

Behavioral, Emotional Problems and Fatigue in Adolescents After COVID-19 Infection: A Cross-Sectional Study

COVID-19 Enfeksiyonu Sonrası Ergenlerde Davranışsal, Emosyonel Problemler ve Yorgunluk: Kesitsel Bir Çalışma

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ABSTRACT

Objective: This study aimed to investigate behavioral, emotional problems and fatigue in adolescents after COVID-19 infection. Also, we examined relationships between baseline inflammation levels, fatigue, and the current behavioral and emotional problems of adolescents.

Material and Methods: A total of 110 adolescents (56 boys, 50.9%, mean age 14.72 years) and their parents were included in the study. Psychiatric assessments of the adolescents were performed 7.31±2.35 months after discharge from hospital. Behavioral and emotional problems was assessed using the Child Behavior Checklist (CBCL) 6-18 parent-rated questionnaire.

Results: We collected baseline inflammatory markers including C-reactive protein (CRP), the neutrophil/lymphocyte ratio (NLR), the monocyte/lymphocyte ratio (MLR), and the systemic immune-inflammation index (SII). The proportions of adolescents that were in the clinical range in at least one behavioral and emotional domain were as follows: 44.5% in the entire sample, 35.7% in boys, and 53.7% in girls. Thought problems were the most common problems in the entire sample (25.5%). The rates of internalizing and externalizing symptoms were 33.6% and 16.4%, respectively. Somatic and attention symptoms were more frequent in females than in males. Inflammatory marker levels did not correlate with behavioral and emotional scores. Fatigue symptoms were determined in 36.4% of all adolescents. We found that somatic and attention problems are more common in fatigued adolescents.

Conclusion: Our findings demonstrated that screening for behavioral, emotional problems, and fatigue in adolescents with COVID-19 infection is necessary. Future studies with a follow-up design are needed to determine whether a relationship exists between behavioral, emotional problems and baseline inflammation levels after COVID-19 infection.

Key Words: Adolescent, COVID-19, Fatigue, Inflammation, Mental health



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ÖZ

Amaç: Bu çalışma, COVID-19 enfeksiyonu sonrası ergenlerde davranışsal, emosyonel problemler ve yorgunluk belirtilerini araştırmayı amaçlamıştır. Ayrıca, ergenlerin başlangıç inflamasyon düzeyleri ile mevcut davranış, emosyonel problemler ve yorgunluk belirtileri arasındaki ilişkiler incelenmiştir.

Gereç ve Yöntemler: Çalışmaya toplam 110 ergen (56 erkek, %50.9, yaş ortalaması 14.72 yıl) ve ebeveynleri dahil edildi. Ergenlerin psikiyatrik değerlendirmeleri hastaneden taburcu olduktan 7.31±2.35 ay sonra yapılmıştır. Ergenlerdeki davranış, emosyonel problemler, Çocuk Davranışı Kontrol Listesi (CBCL) 6-18 ebeveyn formu kullanılarak değerlendirilmiştir.

Bulgular: COVID-19 tanı anındaki C-reaktif protein (CRP), nötrofil/lenfosit oranı (NLR), monosit/lenfosit oranı (MLR) ve sistemik immün-enflamasyon indeksi (SII) dahil olmak üzere temel inflamatuvar belirteçleri geriye dönük olarak saptanmıştır. En az bir davranışsal ve emosyonel problem alanında klinik aralıkta olan ergenlerin oranı tüm örnekleme %44.5, erkeklerde %35.7 ve kızlarda %53.7 olarak bulunmuştur. Düşünce sorunları tüm örnekleme (%25.5) en sık görülen sorunlar olarak bulunurken; içe yönelim ve dışa yönelim belirtilerinin oranları sırasıyla %33.6 ve %16.4 olarak saptanmıştır. Somatik ve dikkat belirtileri kadınlarda erkeklere göre daha sık olduğu bulunmuştur. İnflamatuvar belirteç düzeyleri ile davranışsal ve emosyonel problem skorları arasında korelasyon saptanmamıştır. Tüm ergenlerin %36.4'ünde yorgunluk belirtileri saptanmıştır. Yorgunluk olan ergenlerde somatik ve dikkat problemlerinin daha fazla olduğu bulunmuştur.

