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EVALUATION OF MOLECULAR FINDINGS WITH CLINICAL SYMPTOMS, ACUTE INFLAMMATORY MARKERS AND HAEMATOLOGICAL PARAMETERS IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER IN NINEVEH PROVINCE

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ABSTRACT

Background: Familial Mediterranean fever (FMF) also known as recurrent polyserositis, is an autosomal recessive autoinflammatory disorder characterized mainly by brief recurrent episodes of peritonitis, pleuritis, and arthritis, usually with accompanying fever. Attacks often begin in childhood; in approximately 90% of cases, clinical onset is before age 20 years. As the name indicates, FMF occurs within families and is most common in individuals of Mediterranean descent. **Objectives:** To investigate the relationship between genetic mutations, clinical symptoms, and acute phase reactants, as well as haematological parameters for patients with familial Mediterranean fever in Nineveh province. **Methods:** This retrospective cohort study included sixty patients aged above 15 years, with clinical features of Familial Mediterranean Fever according to Tel Hashomer and Livneh criteria for adults, and the genetic mutations MEFV GENE (homozygous and heterozygous). The patients were clinically evaluated and screened for the most common 12 MEFV different mutations frequently detected in the Mediterranean region using the CE/IVD-labelled FMF Strip Assay (Vienna Lab Diagnostics, Vienna, Austria). This test is based on reverse hybridization of biotinylated PCR products on immobilized oligos for mutations and controls in a parallel array of allele-specific oligonucleotides. **Results:** Among 60 patients with FMF with MEFV gene mutations (heterozygous and homozygous), it demonstrated that the most frequent heterozygous was M694I in 12 patients, while homozygous was M694V in 12 patients. The most frequent double mutation was double heterozygous E148Q and M694I in 6 patients. Males were more common than females in both groups of mutations. Abdominal pain and fever were more frequently in heterozygous group of mutations. At the same time, acute phase reactants erythrocyte sedimentation rate (ESR) and c-reactive protein (CRP) as well as complete blood count (CBC) (neutrophils and lymphocytes) were significantly elevated in the homozygous group of mutations. **Conclusions:** The most common mutations were M694V and M694I, homozygous and heterozygous, respectively. Whereas acute-phase reactants and white blood cells (WBC) were more significantly elevated in the homozygous group than in the heterozygous group. Heterozygous mutations express more symptoms.

KEYWORDS: Familial Mediterranean fever; MEFV mutations; Inflammatory markers; Haematological parameters.

1- INTRODUCTION

Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disorder, characterized by recurrent, self-limited episodes of fever and serosal inflammation involving the peritoneum, pleura, and synovial membranes. It follows an autosomal recessive inheritance pattern and predominantly affects populations originating from the Mediterranean basin, including Arabs, Turks, Armenians, and Jews.[1-2] The disease typically manifests in childhood or adolescence, with approximately 90% of patients presenting before the age of 20 year.[3]

The molecular basis of FMF lies in mutations of the Mediterranean fever (MEFV) gene located on chromosome 16p13.3, which encodes the protein pyrin. Pyrin plays a crucial role in regulating innate immunity through modulation of inflammasome activation and interleukin-1 beta (IL-1β) production.[4-5] Mutations in the MEFV gene lead to dysregulated pyrin function, resulting in excessive activation of the inflammasome complex and overproduction of pro-inflammatory cytokines, particularly IL-1β, which is central to the pathogenesis of FMF.[6-7] This inflammatory cascade contributes to both acute attacks and persistent subclinical inflammation observed in affected individuals.

More than 300 MEFV gene variants have been identified, with certain mutations showing strong genotype–phenotype correlations. Among these, M694V, M694I, V726A, and E148Q are the most commonly reported mutations in Mediterranean populations.[8-9] Homozygous mutations, particularly M694V, have been consistently associated with more severe disease, higher frequency of attacks, increased inflammatory markers, and a greater risk of complications such as secondary (AA) amyloidosis.[10-11] In contrast, heterozygous mutations may present with milder or atypical clinical features, although their clinical significance remains a subject of ongoing debate.[12]

