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ORIGINAL ARTICLE

The impact of peer victimization and psychological symptoms on quality of life in children and adolescents with FMF

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Abstract

Background: Familial Mediterranean fever (FMF) is an inherited, chronic, autoinflammatory disease that causes fever, arthritis, and inflammation of serous membranes. The aim of this study was to investigate the effects of peer bullying and psychological symptoms on the quality of life of children and adolescents with FMF.

Methods: Forty-three children and adolescents aged 8–18 followed up with diagnoses of FMF and volunteering to take part, and 32 healthy controls were included in this study. Subjects who agreed to participate completed the Child Depression Inventory (CDI), Screen for Child Anxiety-Related Emotional Disorders (SCARED), Olweus Bully/Victim Questionnaire (OBQ), and Pediatric Quality of Life Questionnaire (PedsQL)-child form. Parents also completed the Pediatric Quality of Life Questionnaire (PedsQL)-parent form.

Results: Peer bullying victim role, CDI, total SCARED, and SCARED school fear scores were significantly higher in the group diagnosed with FMF than in the healthy controls, while scores for PedsQL completed by children and parents were significantly lower. Spearman correlation analysis revealed a significant negative correlation between the CDI scores, SCARED scores, and total PedsQL scores of children with FMF. Quality of life was lower in children and adolescents with FMF exposed to peer bullying in the victim, bully, and bully/victim roles.

Conclusions: This study suggests that the presence of peer bullying, depression, and anxiety may have an adverse impact on the quality of life of children and adolescents with FMF.

KEYWORDS
anxiety, depression, familial Mediterranean fever, peer victimization, quality of life

INTRODUCTION

Familial Mediterranean fever (FMF) is a chronic, autosomal recessive, autoinflammatory disease that causes inflammation of serous membranes such as the peritoneum and pleura, with symptoms including fever and arthritis.[1] It is frequently seen in Eastern Mediterranean ethnic communities, such as Turkish, Arab, Jewish, and Armenian populations.[1] It has a reported prevalence of approximately 0.1% in Turkey.[2] Frequently observed symptoms include fever, peritonitis, arthritis, myalgia, pleuritis, and erysipelas-like erythema.[2] Diagnosis is usually made in childhood.[2] Colchicine therapy is frequently used in the treatment of FMF, although interleukin-1 antagonists such as anakinra and canakinumab are also used in cases that do not respond to colchicine.[3]

Studies have shown that greater depression and future anxiety, lower self-esteem, and poorer body image may be expected in individuals with chronic diseases.[4,5] One of the problems caused by such diseases is a decreased quality of life.[6] Research has also reported a decreased quality of life in patients with FMF compared to healthy controls.[7,8] Numerous factors reduce the quality of life of FMF patients, including depression and anxiety.[8,9] A greater incidence of depression (6.22–33%) and anxiety (4.93–12%.) has also been reported in patients with FMF than in healthy controls.[8,10–12]

Another problem that individuals with chronic diseases in the child and adolescent age group may encounter is peer bullying.[13] This is a very common global health problem in school-age children. Although the prevalence of peer bullying varies, a figure of approximately 32–38% has been reported.[14] Such bullying can lead to anxiety, depression, loneliness, emotional difficulties, somatic complaints, concerns about going to school, and physical health-related problems.[15,16] However, to the best of our knowledge, no previous studies have addressed peer bullying in children and adolescents with FMF, although a high rate of peer bullying has been described in individuals with chronic diseases such as type 1 diabetes mellitus (85.7%), systemic lupus erythematosus, acne (5.4%), psoriasis (27%), and atopic dermatitis (18–60%).[17–20]

We anticipated that children and adolescents with FMF might be more exposed to peer bullying due to the difficulties they experience. We therefore also thought that depression and anxiety disorders might be more common in such individuals, and this might reduce their quality of life. The purpose of this study was to compare the levels of depression, anxiety, peer bullying, and quality of life in children and adolescents with FMF with those of healthy controls and to investigate the effects of peer bullying and psychological symptoms, which have not been previously studied, on quality of life. The research will thus facilitate the evaluation of psychiatric monitoring and support needs of children and adolescents with FMF and contribute to the literature in this hitherto neglected area.