Sonuç: Bulgularımız, COVID-19 enfeksiyonu olan ergenlerde davranışsal, emosyonel problemler ve yorgunluk belirtileri taramasının gerekli olduğunu göstermiştir. COVID-19 enfeksiyonu sonrası davranışsal, emosyonel problemler ile başlangıç inflamasyon seviyeleri arasında bir ilişki olup olmadığını belirlemek için izlem çalışmalarına ihtiyaç vardır.

Anahtar Sözcükler: Ergen, COVID-19, Yorgunluk, İnflamasyon, Ruh sağlığı

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SAR-CoV-2) infection, which the World Health Organization (WHO) declared as the source of a global pandemic on March 11th, 2020 (1). As the pandemic spreads worldwide, its effects on mental health become more evident (2-4). Preliminary results have shown that COVID-19 is associated with delirium, depression, anxiety, post-traumatic stress disorder (PTSD), obsessive-compulsive symptoms, fatigue, insomnia, and cognitive dysfunction at an early period after infection (4-8).

As the number of the recovered cases increases, there is rising concern regarding the long-term sequelae after COVID-19 infection. In a recent study, 35.8% of patients still had symptoms in the clinical range in at least one psychopathologic dimension 3 months after a COVID-19 infection. Moreover, persistent depressive symptoms and cognitive impairment, including attentional problems and dysfunction in information processing, have been reported in long-term follow-up after a COVID-19 infection (9). Recent evidence has shown that survivors of COVID-19 have an increased risk of mood and anxiety disorders in 3-month follow-up (2). In a retrospective cohort study, the risk of mood and anxiety disorders continued 6 months after COVID-19 infection, and the risk for psychotic disorder increased significantly (10). In a long-term follow-up study, an association was found between depression, cognitive impairment, and baseline inflammation markers of COVID-19 (9). Another recent study showed a significant burden of post-viral fatigue in survivors of COVID-19 and female preponderance in the development of fatigue in medium-term follow-up. However, no correlation has been found between fatigue and inflammation scores (8).

Despite evidence of the mental impact of COVID-19 on adults, there has been very limited research on the mental health

of children and adolescents. In this context, we intended to determine the adolescent behavioral, emotional problems, feelings of fatigue, and relationships between these factors, and baseline inflammation levels after COVID-19 infection.

MATERIAL and METHODS

We retrospectively screened the health records of 504 patients who had COVID-19 infections between April 1st and December 25th, 2020, in our Pediatric Infectious Disease Unit. A total of 110 adolescents (56 boys, 50.9%) with a mean age of 14.72 (range, 11 - 18) years and their parents (74 mothers, 67.3%) who agreed to participate in the study were assessed for psychiatric symptoms.

An online survey was used that included a parent-rated questionnaire screening child behavioral and emotional problems along with socio-demographic variables. Other information (presence of fatigue for at least one month, sleep duration, relative's death due to COVID-19 infection) was collected from the adolescents through phone call interview. The presence of fatigue symptoms was determined with the question "Do you feel tired in a great part of the day?" Information was first given verbally on the phone, and then a survey link was sent to those who agreed to participate in the study. The survey data were collected between February 18th and February 28th, 2021.

For the evaluation of behavioral and emotional problems in adolescents, the Turkish version of the Child Behavior Checklist (CBCL) 6-18 parent-report questionnaire was used (11). Thomas M. Achenbach developed the CBCL, which consists of 113 items rated on a three-point scale (12). The CBCL consists of eight subscales; anxious/depressed, withdrawn/depressed, somatic problems, social problems, thought problems, attention problems, rule-breaking behavior, and aggressive behavior subscales. Raw scores are converted to sex- and