Clinically, FMF is characterized by recurrent febrile episodes accompanied by abdominal pain, chest pain, arthritis, and, less commonly, erysipelas-like skin lesions.[13] These attacks are typically self-limiting, lasting between 12 hours and 3 days, but may significantly impair quality of life and lead to misdiagnosis, particularly in regions where awareness is limited.[14] One of the most serious long-term complications of FMF is amyloidosis, resulting from chronic elevation of serum amyloid A protein, which can lead to progressive renal failure if untreated.[15]

Acute phase reactants, including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), are widely used as markers of inflammation in FMF and are typically elevated during attacks. In addition, haematological parameters such as leukocyte count, neutrophils, and lymphocytes may reflect the degree of inflammatory activity and disease severity.[16-17] Several studies have suggested that these laboratory markers correlate with specific MEFV genotypes, supporting the concept of genotype–phenotype association in FMF.[18]

Despite the high prevalence of FMF in Middle Eastern populations, including Iraq, there is a paucity of data regarding the relationship between genetic mutations, clinical manifestations, and inflammatory markers in Nineveh Province. Most available studies have been conducted in Turkish, Iranian, or North African populations, with limited representation of Iraqi cohorts.[9,19] Given the potential ethnic and environmental influences on disease expression, regional studies are essential to better understand the clinical and molecular characteristics of FMF.

Therefore, this study aimed to evaluate the correlation between MEFV gene mutations, clinical symptoms, acute inflammatory markers, and haematological parameters in patients with FMF in Nineveh Province, with the goal of improving diagnostic accuracy and contributing to the understanding of genotype–phenotype relationships in this population.

2-PATIENTS AND METHODS

This retrospective analytical cohort study was conducted in Nineveh Province, Iraq, over the period from November 2021 to December 2022. The study included 60 patients diagnosed with familial Mediterranean fever (FMF), comprising both males and females aged above 15 years. Diagnosis was established based on the Tel Hashomer and Livneh criteria, which are widely accepted clinical standards for FMF classification. Patients were recruited from available clinical records obtained from private laboratories and healthcare facilities.

Eligible participants were required to have documented clinical features consistent with FMF, including recurrent fever, abdominal pain, chest pain, or joint involvement. In addition, all included patients had laboratory evidence of inflammation, specifically elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), as well as confirmed MEFV gene mutations (either homozygous or heterozygous). Patients with other autoimmune or inflammatory diseases, those younger than 15 years, or those with incomplete clinical or laboratory data were excluded from the study.

Clinical and laboratory data were retrospectively collected from patient records. These included demographic characteristics, clinical manifestations, and haematological parameters such as complete blood count (CBC), including white blood cell count, neutrophils, and lymphocytes. Acute phase reactants, namely ESR and CRP, were also recorded as indicators of inflammatory activity.

Genetic analysis was performed using a CE/IVD-labelled FMF Strip Assay (ViennaLab Diagnostics, Vienna, Austria), which detects the most common MEFV gene mutations prevalent in Mediterranean populations. This assay is based on reverse hybridization of biotinylated polymerase chain reaction (PCR) products with allele-specific oligonucleotide probes immobilized on a test strip, allowing simultaneous identification of multiple mutations.

Statistical analysis was carried out using IBM SPSS version 26. Continuous variables were expressed as mean ± standard deviation, while categorical variables

were presented as frequencies and percentages. The normality of data distribution was assessed using the Shapiro–Wilk test. Comparisons between groups were performed using the independent samples t-test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables, as appropriate. A p-value of ≤ 0.05 was considered statistically significant.

The study protocol was reviewed and approved by the Scientific Council of Internal Medicine, Iraqi Board of Medical Specializations. Patient confidentiality was maintained throughout the study, and all data were handled in accordance with ethical research standards.

3-RESULTS

The study sample includes 60 patients with a female ratio of 1:0.62. The sample was subdivided into 2 groups according to the MEFV gene mutations; group one, which had the heterozygous gene, consisted of 40 patients, and group two, which had the homozygous gene, consisted of 20 patients. The mean age for group one was 15.149±2.216 years, while the mean age for group two was 15.000±1.000 years. Types of gene mutations among the present sample were illustrated in figure (3.1) which demonstrated that the most frequent heterozygous was the heterozygous M694I in 12 patients, the most frequent double mutation was double heterozygous E148Q&M694I in 6 patients. The most frequent homozygous was homozygous M694V in 12 patients.

