

# The effects of working conditions on work life in Familial Mediterranean Fever (FMF) patients

Savaş Kanbur<sup>1</sup>, Burcu Albuz<sup>2</sup>, Irmak Sayin Alan<sup>3</sup>, Miraç Fatma Uzun<sup>4</sup>

<sup>1</sup>Department of Gynecology, İstanbul Zeynep Kamil Women and Children Training and Research Hospital, İstanbul, Turkey

<sup>2</sup>Department of Medical Genetics, Denizli State Hospital, Denizli, Turkey

<sup>3</sup>Department of Internal Medicine, Ankara Güven Hospital, Ankara, Turkey

<sup>4</sup>Institute of Science and Technology, Yıldız Technical University, İstanbul, Turkey

## ABSTRACT

**Objectives:** Familial Mediterranean Fever (FMF) is a common autoinflammatory disease, especially in Mediterranean populations. FMF typically occurs with fever and serositis attacks and can negatively affect the individual's life. In our study, we aimed to investigate the effects of working conditions and the disease course on the work life of FMF patients.

**Methods:** The adult patients with pathogenic or likely pathogenic mutations in the MEFV gene who applied to our medical genetic outpatient clinic of the Faculty of Medicine, Çanakkale Onsekiz Mart University between 01.01.2010 and 01.08.2020 were included in our study. We created a questionnaire of 34 questions, which included sociodemographic data, information about the FMF course of the patients, and the effects of work conditions and FMF on the work life of these patients. The questionnaire link, created over Google Drive, was sent to the patient's current mobile phone numbers via text message, and the answers received until 31.12.2020 were evaluated.

**Results:** A total of 154 survey responses were obtained, and 113 were eligible for our study. Twenty-four of 104 (23.1%) participants who have worked in any job so far stated that they have changed or quit their jobs because of increased or worsening FMF attacks. Of 72 participants who have been working actively for the last year, 4 (5.6%) of them we are reported that they have a health problem in the workplace due to FMF disease. The statistically significant relationships were found between the FMF-induced changing or quitting job and the attack number in the last year regardless of attack severity, work-related adverse psychological effects, the mode of transportation to work, and the physical conditions in the working environment.

**Conclusion:** We suggest that the regulation of work environments, considering the factors that trigger attacks in FMF patients, will contribute to the increase in quality of life and work performance in these patients.

**Keywords:** Familial Mediterranean Fever, FMF, Job, Work, Working Conditions.

Familial Mediterranean fever (FMF) is the most common autoinflammatory disease characterized by recurrent episodes of fever and inflammation.<sup>1</sup> Although it is primarily seen in Mediterranean populations, there are many reports of FMF patients

all over the world. However, the highest disease prevalence is in Turks 1 / 400-1000, and Turkey is the country where there is probably the highest number of FMF patients in the world.<sup>1,2</sup> The disease diagnosis is based on clinical findings, and molecular genetic

*Received:* .October 3, 2023; *Accepted:* October 18, 2023; *Published Online:* October 29, 2023

*How to cite this article:* Kanbur S, Albuz B, Sayin Alan I, Miraç Fatma Uzun MF. The effects of working conditions on work life in Familial Mediterranean Fever (FMF) patients. DAHUDER MJ 2023,3(4):123-131. DOI: 10.56016/dahudermj.1370647

*Address for correspondence:* Irmak Sayin Alan, Department of Internal Medicine, Ankara Güven Hospital, Ankara, Turkey. E-mail: irmaksayin@yahoo.com

©Copyright 2023 by DAHUDER  
Available at <http://dergipark.org.tr/en/pub/dahudermj>

analysis of the MEFV gene is vital in confirming the diagnosis.<sup>3,4</sup> Although FMF is an autosomal recessive inherited disease, mutations that present autosomal dominant inheritance patterns have been reported in the literature.<sup>5,6</sup>

Although FMF attacks are generally characterized by fever, abdominal pain, and joint pain due to arthritis, symptoms such as pleuritis, pericarditis, erysipelas-like erythema, and meningitis can be observed. In addition, the most critical complication of FMF is amyloidosis, which can lead to renal failure and may appear as the first and only finding in asymptomatic individuals.<sup>3</sup> FMF attacks can be triggered by many environmental, psychological, or physiological factors (stress, menstruation, cold, Etc.).<sup>7</sup>

In today's society, business life has an essential place in the lives of individuals. In the developing world, employees have to adapt to these changes as business environments change in the face of economic, political, and technological developments.<sup>8</sup> To the best of our knowledge, there is no study in the literature on the effects of working conditions on FMF attacks and the work life of these individuals. Our study aimed to investigate how working conditions affect the work life of individuals diagnosed with FMF.