age-standardized scores (T scores). The clinical cut-offs of the eight subscales' T scores are 65-69 (borderline clinical) and >70 (clinical). Additionally, the CBCL consists of three summary scales: internalizing (anxious/depressed, withdrawn/depressed, somatic problems subscales), externalizing (rule-breaking behavior and aggressive behavior subscales), and total problems. The clinical cut-offs of the three summary scales' T scores are 60-63 (borderline clinical) and >63 (clinical). Higher scores indicate greater behavioral and emotional problems in adolescents. The reliability and validity of the CBCL for Turkish children and adolescents aged 6-18 years have been confirmed (11). The Depression Anxiety and Stress Scale (DASS-21) was used to determine the parents' current psychological status. DASS-21 is a self-report questionnaire that consists of three subscales (depression, anxiety, and stress) including seven items per subscale, which classify depression, anxiety, and stress according to cut-off scores (normal range: 0-9 points for depression; 0-7 points for anxiety; and 0-14 points for stress) (13). Higher scores indicate greater behavioral and emotional problems in parents. The reliability and validity of DASS-21 have been confirmed for the Turkish population (14).

The first hematologic analysis results of all patients at the time of COVID-19 positivity were obtained from our hospital records. These hematologic analyses associated with COVID-19 inflammation were highlighted in a recent meta-analysis [C-reactive protein (CRP), neutrophil/lymphocyte ratio (NLR), monocyte/lymphocyte ratio (MLR), and the systemic immune-inflammation index (SII) (SII = platelets X neutrophils/lymphocytes)] as baseline inflammation markers (15). Regardless of the severity of the infection, all patients were hospitalized and isolated in our pediatric infectious diseases unit. Psychiatric assessments were performed 7.31 ± 2.35 (range, 2 - 11) months after discharge.

Online informed consent was obtained from the parents, and assent was obtained from the children and adolescents. The study was approved by the Ankara City Hospital No. 2 Clinical Research Ethics Committee (Ethics ID-No: E2-21-21).

Data analyses

We used the Shapiro-Wilk test to analyze whether data were normally distributed. According to the normality of distribution, descriptive statistics are presented as mean \pm standard deviation or median (min-max). Continuous clinical variables were analyzed using the Mann-Whitney U test according to their distribution characteristics in group comparisons. Differences in categorical variables in group comparisons were examined using Pearson's Chi-square and Fisher's exact analysis. The data were analyzed using the SPSS version 23 software package, and all statistical tests were two-tailed with the significance level set at $\alpha = .05$. Spearman's correlation coefficient was calculated to investigate the association among the clinical variables.

RESULTS

One hundred ten adolescents (56 males, 50.9%) with a mean age of 14.72 (range, 11-18) years and their parents (74 mothers, 67.3%) were included in the study. The parents were all literate and had at least primary education. The rate of parents having COVID-19 at the same time as their adolescents was 67.2%. Before the COVID-19 infection, 15 (13.6%) adolescents had psychiatric histories. Of the adolescents, 17.3% had a relative who died of COVID-19 infection and 34.5% of the parents had lost their jobs during the COVID-19 pandemic. Fatigue symptoms were determined in 36.4% of all adolescents ($n=40$) and 46.3% of the female adolescents. There were no differences in age, duration after COVID-19 infection, sleep time per day, relatives death of COVID-19 infection, parents' job loss, and family income levels between the sexes ($p > .050$). However, there were differences in the presence of fatigue symptoms and psychiatric history before COVID-19 infection between the sexes ($p = .030$ and $p = .010$, respectively). The socio-demographic information of the sample is presented in Table I.