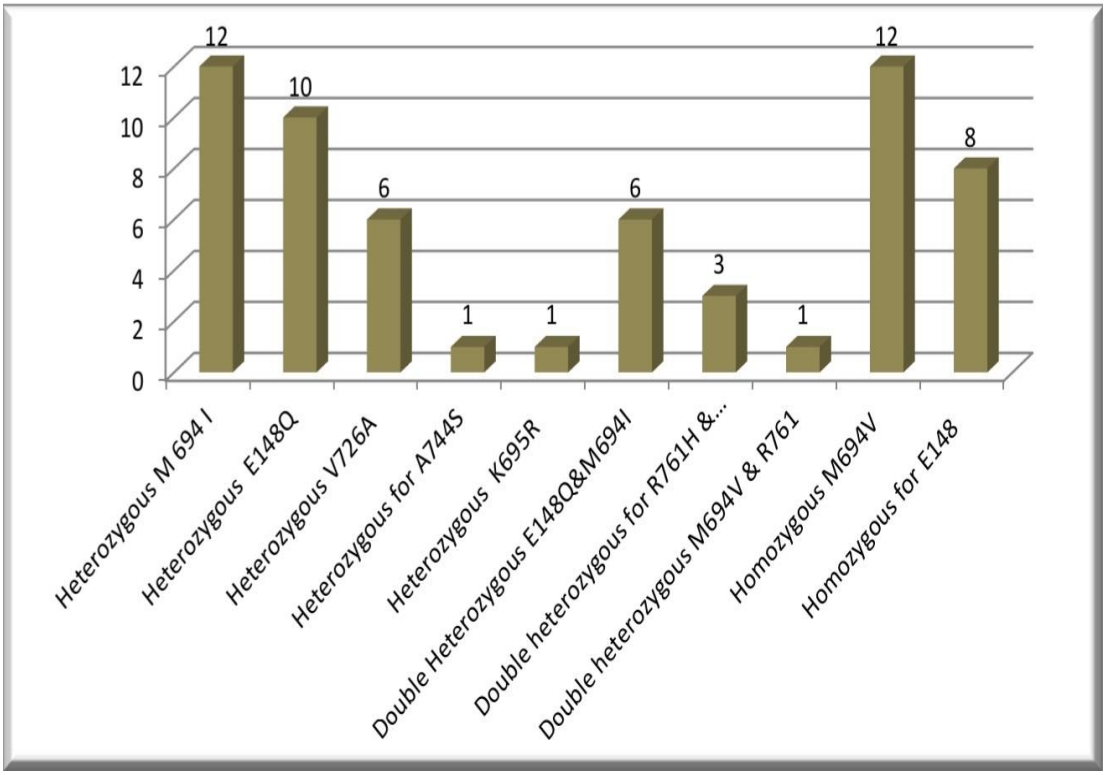

Figure (3.1): Types of gene mutations among the present sample.

Comparison of gender between the study groups was demonstrated in Table 1 and revealed that 72.5% and 27.5% of the heterozygous group were males and females, respectively, while among the homozygous group, the males were 80.0% and females were 20.0%; the difference between the study groups was statistically significant at (p=0.035).

Table 1: Comparison of gender between the study groups.

Gender	Heterozygous group (no= 40)	Homozygous group (no=20)	P-value *
	No.(%)	No.(%)	0.035
Males	21(72.5)	16(80.0)	
Females	19(27.5)	4(20.0)	

***Chi square test has been used**

Comparison of clinical features between the study groups was demonstrated in table 2. It revealed that most of the patients with heterozygous presented with abdominal pain (70.0%), which was significantly lower (p=0.043) than those among the homozygous group (95.0%). Fever was found among 35.0% of the heterozygous patients

and 65.0% of the homozygous patients, with a statistically significant difference (p=0.028). Moreover, joint pain was found among 17.5% of the heterozygous group, significantly differing (p=0.003) from the homozygous group found in 55.0% of the patients. Chest pain showed no statistically significant difference between the study groups.

Table 2: Comparison of clinical features between the study groups.