## METHODS

The adult individuals ( $\geq 18$  years old) who applied to the Canakkale Onsekiz Mart University (COMU) Faculty of Medicine (FoM) Genetic Diseases Diagno-

sis and Treatment Center (GDDTC) with a (pre-)diagnosis of FMF between 01.01.2010 and 01.08.2020 and detected pathogenic or likely pathogenic mutations in the MEFV gene are included in our study. Although there are conflicting interpretations regarding its clinical significance, individuals carrying the E148Q mutation, common in FMF patients in our country, were also included in the study.<sup>9</sup>

The mobile phone numbers of the patients eligible for our study were obtained from the records of our COMU-FoM GDDTC or the hospital information system, MIA-MED, of the COMU-Health Practice and Research Hospital. A questionnaire form with 34 questions was created over Google Drive, and the link was sent to the patients via text message to their mobile phone number. The participants who started to fill out the questionnaire by clicking on the link were asked first of all whether they gave their consent for the study, and only those who approved were allowed to continue the survey.

Survey responses from the participants until 31.12.2020 were evaluated. The survey responses obtained through the Google Drive link were uploaded to the IBM SPSS Statistics 25 program, and appropriate parametric and non-parametric statistical evaluations (Independent T-test, Mann-Whitney Test, Kruskal Wallis Test, Chi-square test) were made after the normality tests. The questionnaires of individuals who do not consent to participate, repeatedly answered questionnaires by the same individual, questionnaires of individuals under the age of 18, and questionnaires of individuals whose mutation and disease informa-

**Table 1. MEFV mutation profiles of the participants**

Mutation	n (%)	Mutation	n (%)
M694V / -	33 (29.2%)	M694V / R761H	1 (0.9%)
E148Q / -	20 (17.7%)	M680I / V726A	1 (0.9%)
M680I / -	12 (10.6%)	M680I / E148Q	1 (0.9%)
M694V / M694V	5 (4.4%)	M680I / M680I	1 (0.9%)
K695R / -	5 (4.4%)	V726A / P369S	1 (0.9%)
M694V / M680I	4 (3.5%)	V726A / V726A	1 (0.9%)
M694V / V726A	4 (3.5%)	E148Q / E148Q	1 (0.9%)
P369S / R408Q	4 (3.5%)	E148Q / L110P	1 (0.9%)
M694V / E148Q	3 (2.7%)	P369S / P369S	1 (0.9%)
V726A / -	3 (2.7%)	R761H / E148Q	1 (0.9%)
R761H / -	2 (1.8%)	F479L / Q405R	1 (0.9%)
P369S / -	2 (1.8%)	P369S / R408Q / E148Q	1 (0.9%)
M694I / -	2 (1.8%)	M680I / F479L / E167D	1 (0.9%)
A744S / -	1 (0.9%)		

-:Wild type allele

tion cannot be accessed because their names are not included in our text message list are excluded from the study. In the repeatedly filled questionnaires belonging to the same individual, the responses of the participant's most recent questionnaire were considered, and other answers were excluded from the study.

Our study was approved by the Canakkale Onsekiz Mart University Faculty of Medicine Ethics Committee.

## RESULTS

A total of 154 survey responses were obtained through the Google Drive link. Two participants did not approve to participate in the survey. A total of 39 survey responses that were repeatedly filled by the same individual, belonging to individuals under the age of 18 and belonging to individuals whose mutation and disease information could not be reached because their names were not included in our text message list were also excluded from the study. The questionnaire data eligible for our study from 113 patients were evaluated. The MEFV gene mutations of these patients analyzed with different techniques (next-generation sequencing, fragment analysis, Sanger sequencing, real-time PCR, pyrosequencing, and strip test) are shown in Table 1.