A significant proportion of the adolescents' parent-rated symptoms were in the clinical range in at least one problematic domain: 44.5% ($n = 49$) in the entire sample, 35.7% ($n = 20$) in the boys, and 53.7% ($n = 29$) in the girls. There was a marginally significant difference in the clinical range in at least one problematic domain between the boys and girls ($\chi^2 (1, N = 110) = 3.60, p = .058$). The rates of internalizing and externalizing symptoms were 33.6% and 16.4%, respectively. There were no sex differences in internalizing and externalizing symptoms. Thought problems were the most common problems in the entire sample (25.5%) and the boys (25.0%); the majority of the behavioral and emotional problems in the girls was somatic problems (27.8%). There was a significant difference in somatic problems ($\chi^2 (1, N = 110) = 4.01, p = .040$), attention problems ($\chi^2 (1, N = 110) = 5.57, p = .010$) and fatigue ($\chi^2 (1, N = 110) = 4.52, p = .033$) between the boys and girls; the other CBCL subscales were not different between the sexes. Adolescents with fatigue had more somatic symptoms ($\chi^2 (1, N = 110) = 6.13, p = .010$), attention problems ($\chi^2 (1, N = 110) = 5.40, p = .020$), and parental depression ($\chi^2 (1, N = 110) = 4.20, p = .040$). Additionally, parent symptoms in the clinical range according to DASS-21 did not differ between the sexes. The percentage of adolescents and parents in the clinical range of psychiatric symptoms is shown in Table II.

Measures of inflammation at the first clinical assessment with the COVID-19 diagnosis and psychiatric symptoms scores after infection in the survivors of COVID-19 are presented in Table III. Inflammatory markers (CRP, NLR, MLR, and SII) were not significantly different between the boys and girls ($p > .050$). There was a marginally significant difference in somatic symptom scores between the boys and girls ($p = .059$); other parent-rated psychiatric symptoms scores were not different between sexes ($p > .050$). Inflammatory marker levels did

Table I: Sociodemographic and clinical information of the sample.

	Gender								Z or χ^2	p
	Whole sample (n=110)		Females (n=54)		Males (n=56)		Mean (SD) or n (%)	Median (Range)		
	Mean (SD) or n (%)	Median (Range)	Mean (SD) or n (%)	Median (Range)	Mean (SD) or n (%)	Median (Range)				
Age (year)	14.72	15 (11-18)	14.63 (1.83)	15.00 (11-18)	14.80 (1.96)	15.00 (11-18)	14.80 (1.96)	15.00 (11-18)	-0.35	.720
Duration after COVID-19 infection to psychiatric assessment (month)	7.31 (2.35)	8.00 (2-11)	7.46 (2.49)	8.00 (3-11)	7.16 (2.24)	7.00 (2-11)	7.16 (2.24)	7.00 (2-11)	-0.69	.480
Presence of psychiatric history prior to COVID-19 infection	15 (13.6)	-	3 (5.6)	-	12 (21.4)	-	12 (21.4)	-	5.88	.010*
Family income (TL/a month)	4014.75 (2745.66)	3000 (500-17000)	3489.06 (2147.61)	3000 (500-12500)	4521.66 (3156.38)	3000 (1000-17000)	4521.66 (3156.38)	3000 (1000-17000)	-1.82	.060
Presence of fatigue symptoms	40 (36.4)	-	25 (46.3)	-	15 (26.8)	-	15 (26.8)	-	4.52	.030*
Duration of sleep (h/day)	8.35 (1.44)	8 (3-12)	8.61 (1.43)	8 (5-12)	8.09 (1.41)	8 (3-11)	8.09 (1.41)	8 (3-11)	-1.71	.080
Parent reports (mother)	74 (67.3)	-	39 (72.2%)	-	35 (62.5)	-	35 (62.5)	-	1.18	.270
Relatives' death due to COVID-19 infection	19 (17.3)	-	9 (16.7)	-	10 (17.9)	-	10 (17.9)	-	.02	.860
Parents' losing job	38 (34.5)	-	21 (30.4)	-	17 (38.9%)	-	17 (38.9%)	-	.88	.340

* $p < .05$; χ^2 value: Chi-Square test, Z value: Mann-Whitney U test, SD: Standard Deviation.

Table II: Percent of adolescents and parents at clinical behavioral and emotional symptoms levels divided according to sex.

