

The relationship between physical activity level, gastrointestinal complaints and quality of life in patients with familial Mediterranean fever

Physical activity level, gastrointestinal complaints and quality of life in familial mediterranean fever

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Abstract

Aim: In this study, we aimed to examine the relationship between physical activity (PA) level, gastrointestinal complaints, and quality of life (QoL) in patients with Familial Mediterranean Fever (FMF) and to compare them with healthy individuals.

Material and Methods: The study included patients diagnosed with FMF and healthy volunteers. Thirty-six FMF patients aged between 18-50 years and 38 healthy subjects were included in the study. The short form of the International Physical Activity Questionnaire (UFAA short form) was used to determine the PA levels of individuals. QoL was evaluated using the Short Form-36 (SF-36), and the Gastrointestinal Quality of Life Index (GIQLI) was used for gastrointestinal complaints.

Results: The mean age of the FMF patients (women=28 and men=8) was 41.27±14.19 years, which is comparable to that of the healthy individuals (43.26 ± 10.72 years; women=32; men=6) ($p > 0.05$). When the group results were compared, there was a significant difference in UFAA short form, SF-36, and GIQLI ($p < 0.05$). A significant correlation was found between UFAA short form and SF-36, GIQLI in FMF patients ($p < 0.05$).

Discussion: It was observed that as the PA level of FMF patients decreased, their gastrointestinal complaints increased and their quality of life decreased. Therefore, recommendations should be made to increase PA levels in FMF patients.

Keywords

Familial Mediterranean Fever, Gastrointestinal Complaints, Physical Activity Level, Quality of Life

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Introduction

Familial Mediterranean Fever (FMF) is a chronic inflammatory disease. FMF patients have fever and inflammation of the serous membranes with recurrent attacks. [1]. The most common symptom is abdominal pain. Today, the most effective treatment of FMF is with lifelong colchicine. The most common side effects of colchicine are diarrhea and nausea [2].

In addition, FMF is a chronic disease. Chronic diseases lead to the loss of various functions over time [3]. They cause many psychiatric disorders such as depression and anxiety, both by reducing the quality of life and their direct biological effects [4-6]. For this reason, it is known that gastrointestinal system functional diseases such as Irritable Bowel Syndrome (IBS) and dyspepsia are more common during the course of chronic diseases [7,8]. However, there are no data in the literature showing the frequency of these disorders in FMF. Chronic disease is not the only reason for the expectation that digestive system complaints will be seen more frequently in patients with FMF. There are studies in the literature that plasma serotonin 2 levels are low in FMF patients [9,10]. In the pathogenesis of IBS and similarly dyspepsia, along with psychosocial factors, dysregulation in serotonergic functions is also involved. Plasma serotonin levels were found to be low in constipation-predominant patients with IBS. Plasma serotonin levels were found to be high in IBS patients with diarrhea [11]. Based on these data, it can be thought that constipation-predominant IBS may be seen more frequently in FMF patients. Although there are digestive system complaints related to both the disease itself and the drug used in the treatment, there are not many studies on the frequency of digestive system disorders in these patients.

Physical activity (PA) and exercise have some benefits and risks for the gastrointestinal tract. Vigorous exercise inhibits gastric emptying, inhibits gastrointestinal absorption, and causes many gastrointestinal symptoms. However, moderately intense exercise is well tolerated and has beneficial effects on inflammatory bowel disease, liver disease, constipation, diverticulosis, and gallstones. PA also increases gastric emptying and reduces the relative risk of PA levels of patients and digestive system complaints in FMF. Considering the benefits of PA, individuals should be encouraged to engage in optimal PA for healthier individuals and healthier societies. It is clear that this is necessary for prolongation of life expectancy and quality of life (QOL) [13]. Since FMF is a chronic disease, it negatively affects the quality of life. A decrease in the level of PA is also expected. However, there is no study examining the effect of PA levels on QOL in FMF patients.

Our aim is to examine the relationship between PA level, gastrointestinal complaints and QOL in patients with FMF and to compare them with healthy individuals.

Material and Methods

Participants

Individuals aged 18 years and over who were treated with the diagnosis of FMF in Pamukkale University Hospital Rheumatological Diseases Polyclinic, as well as volunteers who met the inclusion criteria without any known additional disease

were included in the study. The study included 36 FMF patients aged 18 years and older who were treated with the diagnosis of FMF in Pamukkale University Hospital Rheumatological Diseases Polyclinic, who voluntarily agreed to participate and met the inclusion criteria in the study, and 38 healthy controls of the same age group without any known additional disease. Our study was carried out between March 2021 and June 2023. Patients meeting the inclusion criteria were included. Written consent was obtained from all patients. Permission for our study was given by Pamukkale University Non-Interventional Clinical Research Ethics Committee dated 02.03.2021 (no. 05). Informed consent forms were signed by FMF patients who agreed to participate in this study. We evaluated FMF patients face to face.