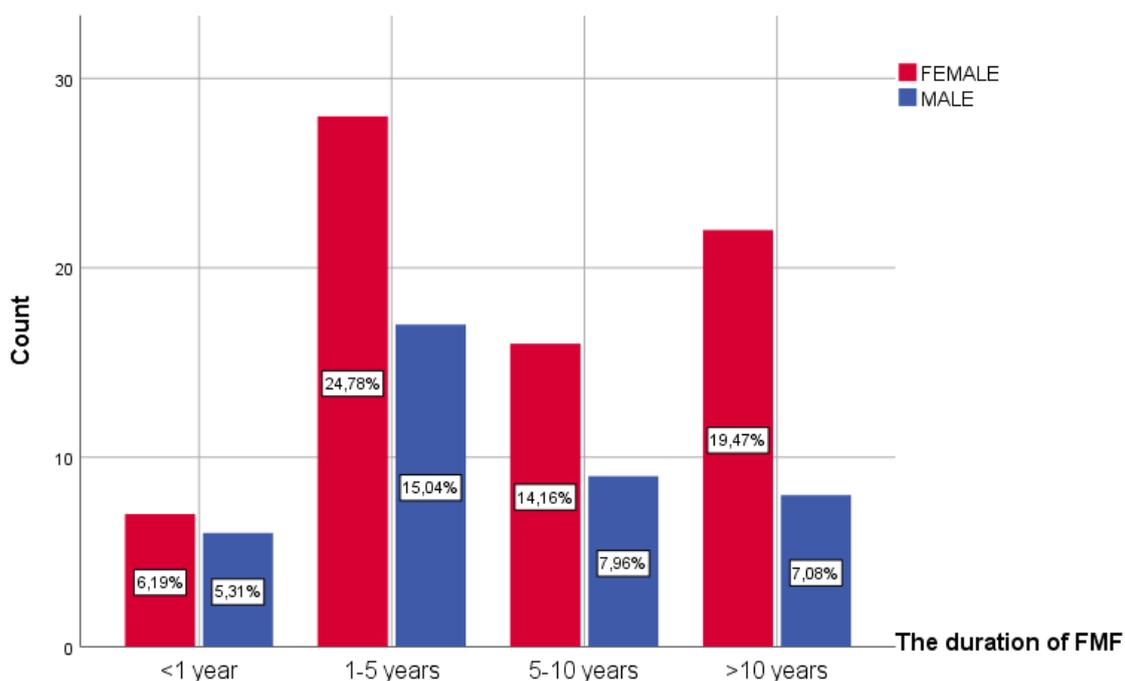
Seventy-three patients (64.6%) were female and

40 (35.4%) were male. Participants' ages ranged from 20 to 63, with a mean of 36.93 and a median of 36. 76 (67.3%) of the patients were married, 29 (25.7%) were single, and 8 (7.1%) were divorced. Seventy of the participants (61.9%) had at least one child. Twenty-two (31.4%) of those with children had a paid caregiver or a family member (such as a mother and mother-in-law) for their children to help. While 7 (6.2%) of the patients lived alone, 77 (68.1%) lived at home with at least two people.

38 (52%) of the female participants and 17 (42.5%) of the male participants had been followed up with a diagnosis of FMF for more than five years (Fig. 1).

92.03% (n: 104) of the participants have worked in any job until today (Table 2). 69.2% (n: 72) of these people have been working actively for the last year, and 4 (5.6%) of these individuals had health problems, such as accidents, injury, mutilation, Etc., in the workplace due to FMF disease. Three of these four participants suffered the loss of workforce (getting the day off from work, rest cure, Etc.) for this reason, and one of them required hospitalization during this time.

23.1% (n: 24) of the participants who have worked in any job so far reported that they have changed or quit their jobs due to increased or worsening attacks. When the participants who changed or quit their jobs due to FMF were examined in detail, 50% of them had not been working actively for the last year, 45.8% of these individuals stated that they had more than



**Fig. 1.** The distribution of participants' FMF durations by gender

**Table 2. The occupations of the participants who have worked in any job until today. Red-bolds (n: 4) present the individuals who had a health problem such as accident, injury, mutilation, Etc. in the workplace due to FMF disease.**

OCCUPATION	COUNT (n)	%	OCCUPATION	COUNT (n)	%
<b>Teacher</b>	<b>1+11</b>	11,5%	Employee	2	1,9%
Public/Officer	7	6,7%	Accountant	2	1,9%
Academician	4	3,8%	Engineer	2	1,9%
Nurse	4	3,8%	Student	2	1,9%
Biologist	3	2,9%	<b>Secretary</b>	<b>1+1</b>	1,9%
Doctor	3	2,9%	Chef	1	1,0%
Sales and marketing	3	2,9%	Lawyer	1	1,0%
Technician	3	2,9%	<b>Barber</b>	<b>1</b>	1,0%
<b>Administrative assistant</b>	<b>1+2</b>	2,9%	Office staff	1	1,0%
Banker	2	1,9%	Esthetician/Beauty Specialist	1	1,0%
Physical worker	2	1,9%	Security guard	1	1,0%
Retired	2	1,9%	Shipper	1	1,0%
Artisan	2	1,9%	Paramedic	1	1,0%
Waiter	2	1,9%	Sociologist	1	1,0%
Food technician	2	1,9%	Tailor	1	1,0%
Graphic designer	2	1,9%	Other	28	26,9%
<b>TOTAL</b>				<b>104</b>	100%

five attacks in the last year, and 95.5% of them stated that the severity of their attacks was 3 points or more. This rate was 81.8% among the individuals without FMF-C/QJ.

When the attack severity of those who had at least one attack in the last year was evaluated, in 87.5% of these, the attack severity (between 1-5 points) was stated as 3 points and above. However, there was no statistically significant relationship between the attack severity and FMF-C/QJ. ( $p > 0.05$ ).

41 (36.3%) of the participants reported that they had no attacks in the last year, while 17 (15.0%) had more than ten attacks. FMF-C/QJ ratio was found to be higher for those who had at least one attack in the last year compared to those who had no attack, and this result was statistically significant ( $p < 0.05$ ).