METHOD

Patient

Forty-three children and adolescents followed up with diagnoses of FMF at the Bezmialem Vakıf University Hospital Child Health and Diseases polyclinic, Turkey, between May 2020 and May 2021, and 32 healthy controls of similar age and gender who presented to the child health and diseases clinic, who consented to take part, were included in the study. Five children and their families refused to participate in the study. Twelve children were excluded from the study because they had chronic diseases other than FMF. Healthy controls without any chronic disease and without an acute infection were included in the control group. All patients met the Tel Hashomer or Ankara diagnostic criteria, had been followed up in our clinic for at least 3 months, and exhibited MEFV (Mediterranean Fever) gene mutation in at least one allele.[21,22] Inclusion criteria were age 8–18, confirmed diagnosis of FMF, consent to participation being given by the child and the family, and the absence of any major neurodevelopmental disease (autism spectrum disorder or cognitive disability) or other chronic diseases. Similar inclusion criteria were applied to the healthy controls.

Study procedures

The research was designed as a case-control study, and ethics committee permission (decision number 07/115 dated 22.05.2020) was obtained before commencement. Patients diagnosed with FMF who met the inclusion criteria and none of the exclusion criteria were asked whether they would participate by submitting an Informed Volunteer Form. Those individuals who agreed to participate in the study completed the Child Depression Inventory (CDI), Screen for Child Anxiety-Related Emotional Disorders for Child (SCARED-C), Olweus Bully/Victim Questionnaire (OBQ), and Pediatric Quality of Life Questionnaire (PedsQL) scales. The parents also completed the Pediatric Quality of Life Questionnaire (PedsQL)-parent form. The average time taken by the children to complete the scales was 30 min, and they were allowed a five-minute break after each scale if they so desired.

Demographic variables and clinical severity

Age at first diagnosis of FMF, treatments applied, duration of the disease, frequency of FMF attacks, number of school absences due to FMF, age of the parents, family income, education level, family type, number of siblings, medical and psychiatric diseases in the family, smoking status, alcohol use in the family, substance use, and the child's height, weight, body mass index, age, academic performance, and any psychiatric and medical illnesses were investigated and recorded. The sociodemographic characteristics of all cases included in the study were obtained using sociodemographic data forms completed by the parents of the children participating in the study.

Psychological measures

Olweus Bully/Victim Questionnaire (OBQ)

The OBQ was created by Olweus in 1996 to measure peer bullying and was developed for students in the 8–16 age group.[23] The Turkish validity and reliability study of the scale was conducted by Hilal Tipirdamaz Sipahi in 2008.[24] It consists of 39 items on a five-point Likert-type scale. The OBQ permits evaluation in terms of being a bully, victim, or bully/victim. The cut-off point was determined as "2–3 times a month". Any answer marked above the cutoff point in questions 4–13 is considered a victim, while marking any answer above the cutoff point for questions 24–33 is considered bullying. Answers marked above the cut-off point in both sections mean being described as a bully/victim, while individuals who are not in the first two groups are referred to as non-bullies and non-victims.

Child Depression Inventory (CDI)

This scale was developed by Kovacs in 1981 to determine the level of depression in children and is used for self-assessment in childhood depression.[25] The validity and reliability study in Turkey was conducted by Öy in 1991.[26] The CDI can be applied to children between the ages of 6 and 17. It consists of 27 items, each scored between 0 and 2. Items B, E, G, İ, J, L, N, O, P, Ş, Ü, and V on the Turkish version are reverse scored. The highest possible score is 54. Higher scores indicate severe depression. A cutoff score of 19 is recommended, with scores of 19 and above being considered pathological.

Screen for Child Anxiety Related Emotional Disorders (SCARED)

This tool measures symptoms of anxiety disorders in children. The original scale was developed by Birmaher et al. in 1997, the validity and reliability of the Turkish-language version being established by Cakmakci in 2004.[27,28] It consists of 41 Likert-type questions, each scored from 0 to 2. Total possible scores range from 0 to 82. There is no cut-off score, and higher scores indicate higher general anxiety levels. SCARED can be applied to children aged 8–18.