Clinical features	Heterozygous group (n=40)	Homozygous group (n=20)	P-value *
	No(%)	No.(%)	
Abdominal pain	28(70.0)	19(95.0)	0.043**
Fever	14(35.0)	13(65.0)	0.028*
Joint pain	7(17.5)	11(55.0)	0.003*
Chest pain	1(2.5)	3(15.0)	0.103**

*** patients presented with more than one feature**
*** Chi-square test has been used; ** Fisher Exact test**

A comparison of proteinuria between the study groups is shown table 3. This table elicited positive proteinuria among 55.0% of the heterozygous group and 85.0% of the homozygous group; the difference was statistically significant at (p=0.022).

Table (3): Comparison of proteinuria between the study groups.

Proteinuria	Heterozygous group (n=40)	Homozygous group (n=20)	p-value*
	No. (%)	No. (%)	
Present	22(55.0)	17(85.0)	0.022
Absent	18(45.0)	3(15.0)	

***The Chi-square test has been use**

Distribution of the clinical features according to gene mutations was demonstrated in table 4 and revealed that abdominal pain was the most frequent clinical feature among all the gene mutations, followed by fever, joint pain, and chest pain.

Table 4: Distribution of the clinical features according to gene mutations.

	Clinical features			
	Abdominal pain	Fever	Joint pain	Chest pain
M694I (n=21)	7(58.3)	4(33.3)	2(16.7)	1.(8.3)
E148Q (n=10)	6(60.0)	3(30.0)	1(10.0)	0(0.0)
V726A (n=6)	4(66.7)	1(16.7)	1(16.7)	0(0.0)
A744S (n=1)	1(100.0)	1(100.0)	1(100.0)	0(0.0)
K695R (n=1)	1(100.0)	1(100.0)	1(100.0)	0(0.0)
E148Q &M694I (n=6)	5(83.3)	2(33.3)	1(16.7)	0(0.0)
R761H &M694V (n=1)	3(100.0)	1(33.3)	1(33.3)	0(0.0)
M694V & R761 (n=1)	1(100.0)	1(100.0)	1(100.0)	0(0.0)
M694V (n=12)	12(100.0)	8(66.7)	7(58.7)	2(16.7)
E148 (n=8)	7(87.5)	5(62.5)	4(50.0)	1(12.5)

A comparison of haematological parameters between the study groups was displayed in table 5 regarding CRP, ESR, WBC, neutrophils, and lymphocytes. The mean erythrocyte sedimentation (ESR) level among the heterozygous group was 38.617±5.643, while among the homozygous group was 52.333±8.737; the difference

was statistically significant at (p=0.001). The mean C-reactive protein (CRP) levels were 28.333±2.887 and 43.638±6.175 among the heterozygous and homozygous groups, respectively, with a statistically significant difference (p=0.001). The mean levels of white blood cells(WBC)including Neutrophils, and Lymphocytes among the heterozygous group were 9.666±0.577, 7.166±0.288, and 2.233±0.642 respectively, which were significantly lower than those among the homozygous group, 10.974±2.057, 9.978±1.375, and 3.883±0.799 in that manner.

Table 5: Comparison of haematological parameters between the study groups.

Haematological parameters	Heterozygous group (n=40)	Homozygous group (n=20)	P-value*
	Mean±SD	Mean±SD	
ESR	38.617± 5.643	52.333±8.737	0.001
CRP	28.333±2.887	43.638±6.175	0.001
WBC	9.666±0.577	10.974±2.057	0.007
Neutrophil	7.166±0.288	9.978±1.375	0.001
Lymphocyte	2.233±0.642	3.883±0.799	0.001

***t-test for Independent two means has been used.**

Distribution of the serum reactant according to gene mutations was shown in table 6; this table elicited that the heterozygous M694I had a higher level of CRP and ESR among the heterozygous, while homozygous M694V had a higher level for CRP and ESR among the homozygous gene mutations.

Table 6: Distribution of the serum reactant according to gene mutations.