While 39% (n:16) of the patients who had no attack in the last 1 year have received active colchicine treatment, this rate was 88.2% (n:15) of those who had more than 10 attacks. FMF-C/QJ ratios were higher in those who received active colchicine treatment than those who did not; this result was statistically significant ( $p < 0.05$ ).

No significant relationship was found between those carrying heterozygous MEFV gene mutations and those with homozygous or compound heterozygous mutations regarding FMF-induced changing or quitting jobs (FMF-C/QJ). This was similar between

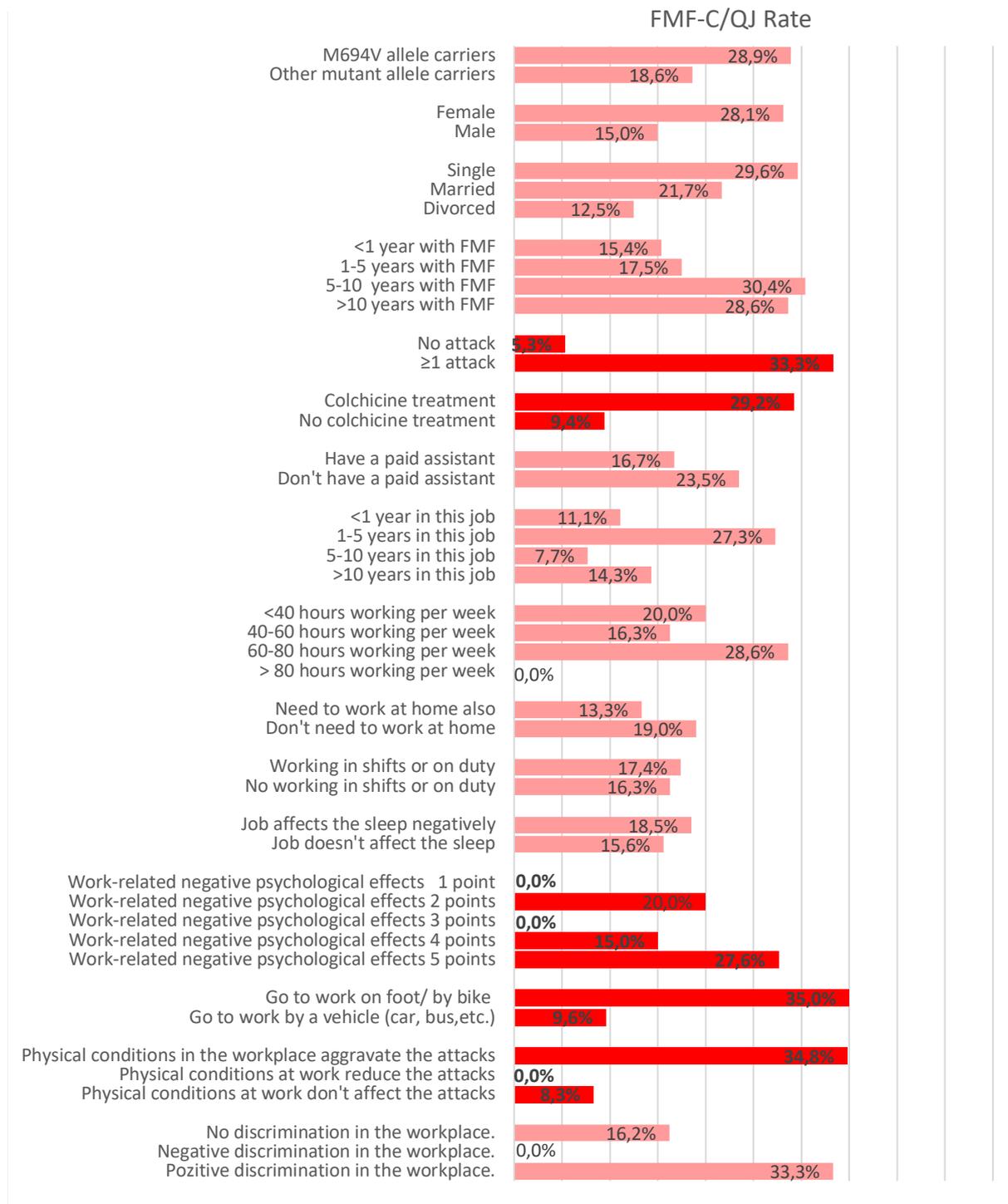
the groups carrying and not carrying the M694V allele ( $p > 0.05$ ).

38.9% (n:28) of the participants who have been actively working for the last year have been working in this business for more than ten years. However, there was no statistically significant relationship between the duration of the current job and FMF-C/QJ ( $p > 0.05$ ).