	Gender				χ^2	p		
	Whole sample (n=110)†		Females (n=54)†				Males (n=56)†	
	n (%)	Median (Range)	n (%)	Median (Range)			n (%)	Median (Range)
Adolescents' CBCL scores at the clinical range								
Anxious/Depressed	26 (23.6)	12 (22.2)	14 (25)	.11	.730			
Withdrawn/Depressed	26 (23.6)	12 (22.2)	14 (25)	.11	.730			
Somatic Complaints	22 (20.0)	15 (27.8)	7 (12.5)	4.01	.040*			
Social Problems	24 (21.8)	14 (25.9)	10 (17.9)	1.04	.300			
Thought Problems	28 (25.5)	14 (25.9)	14 (25.0)	.01	.910			
Attention Problems	14 (12.7)	11 (20.4)	3 (5.4)	5.57	.010*			
Rule-Breaking Behavior	7 (6.4)	2 (3.2)	5 (8.9)	1.25	.260			
Aggressive Behavior	15 (13.6)	7 (13.0)	8 (14.3)	.41	.840			
Internalizing	37 (33.6)	20 (37.0)	17 (30.4)	.55	.450			
Externalizing	18 (16.4)	10 (18.5)	8 (14.3)	.36	.540			
Total problems	32 (29.1)	18 (33.3)	14 (25.0)	.92	.330			
Parents' DASS-21 scores at the clinical range								
Depression	24 (21.8)	18 (33.3)	17 (30.4)	.11	.730			
Anxiety	35 (31.8)	11 (20.4)	13 (23.2)	.13	.710			
Stress	33 (30.9)	16 (29.6)	17 (30.4)	.00	.930			

* $p < .050$; † n(%), χ^2 value: Chi-Square test, DASS-21: Depression and Anxiety Stress Scale, CBCL: Child Behavior Checklist.

Table III: Measures of baseline inflammation at COVID-19 diagnosis and current behavioral and emotional symptoms in COVID-19 survivors, divided according to sex.

	Gender						Z	p
	Whole sample (n=110)		Females (n=54)		Males (n=56)			
	Mean (SD)	Median (Range)	Mean (SD)	Median (Range)	Mean (SD)	Median (Range)		
C-reactive Protein (mg/L)	.017 (.03)	.004 (0-.16)	.014 (.03)	.003 (0-.16)	.020(.033)	.006 (0-.14)	-0.91	.360
Neutrophil/lymphocyte ratio	3.25 (3.24)	2.67 (0.34-27.69)	2.73 (2.10)	1.88 (.55-10.86)	3.75 (4.00)	3.13 (.34-27.69)	-1.45	.140
Monocyte/lymphocyte ratio	.297 (.19)	.293 (.06-1.38)	.27 (.17)	.25 (.06-.85)	0.32 (.21)	0.29 (.06-1.38)	-1.51	.130
Systemic immune-inflammation Index (SII)	787.13 (797.21)	647.18 (28.13-5206.39)	734.04 (793.50)	498.05 (120-4825.79)	838.32 (804.58)	746.67 (28.13-5206.39)	-1.14	.250
CBCL scores								
Anxious/Depressed	58.04 (10.12)	54 (50-90)	57.96 (9.91)	54 (50-83)	58.12 (10.40)	54 (50-90)	-.10	.910
Withdrawn/Depressed	59.89 (11.07)	57(50-100)	60.66 (11.08)	58.43(50-100)	59.16 (11.10)	55.5 (50-100)	-.84	.390
Somatic Complaints	58.49(10.20)	55 (50-90)	59.73 (9.98)	57 (50-90)	57.30 (10.36)	54 (50-89)	-1.88	.050*
Social Problems	57.20 (8.73)	54 (50-82)	58.01 (8.78)	54 (50-80)	56.42 (8.68)	52.5 (50-82)	-1.09	.270
Thought Problems	58.00 (9.35)	55 (50-87)	58.39 (8.89)	55.5 (50-81)	57.62 (9.84)	51 (50-87)	-.68	.490
Attention Problems	56.09 (7.81)	52 (50-93)	57.48 (9.49)	52 (50-93)	54.75 (5.52)	52.5 (50-69)	-.58	.550
Rule-Breaking Behavior	53.31 (6.94)	51 (50-84)	53.24 (6.41)	51 (50-83)	53.37 (7.47)	50 (50-84)	-.50	.610
Aggressive Behavior	54.96 (7.97)	51 (50-86)	55.25 (7.40)	51 (50-77)	54.67 (8.54)	50.5 (50-86)	-1.25	.200
Internalizing	56.22 (13.55)	56 (33-88)	57.17 (13.19)	56.65 (33-82)	55.30 (13.95)	54 (33-88)	-0.93	.340
Externalizing	48.91(11.61)	48 (34-83)	49.90 (10.85)	49 (34-79)	47.96 (12.33)	46 (34-83)	-1.25	.200
Total problems	52.12(14.32)	51 (24-89)	53.26 (14.14)	53.11 (24-82)	51.03 (14.53)	49.5 (24-89)	-1.15	.240
DASS-21 scores of parents								
Depression	5.40 (7.68)	2 (0-32)	5.07 (6.84)	2 (0-28)	5.71 (8.47)	1 (0-32)	-.30	.760
Anxiety	5.38 (7.51)	2 (0-34)	5.51(7.06)	2 (0-24)	5.25 (7.97)	2 (0-34)	-.41	.680
Stress	6.78 (8.15)	4 (0-34)	7.07 (8.16)	4 (0-34)	6.5 (8.20)	2 (0-32)	-.49	.620