Pediatric Quality of Life Questionnaire (PedsQL)

Developed by Varni et al., in 1999, this tool is intended to measure general health-related quality of life in the 2–18 age group.[29] It was originally prepared for four different age groups. The scale developed for the 2–4 age group contains only the parent form, while the scale developed for the 5–18 age group contains both parent and child forms. Memik et al., (2007) concluded that PedsQL is valid and reliable in assessing the quality of life of children aged 8–12 and 13–18.[30] The scale consists of 23 items and is scored in three areas: a total scale score (TS), a physical functionality score (PFS), and a psychosocial functionality score (PFS), which consists of the item scores evaluating emotional, social, and school functionality. Items are scored between 0 and 100. A high total score indicates a high quality of life.

Statistical analyses

Statistical Package Program for Social Sciences version 21.0 software (SPSS 21.0) program was used for statistical analysis. The one-sample Kolmogorov–Smirnov test was used to analyze the distribution of continuous variables. In comparisons between two independent groups, the chi-square test was used for categorical variables. Student's t-test was used if continuous variables conformed to a normal distribution, and the Mann–Whitney U test was used in case of non-normal distribution. Relationships between continuous variables were examined using Spearman correlation analysis. Multivariate linear regression analyses were used to demonstrate predictors of quality of life in children with FMF. In all models, the Child PedsQL total score, physical functioning score, and psychosocial functionality score were used as dependent variables. CDI Total Score, SCARED Total Score, and Olweus Victim Questionnaire, which are correlated with quality of life, were used as independent variables. p values <0.05 were regarded as significant for all analyses.

RESULTS

Girls constituted 51.2% ($n=22$) of the 43 patients diagnosed with FMF and boys 48.8% ($n=21$). The control group consisted of 43.8% ($n=14$) girls and 56.2% ($n=18$) boys ($n=32$). A comparison of the two groups in terms of gender, age, and body mass index (BMI) is shown in Table 1. There was no significant difference between the two groups in terms of gender ($p>0.05$) or age ($p=0.808$). However, BMI was significantly higher in the FMF group than in the control group ($p=0.035$). The school absenteeism rate in the FMF group was significantly higher than that of the control group ($p=0.005$). Absenteeism was significantly higher in the group with FMF attacks

TABLE 1 Sociodemographic data of the FMF and control groups.

	FMF($n=43$)	**Control ($n=32$)**	
	***n* (%)**	***n* (%)**	***p***
Gender			
Female	22 (51.2%)	14 (43.8%)	$p>0.05$*
Male	21 (48.8%)	18 (56.2%)	
	Median (25%–75%)	**Median (25%–75%)**	***p***
Age (years)	14.0 (11.0–15.0)	13.0 (11.0–15.0)	0.808[a]
	Mean ± SD	**Mean ± SD**	***p***
BMI	20.70 ± 5.28	18.41 ± 3.34	**0.035**[b]
	FMF ($n=43$)	**Control ($n=32$)**	***p***
	***n* (%)**	***n* (%)**	
School absence			
Yes	20 (46.5%)	5 (15.6%)	**0.005***
No	23 (53.5%)	27 (84.4%)	

Note: Statistically significant results are shown in bold.

Abbreviations: BMI, body mass index; n=number of cases; p*, Pearson Chi-Square test p value; p^a, Mann–Whitney U test p value; p^b, Independent t-test p value.

TABLE 2 CDI and SCARED Scores in the FMF and control groups.