Gene Mutations		Serum reactants	
		CRP	ESR
Heterozygous mutation	M694I (n=12)	39.3 12±9.533	31.432 ± 5.321
	E148Q (n=10)	39.291±8.714	29.275±4.955
	V726A (n=6)	38.564±9.171	29.021± 5.478
	A744S (n=1)	38. 621±0.000	27.286±0.000
	K695R (n=1)	37.478±0.000	25.235±0.000
	E148Q &M694I (n=6)	39.685±8.934	28.213±4.212
	R761H & M694V (n=3)	40.423±8.792	28.156±3.13
	M694V & R761 (n=1)	48.554±0.000	28.017±3.104
Homozygous mutations	M694V (n=12)	53.405±9.071	43.944±5.698
	E148Q (n=8)	51.261±8.403	43.332±6.652

Distribution of the Leukocytes according to gene mutations is demonstrated in Table 7. It revealed that the highest levels of WBC, neutrophils and lymphocytes were found in about heterozygous M694I and homozygous M694V gene mutations.

Table 7: Distribution of the leukocytes according to gene mutations.

Gene mutations		Leukocytes		
		WBC	Neutrophil	Lymphocytes
Heterozygous mutation	M 694 I (n=12)	11.219±1.019	8.114±0.273	1.675±0.456
	E148Q (n=10)	11.043±0.720	7.136±0.463	2.094±0.758
	V726A (n=6)	8.413±0.413	7.137±0.491	2.011±1.277
	A744S (n=1)	8.675±0.000	6.199±0.000	2.427±0.000
	K695R (n=1)	9.117±0.000	7.081±0.000	2.023±0.000
	E148Q&M694I (n=6)	9.986±0.438	7.325±0.485	2.224±1.253
	R761H & M694V (n=3)	9.684±0.254	7.312±0.592	2.547±1.392
	M694V & R761 (n=1)	9.209± 0.000	7.024±0.000	2.863±0.000
Homozygous mutation	M694V (n=12)	11.983±1.885	10.456±0.897	3.969±0.242
	E148 (n=8)	9.962±2.229	9.5±1.853	3.797±1.356

4- DISCUSSION

Familial Mediterranean Fever (FMF) is a hereditary autosomal recessive disease that is mainly seen in Turks, Armenians, Arabs, and Jews. Recurrent episodes of fever, polyserositis, and rash characterize it. MEFV gene, encoding pyrin protein, is located on the short arm of chromosome 16. FMF is associated with a broad mutational spectrum in this gene. Specific mutations are more common in particular ethnic groups. To date, different mutations of MEFV have been observed in studies carried out in other regions worldwide.

The predominant types of gene mutations observed in the current sample were as follows: heterozygous M694I, which affected 12 patients; double heterozygous E148Q&M694I, which involved 6 patients; and homozygous M694V, which affected 12 patients. These findings are in line with those of El Gezery et al.[20] and Sari et al.[21], respectively, which indicated that M694I, E148Q, M680I, and V726A were the most common mutations in Arabs. El Gezery and Sari also found that M694I was the most common mutation in Arabs, while M680I, M694V, and E148Q were the most common mutations in Arabs. Based on their analysis of 186 individuals diagnosed with FMF before the Syrian civil war, Abuhandan et al.[22] found that the following mutations were most common: R202Q (33.3%), M694V (22.6%), E148Q (22%), V726A (7.5%), R761H (4.3%), M680I (3.8%), and others (6.5%). In addition, a study by Gumus[23] among Turkish patients revealed that the six most common mutations were identical; a survey by Abuhandan et al.[22] indicated a compound heterozygous frequency of 10.8%, despite a rate of 46%; this discrepancy can be explained by next-generation sequencing (NGS), sample size, and most importantly, the study's timing, which was conducted after the migration. R202Q, M694V, E148Q, M680I, V726A, and M694I are the most common mutations in national and regional investigations. R202Q, M694V, E148Q, M680I, R761H, and V726A were the six most common variants found in this investigation.[24-25] Among the genotypes, M694V/R202Q stands out due to its greater incidence (15 cases). Barut K et al[26] examined 708 children diagnosed with FMF and discovered that the most prevalent mutation was homozygous M694V (21.8%), followed by heterozygous M694V (19.2%).[27] This variation was more common place than the M694V pathogenic variant in studies that screened for R202Q polymorphism; nevertheless, it is now widely acknowledged that the common R202Q variant is not linked to FMF morbidity. The frequency of other common genotypes also varies among locations.[25, 28, 29]