Inclusion and exclusion criteria

Individuals over the age of 18, who did not have any additional disease other than FMF, who were oriented and cooperative, who agreed to participate in the study, and who did not have a neurological or physical disease that would prevent them from performing PA were included in the FMF group (FMFG). In the control group (CG), healthy people over 18 years of age, oriented and cooperative, who agreed to participate, and who did not have any problems that would prevent them from performing PA were included. Those with diseases such as Diabetes Mellitus (DM), hypothyroidism, colon cancer, a recent surgery to affect mobility, diagnosed gastrointestinal disease, the integrity of the gastrointestinal tract, and the use of drugs that can change the gastrointestinal motility were not included in the CG and FMFG.

Evaluation Methods

Patient information regarding age, height, weight, gender, disease duration, age of diagnosis, duration of attacks, family history for FMF. The symptoms of the FMF patients were noted. Demographic data were recorded after obtaining consent from the patients. Socio-demographic characteristics of the patients were determined by a face-to-face patient evaluation form. The short form of the International Physical Activity Questionnaire (UFAA) was used to determine the PA levels [14]. QoL was assessed using Short Form-36 (SF-36) [15]. The Gastrointestinal Quality of Life Index (GIQLI) includes 36 parameters. Parameters, the answers were divided into 5 degrees using a Likert scale and scoring was done (0-4; 0: worst and 4: best) [16].

Statistical analysis

It was seen that the effect size obtained in the reference study was at a strong level ($d=1.04$) [4]. Based on the results of the reference study, as a result of the power analysis we made by assuming that we could achieve a lower effect size ($d=0.8$), it was calculated that 95% power could be achieved at the 95% confidence level, when at least 70 people (at least 35 people for each group) were included in the study. The data were analyzed with the SPSS package program. Continuous variables were presented as mean \pm standard deviation and categorical variables as numbers and percentages. In the comparison of differences, the significance of the Man-Whitney U Test was used when the non-parametric test assumptions were not met, and Spearman's Correlation analysis was used when the non-

parametric test assumptions were not met.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

Of the 39 FMF patients, 1 patient was deemed ineligible for this study and 2 patients declined to participate. As a result, 36 FMF patients were analyzed. Of the 40 healthy individuals, 2 were deemed ineligible for this study. As a result, 38 healthy individuals were analyzed (Figure 1).

Thirty-six patients with FMF (men=8 / women=28) and 38 healthy individuals (Men=6 / women=32) were included (p=0.560). The mean age of the patients with FMF was 41.27±14.19 years, which was comparable to that of the healthy individuals (43.26 ± 10.72) (p >0.05). There was no significant difference in terms of age, weight, height and body mass index (BMI) (p > 0.05). A significant difference was found between the groups in terms of IPAQ, SF36, and GIQLI results (p < 0.05). The results are shown in Table 1.

The evaluation of all participants' results showed a highly positive relationship between IPAQ and physical function (r = 0.563, p = 0.000), physical role (r = 0.462, p= 0.005), general health (r = 0.256, p= 0.132), bodily pain (r =0.407, p=0.014), vitality (r = 0.683, p= 0.000), social functioning (r = 0.317, p= 0.059), emotional role (r = 0.313, p= 0.064) and mental (r = 0.646, p= 0.000) in patients with FMF. The evaluation of all participants' results showed a highly positive relationship between IPAQ and GIQLI (r = 0.726, p=0.000) in FMFG. The relationship between IPAQ, SF36, and GIQLI in patients with FMF is presented in Table 2.