	FMF ($n=43$)	Control ($n=32$)	
	Median (25%–75%)	**Median (25%–75%)**	***p***
CDI Total Score	10.00 (7.00–16.00)	8.00 (5.00–12.00)	**0.046***
SCARED Total Score	26.00 (21.00–43.00)	24.05 (13.25–31.75)	**0.032***
SCARED Panic Disorder Score	5.00 (4.00–12.00)	5.00 (2.00–8.00)	0.151*
SCARED Generalized Anxiety Disorder Score	6.00 (4.00–8.00)	5.00 (1.00–7.00)	0.081
SCARED Separation Anxiety Disorder Score	8.00 (4.00–10.00)	5.50 (4.00–8.00)	0.170*
SCARED Social Anxiety Disorder Score	8.00 (5.00–12.00)	6.00 (4.00–8.00)	0.108*
SCARED School Fear Scores	2.00 (1.00–3.00)	0.00 (0.00–2.00)	**0.001***

Note: Statistically significant results are shown in bold.
Abbreviations: *n*, number of cases; *p**, Mann–Whitney *U* test *p* value.

TABLE 3 PedsQL Scores in the FMF and control groups.

	FMF ($n=43$)	Control ($n=32$)	
	Median (25%–75%)	**Median (25%–75%)**	***p***
Child PedsQL Total Score	73.91 (58.69–78.26)	86.41 (69.02–93.48)	**0.001***
Child PedsQL Physical Functioning Score	78.12 (62.50–87.50)	90.62 (75.00–96.87)	**0.006***
Child PedsQL Psychosocial functionality Score	66.67 (56.67–76.67)	86.67 (65.42–93.33)	**<0.001***
Parent PedsQL Total Score	72.83 (59.78–80.43)	90.21 (77.99–94.56)	**<0.001***
Parent PedsQL Physical Functioning Score	78.12 (53.13–90.63)	93.75 (75.78–96.88)	**0.002***
Parent PedsQL Psychosocial functionality Score	70.00 (58.33–76.67)	88.33 (80.42–95.00)	**<0.001***

Note: Statistically significant results are shown in bold.
Abbreviations: *n*, number of cases; *p**, Mann–Whitney *U* test *p* value.

than in the group without FMF attacks ($p<0.001$). The majority of children with FMF who participated in the study used at least one drug, such as colchicine ($n=39$ (90.7%)). The mean disease duration after diagnosis of FMF was 5.5 (4.0–8.0) years, and the mean age at onset of FMF was 6.6±3.6 years.

No significant differences were determined between the two groups in terms of maternal education levels ($p=0.108$), paternal education levels ($p=0.135$), or the presence of chronic disease other than FMF ($p=0.107$). However, the presence of FMF in the family ($p<0.001$) and the presence of psychiatric disease in the family ($p=0.008$) were significantly higher in the FMF group than in the control group. The presence of FMF in the family was found to be 37.2% in the group with FMF. The rate of psychiatric illness in the family was found to be 25.6% in the group with FMF.

A comparison of patients diagnosed with FMF and the control group in terms of depression (CDI) and anxiety disorders (SCARED) is shown in Table 2. CDI ($p=0.046$) and total SCARED ($p=0.032$) scores, as well as SCARED school phobia scores ($p=0.001$) were higher in the FMF group.

A comparison of PedsQL scores between the FMF and control groups is shown in Table 3. Total PedsQL scores completed by children (p=0.001), PedsQL physical functionality completed by children ($p=0.006$), PedsQL psychosocial functionality scores completed by children ($p<0.001$), PedsQL total scores completed by parents ($p<0.001$), PedsQL physical functionality completed by parents ($p=0.002$), and PedsQL psychosocial functionality scores completed by parents ($p<0.001$) were all higher in the control group.

TABLE 4 Olweus Bully/Victim Questionnaire values in the FMF and control groups.

	FMF ($n=43$)	Control ($n=32$)	
	***n* (%)**	***n* (%)**	***p***
Victim			
None	30 (69.8%)	29 (90.6%)	**0.029***
2–3 times a month	13 (30.2%)	3 (9.4%)	
Bully			
None	39 (90.7%)	32 (100%)	0.131**
2–3 times a month	4 (9.3%)	0 (0%)	
Bully/victim			
None	40 (93%)	32 (100%)	
2–3 times a month	3 (7%)	0 (0%)	0.256**

Note: Statistically significant results are shown in bold.
Abbreviations: *n*, number of cases; *p**, Mann–Whitney *U* test *p* value; *p***, Fisher's exact test *p* value.