While the majority of the participants (68.1%) who have worked actively for the last year reported that they have worked an average of 40-60 hours per week, 8.3% (n: 6) stated that they have worked more than 80 hours per week. However, there was no statistically significant relationship between working time per week and FMF-C/QJ ( $p > 0.05$ )(Fig.2).

31.9% of the participants who have actively worked for the last year reported that they were working in shifts or on duty. In 37.5%, their jobs negatively affected their night sleep. 41.7% of them had to work at home in order to finish their work on time. However, no statistically significant relationship was found between these conditions (working in shifts or on duty, night sleep negatively affected due to job, working at home for the extra) and FMF-C/QJ ( $p > 0.05$ ) (Fig. 2).

While 35% of those who go to work on foot or by bike reported that they had experienced FMF-C/QJ, this rate was 9.6% for those who go to work by any means of transport like car, bus, Etc., and this differ-



**Fig. 2.** The FMF-C/OJ rates of the participants in terms of some variables in the current study (The variables with dark red columns were found to be statistically significant with FMF-C/OJ)

ence is statistically significant ( $p < 0.05$ ).

Age was found to be an essential factor in our study, and this was statistically significant for both FMF-related accidents, injury, mutilation, Etc., in the workplace and FMF-C/QJ condition ( $p < 0.05$ ).

90.3% of the participants who worked actively for the last year stated the adverse psychological effects such as stress, workload, and extreme fatigue as 3

points and above, and a statistically significant relationship was found between the adverse psychological effects and FMF-C/QJ ( $p < 0.05$ ) ((Table 3).

31.9% of the participants who have worked actively reported that physical conditions in their work environment (table, chair, cold, wind, Etc.) increased the frequency of FMF attacks or exacerbated their attacks. While 34.8% of these individuals changed or

**Table 3. The distribution of the work-related variables and the number of attacks according to the business sectors of the participants who have been actively working for the last year.**

Business sector	The number of attacks in the last year		Weekly working time		Working shifts or on duty		Negatively affected night sleep due to job		Adverse psychological effects such as work-related stress, workload, and extreme fatigue		The effect of physical conditions in working environment on FMF attack frequency		FMF-induced changing or quitting a job (FMF-C/QI)		Total
	No attack	At least one attack	Less than 40 hours	More than 40 hours	Yes	No	Yes	No	< 3 points	≥ 3 points	Aggravate the attacks	Reduce or not affect the attacks	Yes	No	
Health	Count 4	6	1	9	5	5	5	5	1	9	2	8	1	9	10
	% 40%	60%	10%	90%	50%	50%	50%	50%	10%	90%	20%	80%	10%	90%	100%
Education	Count 8	6	8	6	1	13	2	12	2	12	8	6	3	11	14
	% 57,15	42,90%	57,10%	42,90%	7,10%	92,90%	14,3	85,7	14,3	85,7	57,10%	42,90%	21,40%	78,60%	100%
Agriculture / Farming	Count 0	1	0	1	0	1	0	1	0	1	0	1	0	1	1
	% 0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	100%
Defense / Security Industry	Count 1	3	0	4	2	2	2	2	1	3	0	4	0	4	4
	% 25%	75%	0%	100%	50%	50%	50%	50%	25%	75%	0%	100%	0%	100%	100%
Trade / Craftsman	Count 6	7	0	13	3	10	7	6	1	12	5	8	2	11	13
	% 46,20%	53,80%	0%	100%	23,10%	76,90%	53,80%	46,20%	7,70%	92,30%	38,50%	61,50%	15,40%	84,60%	100%
Banking	Count 1	0	0	1	1	0	1	0	0	1	0	1	0	1	1
	% 100%	0%	0%	100%	100%	0%	100%	0%	0%	100%	0%	100%	0%	100%	100%
Food Industry	Count 3	1	0	4	2	2	0	4	1	3	1	3	2	2	4
	% 75%	25%	0%	100%	50%	50%	0%	100%	25%	75%	25%	75%	50%	50%	100%
Clothing/Women's Industry	Count 0	1	0	1	0	1	0	1	0	1	1	0	0	1	1
	% 0%	100%	0%	100%	0%	100%	0%	100%	0%	100%	100%	0%	0%	100%	100%
Other	Count 5	19	1	23	9	15	10	14	1	23	5	19	4	20	29
	% 20,80%	79,20%	4,20%	95,80%	37,50%	62,50%	41,70%	58,30%	4,20%	95,80%	20,80%	79,20%	16,70%	83,30%	100%
TOTAL	Count 28	44	10	62	23	49	27	45	7	65	23	49	12	60	72
	% 38,90%	61,10%	13,90%	86,10%	31,90%	68,10%	37,50%	62,50%	9,70%	90,30%	31,90%	68,10%	16,70%	83,30%	100%

quit their jobs due to FMF, this rate was 0% and 8.3%, respectively, for those who stated that the physical conditions reduced or did not affect the frequency and severity of their attacks. A statistically significant relationship was found between physical conditions in the working environment and FMF-C/QJ ( $p < 0.05$ ).