* $p < .05$, **Z value:** Mann Whitney U test, **DASS:** Depression and Anxiety Stress Scale, **CBCL:** Child Behavior Checklist, **Systemic immune-inflammation index (SII)**= platelets X neutrophils/lymphocytes, **SD:** Standart Deviation

not correlate with behavioral and emotional problems scores. Moreover, the adolescents' behavioral and emotional problems scores did not correlate with parent DASS-21 scores and post-COVID-19 time to psychiatric assessments ($p > .050$). Bivariate correlations between current behavioral, emotional symptoms and baseline inflammation markers are presented in Table IV.

DISCUSSION

Our study demonstrated that 44.5% of its sample was in the clinical range of at least one behavioral and emotional problematic domain, with particularly higher rates in girls. In the recent COVID-19 pandemic, various neuropsychiatric problems occurring after COVID-19 infection have been reported in adult samples (2,4,10,16). Preliminary data suggest that patients with COVID-19 may experience delirium, depression, anxiety, and insomnia in the early period (4). Another study reported high rates of PTSD, depression, anxiety, insomnia, and obsessive-compulsive symptoms in survivors of COVID-19 at 1-month of follow-up after hospital treatment (6). Our study found that internalizing symptom rates were higher than externalizing symptom rates in all adolescents. Thought problems involving symptoms such as obsessive thoughts, self-harm, hallucinations, compulsions, and strange behavior or ideas were the most common problems in the entire sample and boys; the majority of the behavioral and emotional problems in girls was somatic problems. Our findings are similar to the results from studies during previous coronaviruses outbreaks,

which reported higher internalizing symptoms in patients with severe acute respiratory syndrome (SARS) in the long-term follow-up (17-19). One-quarter of the patients had PTSD and 15.6% had depressive disorders as late as 30 months after the SARS infection (20). Recent evidence indicated that survivors of COVID-19 were at increased risk of mood and anxiety disorders 3 months after infection (2). In a recent retrospective cohort study, COVID-19 was associated with an increased risk of neuropsychiatric disorders, including anxiety disorders and psychosis 6 months after a COVID-19 diagnosis (10). The high rates of psychiatric problems, particularly internalizing symptoms in the adolescents in our study, were in line with recent studies showing an increased risk for psychiatric disorders.