There are also differences in the frequency of other common genotypes between the regions. E148Q was the most common mutation in a study from the south-eastern region by Ece et al.[28], whereas E148Q was the second most common mutation in the eastern region[27] north-

eastern region[30] and central Anatolia.[25] In Almalky et al.[31] study, M694V was the most prevalent mutation followed by M694I, V726A, M680I, R761H and K695R respectively. A744S, I692del and E148Q mutations were found only in one patient and all were heterozygous and lastly P369S and F479L mutations were not found in any of our patients.

This data aligns with previous research conducted in Turkey (Tunca et al., 2005) and Germany Lainka et al.[32] In both studies, the most common mutation was M694V, followed by M680I and V726A. Other mutations, like E148Q, M694I, R761H, K695R, E148V, and P369S, were found to a lesser degree. With frequency rates of 49% and 37%, respectively, M694V and M694I were the most frequently observed mutations in Morocco.[33] In Algeria, these mutations accounted for 5% of the MEFV mutations, whereas in Tunisia, they accounted for 50% and 25%, respectively.[33] Only the Arab population of Morocco was found to have the M694I mutation. Among a group of children with FMF, 92% of Jewish patients and just 30% of Arab patients had the M694V mutation.[34] In line with this, research conducted in Turkey found that 51.4% of patients had the M694V mutation, 14.4% with the M680I mutation, and 8.6% with the V726A mutation.[23] Another research in Turkey found similar results: M694V (48%), E148Q (18%), M680I (15%), V726A (12.5%), P369S (3.3%), R761H (0.9), K695R (0.9), E148V (0.9), and A744S (0.5%) were the allele frequencies of MEFV mutations.[35] The present investigation demonstrated a statistically significant difference between the sexes among the heterozygous, with a majority of men compared to the homozygous. Among 419 heterozygous and homozygous mutations, 216 were male, and 203 were female, according to research by Mansour et al.[36] In men, the distribution of the alleles E148Q was 34.3%, in females it was 20.4%. Between the sexes, it was 39.4%, 15.8%, and 13.3%. In addition, heterozygous mutations were more commonly linked to men, according to Dundar et al.[37] Talaat et al.[38] found no statistically significant difference between the sexes. However, they did find that homozygous females were more common than heterozygous ones.

Proteinuria was detected in 55.0% of the heterozygous and 85.0% of the homozygous groups among those who participated in the research. Researchers Talaat et al.[38] discovered that proteinuria was linked to mutations in the E148Q, M694V, and M680I-P369S genes in 5.26 percent of their research participants. None of our patients tested positive for amyloidosis when kidney biopsy results were given. Of 403 individuals enrolled in the research, Salehzadeh[39] also documented a single instance of amyloidosis; however, this case was linked to M694I-M694I mutations. Proteinuria was discovered in Turkish FMF patients in a prior investigation by Bilge et al.[40] that used the same registry. Amyloidosis affected over 10% of the sample. Most significantly, this condition was connected with the homozygosity of the M694V genotype. Joint pain and chest discomfort were the most common presenting clinical signs among the homozygous individuals. In contrast, fever and abdomen pain were the most common presenting features among the heterozygous patients. Consistent with this finding are studies by El Gezery et al.[20] Bidari et al.[41] and Tunca et al.[24]; however, contrary to this, Lainka et al.[32] and Yilmaz et al.[42] found that abdominal discomfort was the primary symptom. Our study's findings may differ from Lainka et al.'s[32] since we dealt with patients of the same ethnic background. Furthermore, Öztürk et al.[43] found that out of 3,454 patients, 88.2% experienced stomach pain, 86.7% had fever, 27.7% had arthritis, 20.2% had chest pain, 23% had myalgia, 22.1% had exertional leg pain (ELP), and 13.1% had erysipelas-like erythema. Contrarily, 92 out of 95 patients (96.84%) reported fever as a symptom in the research by Talaat et al.[38], whereas 90 out of 95 patients (94.74%) reported abdominal pain, 75 out of 95 patients (78.95%) experienced arthritis, 19 out of 95 patients (20%) felt erysipelas-like erythema (ELE), and 17 out of 95 patients (17.89%) reported chest pain. According to Manna et al.[44] the primary symptom of FMF in 94% of patients was a high temperature, whereas in 83%, it was stomach discomfort.