Among the participants who have actively worked, none (0.0%) of those who experienced negative discrimination in the distribution of work due to FMF disease, 33.3% of those who experienced positive discrimination, and 16.2% of those who were not exposed to any discrimination reported that they experienced FMF-C/QJ. However, these differences were not statistically significant ( $p > 0.05$ ).

## DISCUSSION

To the best of our knowledge, our study is the first in the literature on the effects of working conditions and the FMF course of the patients on their work life. Four of the 72 participants reported that they have had a health problem in their workplace due to FMF disease. In addition, 23.1% (n:24/104) of the patients stated that they have changed or quit from their jobs because of FMF.

The mutations in the MEFV gene, with ten exons located on the short arm of chromosome 16, play an essential role in the development of FMF. The detection of biallelic pathogenic mutations in the MEFV gene confirms the diagnosis, and identification of the mutations contributes to different FMF phenotype diagnoses.<sup>3,10</sup> A total of 385 current sequence variants in the MEFV gene were reported in the INFEVERS database, and 61 of them (15.8%) were evaluated as "Pathogenic" or "Likely pathogenic".<sup>11</sup> All pathogenic or likely pathogenic mutations in the MEFV gene do not constitute the same clinical phenotype in FMF patients. The significant clinical findings of FMF are observed higher in those who carry one or more M694V or M680I mutant alleles, while fewer clinical symptoms have been reported in those carrying E148Q or V726A mutant alleles.<sup>12</sup> In addition, it has been reported that up to 25% of individuals with a clinical diagnosis of FMF may be heterozygous pathogenic mutation carriers, and FMF findings can be observed in heterozygous carriers even with the mild variants (such as V726A P369S) than the mutations that cause severe phenotype (such as M694V).<sup>13,14</sup>

Our study found no statistically significant difference between individuals with heterozygous MEFV

mutations and with homozygous or compound heterozygous mutations in terms of FMF-C/QJ. However, in our study, different molecular techniques were used to detect mutations in the MEFV gene in the patients, and in most of these techniques, the target exons or mutations were screened, not the whole gene. Since our study was designed retrospectively, it is not known whether the heterozygous pathogenic mutation carriers also had a different pathogenic mutation(s) on the MEFV gene regions that were not screened or whether the two different mutations detected in the same patient were on the same or different alleles. Nevertheless, the most common M694V mutation in FMF patients in our country.<sup>9</sup> is screened even in targeted exon or mutation screening methods of the MEFV gene. However, in our study, no statistically significant difference was found between those carrying the M694V allele and not in terms of FMF-C/QJ.

It is still unknown why FMF progresses with attacks. However, it has been shown that attacks can be triggered by many factors, such as physical or emotional stress, menstruation, physical trauma, exposure to colds, infections, high-fat consumption, starvation, insomnia, and fatigue.<sup>15-18</sup> Factors such as job change and job interviews can be considered among the emotional stress factors.<sup>18</sup> In the study by Gidron *et al.*, the relationship between psychosocial factors and the incidence of FMF attacks has been reported in children.<sup>19</sup> In another study by Kishida *et al.*, 49.4% of 372 FMF patients reported that there were some triggers for FMF attacks. Among these, psychological stress and tiredness were the most frequently reported factors regardless of gender.<sup>7</sup> It has also been reported that depression and anxiety are more common in FMF patients compared to healthy individuals.<sup>20,21</sup> It is suggested that the dose of colchicine can be increased temporarily in such periods, significantly since physical and emotional stress can trigger FMF attacks (15).

In our study, a statistically significant relationship was found between work-related adverse psychological effects and FMF-C/QJ. At the same time, it was found that having an attack was significantly associated with FMF-C/QJ regardless of the severity of the attack.

In contrast to the study by Küçükşahin *et al.*<sup>21</sup>, in which poor sleep quality in FMF patients was associated with the number of attacks in the last three months, fatigue, and inflammatory marker levels during attacks, in our study, no significant relationship was found between FMF-C/QJ and working on duty or shift, working time per week or sleep disturbance

caused by job.