A comparison of OBQ scores between the FMF and control groups is shown in Table 4. The peer bullying victim role was significantly higher in the FMF group than in the healthy controls ($p=0.029$).

Spearman analysis revealed a significant negative correlation ($p<0.001$) between the CDI scores of the children with FMF and the total PedsQL score. A significant negative correlation ($p<0.001$) was found between the SCARED scores of children with FMF and the total PedsQL score. A significant positive correlation ($p<0.001$) was also found between the CDI scores and SCARED scores of children with FMF (Table 5).

There was no significant difference between CDI scores ($p=0.064$) and SCARED scores ($p=0.138$) between children and adolescents with FMF with peer bullying victim roles and those who were not bullied. PedsQL scores for the child ($p=0.006$) and PedsQL psychosocial subscale scores for the child ($p=0.003$) were significantly lower in children and adolescents with FMF with peer bullying victim roles compared to those who were not bullied.

No significant difference was determined between the CDI scores ($p=0.148$) of children and adolescents with FMF who were in a peer bullying-bullying role compared to those who were not bullying. However, SCARED scores ($p=0.036$) were significantly higher among those involved in bullying, whereas PedsQL total scores ($p=0.007$), PedsQL physical functioning subscale scores ($p=0.006$), and PedsQL psychosocial subscale scores ($p=0.012$) completed by the children were significantly lower.

There was no significant difference between the CDI scores ($p=0.251$) and SCARED scores ($p=0.110$) of children and adolescents with FMF in the peer bullying-victim-bullying role and those of children who were not bullied. However, PedsQL scores ($p=0.028$), PedsQL physical functionality subscale scores ($p=0.035$), and PedsQL psychosocial subscale scores ($p=0.040$) completed by children and adolescents with FMF with peer bullying-victim-bullying roles were significantly lower than those among children who were not exposed to bullying.

CDI, SCARED, and PedsQL scores filled out by children and adolescents exposed to peer bullying in the FMF and control groups are shown in Table 6.

According to the results of linear regression, peer victimization, CDI Total Score, and SCARED Total Score

TABLE 5 Correlations between the PedsQL Scores and the CDI SCARED Scores of children with FMF.

	1	2	3	4	5	6	7
1. Age		**$r=0.415$ $p=0.006$***	$r=0.118$ $p=0.314$	$r=-0.224$ $p=0.054$	$r=-0.044$ $p=0.709$	$r=-0.031$ $p=0.795$	$r=-0.032$ $p=0.785$
2. Duration of FMF			$r=0.038$ $p=0.810$	$r=-0.133$ $p=0.394$	$r=0.019$ $p=0.905$	$r=-0.135$ $p=0.388$	$r=0.060$ $p=0.702$
3. CDI Score				**$r=0.519$ $p<0.001$***	**$r=-0.679$** $p<0.001$*	**$r=-0.539$** $p<0.001$*	**$r=-0.681$** $p<0.001$*
4. SCARED Score					**$r=-0.737$ $p<0.001$***	**$r=-0.684$ $p<0.001$***	**$r=-0.722$ $p<0.001$***
5. Total Child PedsQL Score						**$r=0.877$ $p<0.001$***	**$r=0.966$ $p<0.001$***
6. Child PedsQL Physical Functioning Score							**$r=0.750$** $p<0.001$*
7. Child PedsQL Psychosocial Functioning Score							

Note: Statistically significant results are shown in bold.

Abbreviations: p*, Spearman correlation analysis p value; r=correlation coefficient.

TABLE 6 CDI, SCARED, and Child PedsQL Scores in children and adolescents exposed to Olweus peer bullying in the FMF and control groups.