Regarding the difference in results between the sexes in our study, girls were more likely to present with somatic and attention problems. Studies in children and adolescents reported that female adolescents were more anxious and depressive than male adolescents in the COVID-19 pandemic; however, a preadolescent sample showed no sex differences (21-23). Although most studies are about anxiety and depression in the COVID-19 pandemic, children and adolescents could present with various symptoms (3). A study with children and adolescents showed that 6-18-year-olds were more likely to show inattention problems, whereas younger children were more likely to present with clinginess and irritability (24). The girls had more attention problems than the boys in our study, which was discordant with the previous findings (25, 26). Screen exposure was not

Table IV: Correlation analysis between current adolescents' and parents' psychiatric symptoms and baseline inflammation markers of COVID-19 infection in the whole sample.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
1. C-reactive Protein (mg/L)	1	.349**	.223*	.288**	.114	.064	.005	.090	.009	.132	.074	.110	.094	.119	.092	.172	-.007	.090	-.289**	.060	
2. Neutrophil/lymphocyte ratio		1	.755**	.936**	.062	-.100	-.008	-.051	-.146	.071	-.016	.044	-.015	-.019	-.030	-.117	-.056	-.033	-.079	.132	
3. Monocyte/lymphocyte ratio			1	.704**	.063	-.176	.049	-.043	-.151	.018	-.007	-.039	-.032	-.052	-.055	-.084	-.072	-.037	-.051	.104	
4. Systemic immune-inflammation index (SII)				1	.024	-.090	.016	-.083	-.152	.036	.015	-.009	-.023	-.052	-.050	-.119	-.031	-.035	-.043	.064	
5. Anxious/Depressed					1	.713**	.647**	.755**	.688**	.647**	.615**	.748**	.892**	.779**	.853**	.009	-.066	.003	.058	.057	
6. Withdrawn/Depressed						1	.621**	.665**	.718**	.606**	.658**	.718**	.883**	.761**	.853**	.072	.051	.105	.004	-.135	
7. Somatic Complaints							1	.634**	.738**	.592**	.469**	.593**	.824**	.607**	.773**	.029	-.041	.029	-.029	.057	
8. Social Problems								1	.680**	.705**	.588**	.722**	.776**	.745**	.851**	.089	.009	.067	.051	-.083	
9. Thought Problems									1	.596**	.562**	.710**	.794**	.712**	.830**	.068	-.061	.089	-.006	.028	
10. Attention Problems										1	.547**	.697**	.702**	.714**	.809**	.013	-.025	.065	-.023	.100	
11. Rule-Breaking Behavior											1	.656**	.657**	.782**	.707**	.030	-.009	.078	-.042	-.068	
12. Aggressive Behavior												1	.777**	.937**	.866**	.051	-.015	.049	-.053	.053	
13. Internalizing													1	.822**	.947**	.040	-.048	.056	.018	.005	
14. Externalizing														1	.911**	.061	.003	.081	-.074	.068	
15. Total problems															1	.073	.002	.096	-.017	.030	
16. Parents' DASS-21 Depression																1	.747**	.773**	-.028	-.022	
17. Parents' DASS-21 Anxiety																	1	.775**	-.040	.013	
18. Parents' DASS-21 Stress																		1	.005	.078	
19. Duration after COVID-19 infection to psychiatric assessment																			1	-.224*	
20. Age																					1

Spearman correlation analysis with rho coefficient, * $p < .050$, ** $p < .010$

evaluated in our adolescent sample, which could be associated with attention problems during the COVID-19 pandemic (27).

In adolescence, fatigue is a common problem that usually depends on hormonal pubertal changes and psychological problems (28). A pre-COVID-19 epidemiologic study showed that fatigue symptoms were present in 20% of female adolescents and 6% of male adolescents (29). In our study, fatigue symptoms after COVID-19 infection were reported in 36.4% of the entire sample; in particular, 46.3% of girls presented with fatigue symptoms. Prior studies showed that the chronic fatigue symptoms in survivors of SARS continued in long-term follow-up (18,30). Recent study results showed that 53.6% of survivors of COVID-19 presented with fatigue symptoms, 26.8% had anxiety and depression symptoms, and these symptoms had no association with pneumonia severity (31). We found fatigue more common in girls, and the rates of somatic symptoms, attention problems in fatigued adolescents were more than in non-fatigued individuals. Our results are consistent with studies showing that fatigue is often accompanied by other psychological problems, including anxiety, depression, somatic disorder, or physical symptoms such as headaches, stomachaches, and muscle aches,

particularly in females (32-34). Considering that the girls had more attention problems and fatigue than the boys in our study, this could be related to the higher levels of cognitive fatigue in females, as indicated in previous studies (35,36). A recent study showed significant fatigue rates in survivors of COVID-19, and in particular in females at medium-term follow-up. However, no correlation was found between fatigue and inflammation levels (8).