One of the factors that trigger FMF attacks is exposure to cold. In a study with the medical records of 2774 children diagnosed with FMF, possible triggering factors for FMF attacks were reported in 14.9% of the patients, and the cold factor was reported as a triggering factor in 77.2% of these patients.<sup>22</sup> Similarly, in another study, the most common triggering factors for serositis were reported as exposure to cold (59.3%), emotional stress (49.8%), tiredness (40.0%), and menstruation (33.7% in women). In comparison, those triggers for attacks with musculoskeletal symptoms were reported as long-lasting standing (78.8%), long-duration travel (64.1%) and tiredness (47.8%) (17). In a study by Cebicci *et al.*, emotional stress was reported as the most common triggering factor for abdominal pain in FMF patients in two different provinces. Physical activities that were longer than 30 minutes and caused excessive sweating, such as jogging, brisk walking for an extended period of time, climbing stairs with a heavy load, heavy household chores, and fast-paced dancing, were reported as the second trigger factor.<sup>18</sup> In the study by Alaylı *et al.*, they reported that children with FMF not only display lower functional capacity and muscle strength but also manifest lower physical and psychosocial functioning in comparison with healthy children.<sup>23</sup>

In our study, a statistically significant relationship was found between the way of transportation used to work and FMF-C/QJ. Those who go to work on foot or by bike were found to have higher FMF-C/QJ rates than those who use transport vehicles to work. However, there was no significant relationship between the duration of transport and FMF-C/QJ. Karadağ *et al.* reported that standing for a long time can trigger attacks with musculoskeletal pain.<sup>17</sup> In another study, it has been reported that the presence of painful symptoms in the lower extremities after prolonged standing and sitting periods in FMF patients during the absence of attacks may be due to an inflammatory activity.<sup>24</sup> In a study in which a wearable device obtained weekly attack information of FMF patients, it was reported that FMF attacks negatively affected the daily physical life of the patient, and all attacks decreased physical activities by 33% to 84% regardless of the attack duration.<sup>25</sup> Our study suggests that not the duration of transport to work but the mode of transportation may affect work life by triggering FMF attacks due to exposure to physical activity or environmental factors such as cold.

In our study, it was observed that physical condi-

tions at work (table, chair, cold, wind, Etc.) were also associated with FMF-C/QJ. This shows the importance of possible triggering factors in FMF patients' work environments.

The effects of triggers may also vary according to the MEFV gene mutations that are detected in the individual. In the study by Avagyan *et al.*, a statistically significant relationship was reported between emotional stress and three primary pathogenic MEFV mutations: M694V, M680I, V726A, and their homozygous genotypes.<sup>22</sup> In another study, it was reported that the M694V allele was associated with starvation, the E148Q allele with high food intake, and the V726A allele with long-duration travel.<sup>17</sup> However, when the data in our study were analyzed, no significant relationship was found between the two groups that carried the M694V allele or not in terms of the mode of transport to work, affected by physical conditions at work, and the severity of work-related adverse psychological effects. This result was similarly statistically insignificant when patients were grouped as M694V heterozygous, M680I heterozygous, M694V / M680I homozygous or compound heterozygous, and those carrying other mutant alleles.

Although this is the first study in the literature investigating the effect of work conditions and the disease on the work-life of FMF patients, it has some limitations. The most important of these is the low number of participants. Moreover, our questionnaire was filled out individually, not by professionals. While creating the questions, in order to prevent bias due to the length and the boredom of the questionnaire, the questions about the working conditions were asked by generalization. For this reason, no evaluation could be made of the different work conditions that caused FMF-related work problems.

## CONCLUSION

In the regions where there is a high number of patients with FMF, such as Turkey, we propose that the regulation of working conditions of these patients will positively affect the work performance and the quality of life of these patients. However, more comprehensive studies are needed on this subject.

### Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Ethical Approval

The protocol of the study was approved by the Medical Ethics Committee of Çanakkale 18 March University, Çanakkale, Turkey. (Decision number: 2020-12, date: 23.09.2020).

### Authors' Contribution

Study Conception: SK, ISA; Study Design: SK, BA, ISA; Supervision: SK, BA, ISA, BFU; Funding: SK, ISA; Materials: SK, BA, ISA, BFU; Data Collection and/or Processing: SK, ISA; Analysis and/or Data Interpretation: SK, BA, ISA, BFU; Literature Review: SK, BA, ISA, BFU; Critical Review: SK, BA, ISA; Manuscript preparing: SK, BA, ISA.