The following symptoms were reported by patients in Salehzadeh's research[39], among which fever (88.1%), stomach discomfort (93.3%), arthralgia (25.6%), and arthritis (3.7%). In a study conducted by Ebrahimi-Fakhari et al.[45], it was found that 78% of patients experienced fever, 95% reported stomach pain, 59% reported arthritis, 32% reported chest pain, and 23% reported ELE. Mutants M694V and E148Q were associated with a greater frequency of arthritis and arthralgia, whereas mutations M694I were associated with a lower frequency. In study conducted by Seif and Zaki.[46]

Results showed that among Egyptian patients, E148Q was the most common mutant allele in cases of fever (36.3%), followed by M6941 (18.7%), V726A (13.4%), and A744S (11.2%); in cases of abdominal pain, E148Q, M6941, and V726A were the most common mutant alleles (37.5%, 18.5%, and 15.4%, respectively). According to Kincir et al.[47] arthritis is associated with mutations M694V and E148Q. A more significant proportion of patients with the V726A mutation (36.44%) and the M694V mutation (17.65%) exhibited Erysipelas-like erythema (ELE). According to Bodur et al.[48] ELE is a hallmark of FMF, occurring in 3% to 46% of cases, and is frequently linked to the M694V mutation. Chest discomfort was noted in 41.18 percent of patients with the M694V mutation, and pleurisy in 75 percent of patients with the same mutation was described by Özturk et al.[49] By contrasting the most prevalent mutations with clinical data, genotype-phenotype analysis was conducted. Thus, there was no correlation between the frequency of fever and stomach discomfort and any particular mutation. Patients with the following

mutations were more likely to experience chest pain: M694V/M680I ($p < 0.001$), M680I/M680I ($p < 0.001$), M694V/R761H ($p < 0.001$), and M680I/E148Q ($p < 0.001$). The study also found that patients with the M694V/M694V and R761H/-mutations were more likely to have arthritis ($p < 0.001$). Pathologies that are frequently associated with arthralgia, myalgia, and ELP.[49] The current investigation found that the mean levels of acute-phase reactants, such as ESR and CRP, were significantly more significant in the homozygous group than in the heterozygous group. The white blood cells (WBC), lymphocytes, and neutrophils behaved in a similar fashion. Although there was a statistically significant difference in erythrocyte sedimentation rate ESR across the groups, there was no statistically significant difference in CRP or WBC, according to the research by Kosan et al.[50]

On the other hand, the study conducted by Özlü et al.[51] indicated that the homozygote M694V group had substantially higher ESR and CRP levels during episodes compared to the other groups ($p=0.002$ and $p=0.004$, respectively). In contrast, the research by Onder et al.[52] found that homozygous mutations resulted in greater levels of CRP and neutrophils, but heterozygous mutations revealed considerably higher levels of lymphocytes and ESR.

The results showed that M694V had the highest CRP levels at 18%, V726A at 18%, M694I at 11%, E148Q at 11%, M680I (G/C) at 11%, and R761H at 2%. The meal level of CRP was lower among the heterozygous at 10.8±8.11 than the homozygous at 24.55±33.88. Additionally, patients with M694V homozygous or heterozygous genotypes did not vary significantly from one another in terms of WBC count, enhanced serum red blood cells (RBC), CRP, fibrinogen, or procalcitonin (PCT).[53]

5- CONCLUSION AND RECOMMENDATION

The most common mutation was M694V and M694I, homozygous and heterozygous respectively. Whereas acute-phase reactants, such as ESR and CRP, were significantly more significant in the homozygous group than in the heterozygous group. The WBC including lymphocytes, and neutrophils behaved in a similar fashion. Heterozygous mutations expressed more symptoms like abdominal pain and fever compared with homozygous mutations. Based on the gender the males were predominant than females in both groups of mutations. compound heterozygous group of mutations associated with more elevation of acute phase reactants including (CRP and ESR) and lymphocytes and neutrophils.

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