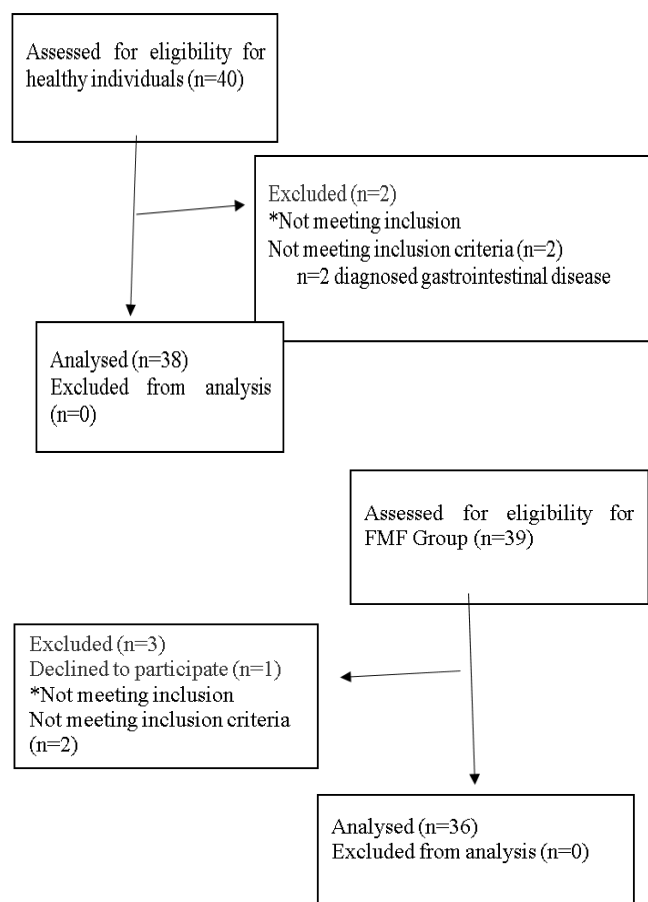


Figure 1. Flow chart of the study design.

Table 1. Demographic and clinical features as well as IPAQ, GIQLI and SF-36 in the FMFG and CG.

Variables	FMFG mean ± SD Percent	CG mean± SD Percent	P
Age (years)	41.27±14.19	43.26 ± 10.72	0.581*
Height (cm)	164.58±10.32	167.52±10.11	0.217*
Weight (kg)	66.94±15.18	62.92±15.67	0.283*
BMI (kg/m ²)	24.56±4.55	22.34±4.99	0.071*
Gender			
Female	28 (77.8%)	32 (84.2%)	0.560**
Male	8 (22.2%)	6 (15.8%)	
Disease duration (years)	21.13±13.55	-	
Age of onset (years)	20.13±12.27	-	
Clinical features			
Peritonitis	25 (69.4%)	-	
Fever	23 (63.8%)	-	
Arthritis	15 (41.6%)	-	
Pleuritis	13 (36.1%)	-	
Erysipelas-like erythema	1 (0.02%)	-	
Disease severity score			
Mild	12 (33.3%)	-	
Moderate	20 (55.6%)	-	
Severe	4 (11.1%)	-	
IPAQ	389.04±537.28	896.39±987.58	0.006*
GIQLI	59.75±26.21	105.34±8.82	0.000*
SF-36 items			
Physical Function	43.63±13.93	88.60±11.99	0.000*
Physical Role	34.52±13.32	83.15±13.78	0.000*
Bodily Pain	28.16±13.69	78.18±11.33	0.000*
General Health	36.05±17.23	86.05±13.96	0.000*
Vitality	21.91±19.61	77.47±20.11	0.000*
Social Functioning	41±9.42	79.92±9.19	0.000*
Emotional Role	41.5±12.14	74.57±14.24	0.000*
Mental	40.72±17.02	71±13.64	0.000*

FMFG: Familial Mediterranean Fever Group, CG: Control Group, BMI:Body Mass Index, SD: Standard Deviation, FMF: Familial Mediterranean Fever, GIQLI: Gastrointestinal Quality of Life Index, SF36: Short Form 36, IPAQ: International Physical Activity Questionnaire; *Mann-Whitney U test, **: Chi-Square, p < 0.05.

Table 2. Relationship between IPAQ, SF36, and GIQLI in FMFG.

Variables	IPAQ	
	R	p
GIQLI	0.726	0.000
SF 36 items		
Physical function	0.563	0.000
Physical role	0.462	0.005
Bodily pain	0.407	0.014
General health	0.256	0.132
Vitality	0.683	0.000
Social functioning	0.317	0.059
Emotional role	0.313	0.064
Mental	0.646	0.000

FMFG: Familial Mediterranean Fever Group, FMF: Familial Mediterranean Fever, GIQLI: Gastrointestinal Quality of Life Index, SF36: Short Form 36, IPAQ: : International Physical Activity Questionnaire; *Spearman's Correlation Analysis, p<0.05, p= Significance level, r= Correlation coefficient.

Discussion

Chronic diseases cause both physical and mental problems. In this case, it impairs the quality of life [5-7]. At the same time, lack of PA is a condition that increases gastrointestinal complaints [17,18]. It is very important to improve the QOL in patients.