	FMF ($n=14$)	**Control ($n=3$)**	
Victim, bully, bully-victim	**Median (25%–75%)**	**Median (25%–75%)**	***p***
CDI Total Score	14.50 (8.75–18.50)	13.00 (12.00–25.00)	0.659*
SCARED Total Score	36.50 (25.50–52.50)	45.00 (31.00–66.00)	0.449*
Child PedsQL Total Score	58.69 (39.68–73.91)	54.34 (32.61–84.78)	0.899*
Child PedsQL Physical Functioning Score	62.50 (42.19–87.50)	31.25 (25.00–93.75)	0.446*
Child PedsQL Psychosocial Functioning Score	56.67 (43.33–66.67)	66.67 (36.67–80.00)	0.410*

Abbreviations: n, number of cases; p*, Mann–Whitney U test p value.

TABLE 7 Linear regression results predicting quality of life scores of children with FMF.

	B	*SE*	*β*	*t*	*p*	Confidence interval (%95)
Model-1: Child PedsQL Total Score as a dependent variable						
CDI Total Score	−0.705	0.210	−0.282	−3.357	<0.001	−1.125 to −0.286
SCARED Total Score	−0.598	0.091	−0.547	−6.565	0.001	−0.779 to −0.416
Olweus Victim Questionnaire	−6.887	2.761	−0.175	−2.494	0.015	−12.393 to −1.380
Model-2: Child PedsQL Physical Functioning Score as a dependent variable						
CDI Total Score	−0.617	0.309	−0.212	−1.996	0.05	−1.234 to −0.001
SCARED Total Score	−0.660	0.134	−0.520	−4.932	<0.001	−0.927 to −0.393
Olweus Victim Questionnaire	−5.571	4.063	−0.122	−1.371	0.175	−13.673 to −2.531
Model-3: Child PedsQL Psychosocial functionality Score as a dependent variable						
CDI Total Score	−0.793	0.221	−0.313	−3.594	0.001	−1.233 to −0.353
SCARED Total Score	−0.547	0.096	−0.495	−5.724	<0.001	−0.737 to 0.356
Olweus Victim Questionnaire	−7.600	2.899	−0.191	−2.621	0.011	−13.381 to −1.819

Note: Model-1: R^2=0.709, adjusted R^2=0.696, F=57.588, p<0.001. Model-2: R^2=0.533, adjusted R^2=0.514, F=27.062, p<0.001. Model-3: R^2=0.687, adjusted R^2=0.673, F=51.839, p<0.001.

predicted Child PedsQL total score and psychosocial functionality score. SCARED Total Score predicted Child PedsQL Physical Functioning Score. The results of linear regression predicting PedsQL scores of children with FMF are shown in Table 7.

DISCUSSION

To the best of our knowledge, this is the first study to compare peer bullying between children and adolescents with FMF and healthy controls, and to examine the effects of peer bullying and psychological symptoms on patients' quality of life. A higher frequency of exposure to peer bullying has been reported among individuals with chronic diseases than in healthy children.[13] A study conducted on children with systemic lupus erythematosus reported that although no significant difference was found compared to healthy controls, peer bullying rates were higher in the SLE group, and concluded that it was difficult to demonstrate the effects of peer bullying in rheumatological diseases.[19] Greater peer bullying has also been observed in children with type 1 diabetes mellitus than in healthy controls (85.7%).[20] Type 1 diabetes may be more likely to be bullied because of the needs and particularities of the disease (such as frequent insulin administration and blood sugar monitoring). Peer bullying is more common in patients with skin diseases such as acne (5.4%), psoriasis (27%), and atopic dermatitis (18–60%). Because acne rather than other skin diseases is more common among young people, it may be more normalized, which may be why bullying rates are lower. This may be attributable to skin diseases being easily visible from the outside and bullying being more related to appearance.[18] In this study, school absenteeism was significantly higher in the group with FMF than in the healthy controls and in the group with FMF with disease attacks compared to those without attacks. Studies of individuals with chronic diseases such as asthma and juvenile rheumatoid arthritis have reported significantly higher school absenteeism than in healthy controls.[31,32] Although children with FMF have no externally visible disease, we believe that they are more likely to be victims due to reasons such as school absenteeism and subsequent academic failures, and physical retardation, if present. In the present study, the peer bullying victim role was significantly higher in the FMF group than in the healthy controls (%30.2). A similar situation has been observed in many chronic diseases in the literature.

