**	33 (30-47) 32.5(31-39)	0.323**
Boy	n=5 n=13		n=5 n=13	
Median (IRQ)	29(26.5-30.5) 28(27.5-30)		(28.5-39.5) 30 (27.5-35)	
	Study gr. Control gr.		**Study gr. Control gr.**	
13-18 years	n=6 n=22		n=6 n=22	
Median (IRQ)	29(27.8-32.3) 41.5(35.5-46.3)	**0.003****	34 (30.8-36.5) 39 (32-42.3)	0.354**

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**Independent Sample T test* ***Mann-Whitney U test*

Table 4. Comparison of anxiety status of mothers between study and control group.

	Mothers in study gr. **(n=45)**	Mothers in control gr. **(n=90)**	**P**
State anxiety score			0.803*
mean±sd	48.3 ± 10.5	47.7 ± 12.5	
Trait anxiety score			**0.001***
mean±sd	41.7 ± 8.9	36.2 ± 8.3	
Percentage of correct answered questions about COVID-19			**0.001****
median (IRQ)	64.3 (57.1-78.6)	78.6 (71.4-85.7)	
Children aged 0-8 years			
State anxiety score	45 (41-53)	46.5 (40.5-60)	0.616**
median (IRQ)	41 (35-47)	36 (30.8-42)	**0.030****
Trait anxiety score			
median (IRQ)			
Children aged 9-12 years			
State anxiety score	50.5 (47.8-61.8)	44 (36-59.5)	0.216**
median (IRQ)	43.5 (40.8-47.3)	33(29.5-39)	**0.002****
Trait anxiety score			
median (IRQ)			
Children aged 13-18 years			

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State anxiety score	43 (39.8-57.5)	48 (39-59)	0.947**
median (IRQ)	35.5 (33-40.8)	34 (30-42)	0.674**
Trait anxiety score			
median (IRQ)			

**Independent Sample T test* **Mann-Whitney U test*

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