This is the first study to examine the relationship between PA level, and gastrointestinal findings. As a result of our study, we determined that gastrointestinal system (GIS) symptoms increased as PA decreased. At the same time, we found that the PA level of FMF patients was lower than that of healthy individuals, their GIS findings were higher, and their quality of life was more impaired.

As a result of this study, physical function, physical role, bodily pain and vitality of SF36 were lower in FMF patients than in health controls. Previous studies have shown that the quality of life of pediatric and adult FMF patients is impaired [19,20]. Our findings on quality of life are consistent with previous studies. Decreased quality of life may be associated with episodes of illness, and PA may also be associated with symptoms of depression, anxiety, and GIS symptom [4-6].

We determined that their PA was lower than that of healthy individuals. In a study, it was reported that the level of depression and fatigue in FMF patients was higher than in healthy individuals [4]. This can reduce the PA level in people and reduce their desire to exercise. At the same time, musculoskeletal symptoms are common in FMF patients. Arthritis, arthralgia, and myalgia can mostly affect the knee or hip [21]. Since the attacks in these patients are painful and physical exertion ultimately causes attacks, this forces patients to a sedentary lifestyle [22]. This can cause a decrease in PA. Therefore, patients with FMF have more problems in performing activities of daily living than healthy individuals due to their low level of PA. In a study, it was reported that the exercise capacity of patients with FMF also decreased [23]. In the study Babaoğlu et al., patients with FMF were physically inactive during the attack [22]. In addition, the EULAR (Europa League Against Rheumatism) recommendations stipulated that FMF patients should be informed by physicians that physical stress triggers FMF episodes [24]. All this lowers the level of PA. Therefore, the level of PA was evaluated. In this study, the PA level in patients with FMF was found to be lower than in healthy individuals. There are not many studies comparing PA with healthy individuals [23]. In the previous study, a decrease was found in exercise capacity and PA level [24].

Joint pain is the third most common clinical finding of FMF after abdominal pain and fever. Episodic abdominal pain, which generally lasts less than 72 hours, is frequently seen in the course of FMF with a frequency of 89.2–93.7% [1]. Constipation and abdominal pain are seen in FMF. However, it is sometimes difficult to distinguish abdominal pain from an attack of FMF or from organic GIS disorders with visceral inflammation [25]. In addition, studies have previously found FMF to be associated with a higher risk of inflammatory bowel disease [7,8]. It was uncertain whether MEFV mutations were the cause [1,7,8]. Complaints such as constipation and diarrhea have been reported in FMF patients [20].

Limitation

Limitations of the current study were the small number of patients and the fact that most of the patients were under colchicine treatment. Colchicine treatment has controlled most of the FMF symptoms and we cannot know whether colchicine has a positive or negative impact on GIS symptoms. There are no studies examining the relationship between PA and GIS findings in FMF patients. However, it was observed that low PA levels negatively affected the QOL and increased GIS complaints [18]. For this reason, we think that GIS findings in FMF patients should be considered and studies should be conducted to increase the PA levels in FMF patients.

Conclusion and Recommendations

It was seen that as the PA level of FMF patients decreased, their gastrointestinal complaints increased and their QOL decreased. Therefore, recommendations should be made to increase PA levels in FMF patients. At the same time, it was observed that gastrointestinal complaints of FMF patients were higher than in healthy individuals. It is important to evaluate these patients' GIS complaints.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of interest

The authors declare no conflict of interest.