## REFERENCES

- Alghamdi M. Familial Mediterranean fever, review of the literature. *Clin Rheumatol*. 2017;36(8):1707–13.
- Ben-Chetrit E, Touitou I. Familial Mediterranean fever in the world. *Arthritis Care Res*. 2009;61(10):1447–53.
- Shohat M. Familial Mediterranean Fever. 2000 Aug 8 [Updated 2016 Dec 15]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. *GeneReviews®* [Internet]. Seattle (WA): University of Washington S 1993-2021. A from: <https://www.ncbi.nlm.nih.gov/books/NBK1227>. No Title.
- Sönmez HE, Batu ED, Özen S. Familial mediterranean fever: Current perspectives. *J Inflamm Res*. 2016;9:13–20.
- Rowczenio DM, Iancu DS, Trojer H, Gilbertson JA, Gillmore JD, Wechalekar AD, et al. Autosomal dominant familial Mediterranean fever in Northern European Caucasians associated with deletion of p.M694 residue-A case series and genetic exploration. *Rheumatol (United Kingdom)*. 2017;56(2):209–13.
- Stoffels M, Szperl A, Simon A, Netea MG, Plantinga TS, Van Deuren M, et al. MEFV mutations affecting pyrin amino acid 577 cause autosomal dominant autoinflammatory disease. *Ann Rheum Dis*. 2014;73(2):455–61.
- Kishida D, Nakamura A, Yazaki M, Oka K, Tsuchiya-Suzuki A, Ichikawa T, et al. Triggering factors for febrile attacks in Japanese patients with familial Mediterranean fever. *Clin Exp Rheumatol*. 2020;38(5):76–9.
- Kaplanoglu E. Mesleki Stresin Temel Nedenleri Ve Muhtemel Sonuçları: Manisa İlindeki SMMM'ler Üzerine Bir Araştırma. *Muhasebe ve Finans Derg*. 2014;(64):131–50.
- Yaşar Bilge NŞ, Sari İ, Solmaz D, Şenel S, Emmungil H, Kiliç L, et al. The distribution of MEFV mutations in Turkish FMF patient multicenter study representing results of anatolia. *Turkish J Med Sci*. 2019;49(2):472–7.
- Soriano A, Manna R. Familial Mediterranean fever: New phenotypes. *Autoimmun Rev* [Internet]. 2012;12(1):31–7. Available from: <http://dx.doi.org/10.1016/j.autrev.2012.07.019>
- INFEVERS: an online database for autoinflammatory mutations. [Internet]. Available from: <https://infEVERS.umai-montpellier.fr/> Accessed ( 2021-03-23 )
- Cekin N, Akyurek ME, Pinarbasi E, Ozen F. MEFV mutations and their relation to major clinical symptoms of Familial Mediterranean Fever. *Gene* [Internet]. 2017;626:9–13. Available from: <http://dx.doi.org/10.1016/j.gene.2017.05.013>
- Marek-Yagel D, Berkun Y, Padeh S, Abu A, Reznik-Wolf H, Livneh A, et al. Clinical disease among patients heterozygous for familial Mediterranean fever. *Arthritis Rheum*. 2009;60(6):1862–6.
- Moradian MM, Sarkisian T, Ajrapetyan H, Avanesian N. Genotype-phenotype studies in a large cohort of Armenian patients with familial Mediterranean fever suggest clinical disease with heterozygous MEFV mutations. *J Hum Genet* [Internet]. 2010;55(6):389–93. Available from: <http://dx.doi.org/10.1038/jhg.2010.52>
- Ozen S, Demirkaya E, Erer B, Livneh A, Ben-Chetrit E, Giancane G, et al. EULAR recommendations for the management of familial Mediterranean fever. *Ann Rheum Dis*. 2016;75(4):644–51.
- Yenokyan G, Armenian HK. Triggers for attacks in familial mediterranean fever: Application of the case-crossover design. *Am J Epidemiol*. 2012;175(10):1054–61.
- Karadag O, Tufan A, Yazisiz V, Ureten K, Yilmaz S, Cinar M, et al. The factors considered as trigger for the attacks in patients with familial Mediterranean fever. *Rheumatol Int*. 2013;33(4):893–7.
- Cebicci H, Aykac Cebicci M, Sahan M, Gurbuz S, Karaca B, Karakus A, et al. Triggers for attacks in familial Mediterranean fever: Are there any regional or ethnic differences? *Acta Medica Mediterr*. 2014;30(6):1349–53.
- Gidron Y, Berkovitch M, Press J. Psychosocial correlates of incidence of attacks in children with Familial Mediterranean Fever. *J Behav Med*. 2003;26(2):95–104.
- Deger SM, Ozturk MA, Demirag MD, Aslan S, Goker B, Haznedaroglu S, et al. Health-related quality of life and its associations with mood condition in familial Mediterranean fever patients. *Rheumatol Int*. 2011;31(5):623–8.
- Kucuksahin O, Omma A, Ozdemirel AE, Tecer D, Ulutas S, Maras Y, et al. Incidence of sleep disturbances in patients with familial Mediterranean fever and the relation of sleep quality with disease activity. *Int J Rheum Dis*. 2018;21(10):1849–56.
- Avagyan T, Amaryan G, Budumyan A, Hayrapetyan A TA. Influence of some environmental factors on manifestation of familial Mediterranean fever in children: clinical and genetic aspects. *Caucas J Heal Sci Public Heal*. 2018;2(2).
- Alayli G, Durmus D, Ozkaya O, Sen HE, Nalcacioglu 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.
- Dinc A. Non-periodic leg pain in patients with familial Mediterranean fever. *Ann Rheum Dis*. 2000;59(400).
- Babaoglu H, Varan O, Atas N, Satis H, Salman R, Ozturk MA, et al. 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