Psychiatric symptoms after COVID-19 infection can result from an immune response related to the virus and or psychosocial factors (37). Neuroinflammation, blood-brain-barrier impairment, neurotransmission changes, hypothalamic-pituitary-adrenal (HPA) axis dysfunction, cytokine dysregulation, and microglia activation are known to be associated with psychiatric problems (36,38-40). In a recent study, COVID-19 RNA in cerebrospinal fluid showed its neuroinvasive features (41). Patients with COVID-19 may present with neurologic manifestations such as headache, dizziness, hypogeusia, and hyposmia, supporting its neuroinvasive potential (37). A recent systematic review and meta-analysis reported that COVID-19 infection could activate immune responses and immune-inflammatory parameters such

as white blood cells (WBCs), lymphocytes, NLR, and CRP were correlated with disease severity (15). In a study of survivors of COVID-19 that investigated the role of inflammatory and clinical predictors, correlations were found between obsessive-compulsive symptoms and MLR at one-month follow-up (6). In our study, inflammatory markers at COVID-19 diagnosis (CRP, NLR, MLR, and SII) did not correlate with current behavioral and emotional problems. Furthermore, there were no significant differences between the girls and boys. In a recent retrospective cohort study of electronic health records, common psychiatric symptoms, including mood and anxiety disorders, continued beyond 6 months after COVID-19 infection. However, psychiatric symptoms showed a weaker association with the severity markers of COVID-19 than neurologic symptoms (10). These results may indicate the psychosocial impacts of COVID-19, rather than the direct effects of the infection and its severity.

Our study had the following limitations: it was conducted in a single center with a small sample, thus our findings cannot be generalized to other populations. Its cross-sectional design does not allow interpretation for causality. The general limitations of online surveys also apply to our study. Considering those who did not have internet access, our sample may not represent all survivors of COVID-19. Adolescents' behavioral and emotional states before COVID-19 infection were not known. In addition, only about 20% of children with COVID-19 infection were assessed, and the post-infection period was in a wide range (2-11 months). The behavioral and emotional problems of the adolescents and their parents could not be evaluated with face-to-face psychiatric interviews. Unfortunately, the pandemic continues, and there are many difficulties in making face-to-face evaluations of patients during this period. Although there were data on the presence of previous psychiatric diagnoses, no detail about which diagnoses were not reported in the online survey. The presence of fatigue was asked as 'yes' and 'no' to the adolescents, but no assessment was made regarding the fatigue's physical and mental characteristics. Another limitation of our study is that the CBCL scale's clinical cutoff scores were not validated for Turkish adolescents.

Despite the limitations mentioned above, our study contributes to the literature in several ways. To our knowledge, this is the first study to evaluate behavioral and emotional problems in adolescents after COVID-19 infections in the long term. This study may be important to demonstrate the long-term mental effects of COVID-19 infections on adolescents. Future studies are needed to confirm the high rates of behavioral and emotional problems in adolescents recovering from COVID-19 in comparison with non-infected adolescents. A follow-up design with larger samples may reveal the relationship between behavioral, emotional problems and inflammation in future studies.

CONCLUSION

Our results support that survivors of COVID-19 present with a high prevalence of behavioral and emotional problems; 44.5% of the sample was in the clinical range of at least one problematical domain. Additionally, the rate of fatigue reported by the adolescents was higher, especially among girls. Somatic symptoms and attention problems were more common in girls and fatigued adolescents. Considering the impact of COVID-19 infection on adolescent mental health, screening of behavioral, emotional problems and fatigue symptoms seems necessary in survivors of COVID-19.

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