References

- Lachmann HJ, Sengul B, Yavuzsen TU, Booth DR, Booth SE, Bybee A, et al. Clinical and subclinical inflammation in patients with familial Mediterranean fever and in heterozygous carriers of MEFV mutations. *Rheumatology*. 2006;45(6):746-50.
- Özdoğan H. Ailevi Akdeniz Ateşi Tedavisi ve Prognozu (Familial Mediterranean Fever Treatment and Prognosis). *Turkiye Klinikleri J Int Med Sci*. 2006;2(8):51-6.
- Anderson E, Durstine JL. Physical activity, exercise, and chronic diseases: A brief review. *Sports Med Health Sci*. 2019;1(1):3-10.
- Guler T, Garip Y, Dortbas F, Dogan YP. Quality of life in Turkish patients with Familial Mediterranean Fever: Association with fatigue, psychological status, disease severity and other clinical parameters. *Egypt Rheumatol*. 2018;40(2):117-21.
- McDougall J, Wright V, Schmidt J, Miller L, Lowry K. Applying the ICF framework to study changes in quality-of-life for youth with chronic conditions. *Dev Neurorehabil*. 2011;14(1): 41-53.
- Gagnon LM, Patten SB. Major depression and its association with long-term medical conditions. *Can J Psychiatry*. 2002;47(2):149-52.
- Palsson OF, Drossman DA. Psychiatric and Psychological Dysfunction in Irritable Bowel Syndrome and the Role of Psychological Treatments. *Gastroenterol Clin N Am*. 2005;34(2):281-303.
- Yildiz A, Kizil E, Yildiz A. Quality of life and psychometric evaluation of patients diagnosed with irritable bowel syndrome: an observational cohort study. *Sao Paulo Med J*. 2020;138(4):282-6.
- Onat AM, Öztürk MA, Özçakar L, Üreten K, Kaymak SU, Kiraz S. Selective serotonin reuptake inhibitors reduce the attack frequency in familial mediterranean Fever. *Tohoku J Exp Med*. 2007;211(1):9-14.
- Onat AM, Ozçakar L, Oztürk MA, Uçar G, Ureten K, Dagli N, et al. Plasma and platelet serotonin levels in familial Mediterranean fever. *Clin Exp Rheumatol*. 2007;25(4Suppl.45):S16-20.
- Dunlop SP, Coleman NS, Blackshaw E, Perkins A, Singh G, Marsden CA, et al. Abnormalities of 5 hydroxytryptamine metabolism in irritable bowel syndrome. *Clin Gastroenterol Hepatol*. 2005;3(4):349-57.
- de Oliveira LDSSCB, Souza EC, Rodrigues RAS, Fett CA, Piva AB. The effects of physical activity on anxiety, depression, and quality of life in elderly people living in the community. *Trends Psychiatry Psychother*. 2019;41(1):36-42.

13. Singh S, Devanna S, Edakkanambeth Varayil J, Murad MH, Iyer PG. Physical activity is associated with reduced risk of esophageal cancer, particularly esophageal adenocarcinoma: a systematic review and meta-analysis. *BMC Gastroenterol.* 2014;14:101.
14. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc.* 2003;35(8):1381-95.
15. Maurischat C, Ehlebracht-König I, Kühn A, Bullinger M. Structural validity of the Short Form 36 (SF-36) in patients with rheumatic diseases. *Z Rheumatol.* 2005;64(4):255-64.
16. Yılmaz-Sahin S, Oztas B, Kural E, Iyigun E. Transcultural adaptation and validation of the Turkish version of the gastrointestinal quality of life index. *Indian J Surg.* 2022;84(4):707-14.
17. Aya V, Flórez A, Perez L, Ramírez JD. Association between physical activity and changes in intestinal microbiota composition: A systematic review. *PLoS One.* 2021;16(2): e0247039.
18. Martin D. Physical activity benefits and risks on the gastrointestinal system. *South Med J.* 2011;104(12):831-7.
19. De Schryver AM, Keulemans YC, Peters HP, Akkermans LM, Smout AJ, De Vries, et al. Effects of regular physical activity on defecation pattern in middle-aged patients complaining of chronic constipation. *Scand J Gastroenterol.* 2005;40(4):422-9.
20. Alaylı G, Durmuş D, Özkaya O, Şen HE, Nalcacioğlu H, Bilgici A, et al. Functional capacity, strength, and quality of life in children and youth with familial Mediterranean fever. *Pediatr Phys Ther.* 2014;26(3):347-52.
21. Brik R, Shinawi M, Kasinetz L, Gershoni-Baruch R. The musculoskeletal manifestations of familial Mediterranean fever in children genetically diagnosed with the disease. *Arthritis Rheumatol.* 2001;44(6):1416-19.
22. Babaoğlu H, Varan Ö, Ataş N, Satiş H, Salman R, Ozturk MA. Detection of Familial Mediterranean Fever attacks by using a connected activity tracker and assessment of impact of attacks to daily physical activities: a pilot study. *Clin Rheumatol.* 2019;38(7):1941-6.
23. Tore NG, Sari F, Sarac DC, Bayram S, Satiş H, Karadeniz H, et al. Decreased exercise capacity, strength, physical activity level and quality of life in adult patients with familial Mediterranean fever. *Turk J Med Sci.* 2021;51(4):1712-18.
24. Özen S, Demirkaya E, Erer B, Livneh A, Ben-Chetrit E, Ben-Chetrit E, et al. EULAR recommendations for the management of familial Mediterranean fever. *Ann Rheum Dis.* 2016;75(4):644-51.
25. Mor A, Gal R, Livneh A. Abdominal and digestive system associations of familial Mediterranean fever. *Am J Gastroenterol.* 2003;98(12):2594-260.

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