Studies have reported that peer bullying may cause internalizing disorders such as depression and anxiety.[15,16] In the present study, anxiety scores were higher in children and adolescents with FMF in the presence of a peer bullying-bullying role. However, we found that peer bullying was not associated with depression. Although these children might be expected to register high anxiety scores due to fear of attacks or chronic stress, the absence of a significant difference in their depression scores suggests that these children's ability to cope with depression has developed positively due to the difficulties they experience as a result of physical health problems. To the best of our knowledge, no other studies to date have examined the relationship between peer bullying and psychological symptoms in children and adolescents with FMF. Further research on this issue is therefore needed.

Mean depression (CDI) and total anxiety (SCARED) scores, and anxiety (SCARED) school fear scores were higher in the FMF group in the present research. While some studies examining the frequency of depression and anxiety disorders in children and adolescents diagnosed with FMF have reported that only depression scores were higher than in control groups,[11] others have detected anxiety disorders only more frequently.[9] Higher depression and anxiety scores than healthy controls have also been determined in other research.[33] In one study, no significant difference was observed between a group diagnosed with FMF and healthy controls. The authors attributed this to all patients receiving colchicine therapy and the disease being in remission.[34] In studies conducted on children and adolescents, depression was reported as 6.22–33% and anxiety as 4.93–12% in patients with FMF. In our study, depression was seen at a frequency of 14%.[8–12] The frequency of depression is consistent with the literature. Adult studies have observed significantly higher depression and anxiety scores in patients diagnosed with FMF compared to controls.[12,35–37] Researchers have suggested that patients with FMF may have a fear of attacks, thus leading to anxiety disorders, and have recommended that the biopsychosocial aspect of FMF be investigated in a comprehensive manner.[36] Previous studies have suggested various possible mechanisms involved in the frequent accompaniment of depression and anxiety in FMF patients. These include proinflammatory cytokines such as IL-1, IL-6, and TNF-α playing a role in the pathophysiology of FMF as an auto-inflammatory disease,[38] with these cytokines also being implicated in the pathophysiology of depression and anxiety. These proinflammatory cytokines increase the permeability of the blood–brain barrier, allowing inflammation to pass into the central nervous system, thus might cause psychiatric symptoms.[39] Another suggested mechanism involves inflammation causing anxiety by increasing amygdala activity,[39] with a significant decrease being observed in the frequency of FMF attacks after selective serotonin reuptake inhibitors are used by patients with FMF.[40,41] In the light of this information from the literature, we think that our findings are compatible with the previous research and that biopsychosocial evaluation of FMF patients and consultations with a child psychiatrist may be important for determining the presence of comorbid psychiatric diseases.

The presence of psychiatric disease in the families of children diagnosed with FMF was significantly higher than in the control group(25.6%). A previous study evaluating psychiatric diseases in the families of children with FMF reported a higher incidence in the FMF group than in healthy controls.[42] In another study, no significant difference was found in terms of psychiatric disease between the families of child and adolescent patients with FMF and healthy controls.[34] We think that the presence of painful attacks that may occur at unpredictable times in children with chronic diseases may increase the risk of anxiety and depressive disorders due to the fact that it creates a kind of anticipatory anxiety in the parents and that they are exposed to more stress.

According to the linear regression analysis, peer victimization, CDI total score, and SCARED total score significantly predicted the child-reported PedsQL total and psychosocial functioning scores. Additionally, the SCARED total score was a significant predictor of the child-reported PedsQL physical functioning score. Peer victimization and depression and anxiety scores may have negative effects on quality of life, as expected. The PedsQL total scores completed by the children and the total PedsQL scores completed by the parents were significantly lower in the FMF group in this study. Additionally, Spearman correlation analysis revealed a significant negative correlation between depression (CDI) scores and the total PedsQL score, a significant negative correlation between anxiety (SCARED) scores and the total PedsQL score, and a significant positive correlation between the depression (CDI) scores and anxiety (SCARED) scores of children with FMF. Several studies examining the quality of life of children and adolescents with FMF have described it as significantly lower than that of healthy controls.[9,10,43–45] Studies of adults with FMF have also shown a significantly lower quality of life than that of healthy controls.[7,8,36] Research has concluded that the presence of depression and anxiety may reduce the quality of life in patients with FMF.[8,9] FMF is a lifelong autoimmune chronic disease. As expected, the FMF patients' PedsQL scores were lower than those of healthy controls in this study, for reasons such as physical distress in children with chronic diseases and the inability to attend school, resulting in course failure and pain. Although our findings are compatible with the previous literature, the quality of life of children and adolescents with FMF who were subjected to peer bullying in the victim, bully, and bully/victim roles was lower than that of those who were not bullied. We concluded that depression and anxiety disorders are more common in children and adolescents with FMF due to the difficulties they experience, that this in turn impacts their quality of life, and that this deterioration may expose them to more peer bullying. However, we detected a significant difference between the CDI, SCARED, and PedsQL Scores completed by the children and adolescents who were exposed to peer bullying between the FMF and control groups. This may perhaps be attributable to the low numbers of patients and controls subjected to peer bullying. Further studies are now needed to evaluate the relationship between peer bullying and quality of life in children with FMF. Makay et al., observed no relationship between the duration of FMF and depression and anxiety scores.[11] In the present study, no significant correlation was found between disease duration and depression, anxiety, or PedsQL scores of children with FMF. We think that the adaptation process to the disease may

have improved as the duration of the disease increased and that quality of life may have been preserved with the development of better coping skills.

There are a number of limitations to this study. First, the research was conducted as a cross-sectional study. When interpreting our findings, it should be remembered that the number of cases of peer bullying in the FMF and control groups was low, and that the data may not be statistically significant. Depression and anxiety were evaluated using self-report scales, and no structured or semi-structured interviews were conducted.

In conclusion, we think that it may be important for pediatricians to consider the possibility of psychiatric disorders worsening in children and adolescents with FMF during evaluation, treatment, and follow-up, to exhibit the requisite sensitivity, and to seek child psychiatry consultations when necessary. It would be good for both the parents and the child's best interests if pediatricians warned parents about peer bullying and raised awareness. So far as we are aware, this study is the first to compare children and adolescents with FMF with healthy controls in terms of peer bullying and to compare the effects of peer bullying and psychological symptoms on quality of life between such patients and healthy controls. The peer bullying-victim role was significantly higher in the FMF group than in the healthy controls. At the same time, depression and anxiety scores in the FMF group were significantly higher than in the healthy control group. PedsQL scores completed by children and parents were significantly lower in the FMF group than in the control group. According to the results of linear regression, peer victimization, CDI Total Score, and SCARED Total Score predicted Child PedsQL total score and psychosocial functionality score. Our findings showed that peer victimization, comorbid depression, and anxiety reduce the quality of life of patients with FMF. The quality of life of children and adolescents with FMF who were subjected to peer bullying in the victim, bully, and bully/victim roles was lower than in those who were not bullied. Anxiety scores in the presence of peer bullying-bully roles in children and adolescents with FMF were higher than in those who were not bullies, although no association was determined with depression. This study suggests that the presence of peer bullying, depression, and anxiety may have an adverse impact on the quality of life of children and adolescents with FMF. It may be useful for future studies to evaluate the effects of peer bullying on FMF patients in a larger population.

AUTHOR CONTRIBUTIONS

Ayşenur Gülcü was responsible for the study planning, conception, design, data collection, and literature review. Ali Güven Kılıçoğlu was responsible for the study planning, conception, design, and revision of all drafts of the manuscript. Nurver Akıncı was responsible for the study planning, conception, design, and data collection. Nur Seda Gülcü Üstün was responsible for data collection, literature review, and the English writing of the manuscript. All authors read and approved the final manuscript.

INFORMED CONSENT

Informed consent was obtained from all individual participants included in the study.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

ETHICS STATEMENT

All procedures performed in studies involving human participants were in accordance with the ethical standards of the ethical committee of Bezmialem Faculty of Medicine and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

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