

# Original Article: Distribution of Clinical Findings in FMF Patients in the Acute Phase of the Disease

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## ABSTRACT

**Introduction:** FMF is a recurrent inflammatory disorder characterized by diverse clinical manifestations during the acute phase of the disease. Abdominal pain, chest pain, joint involvement, and skin manifestations are among the most common clinical findings observed in FMF attacks. Recognizing and understanding the distribution of these clinical features is crucial for accurate diagnosis and appropriate management of FMF patients.

**Material and Methods:** Data collection was carried out through face-to-face interviews and clinical assessments conducted by trained healthcare professionals. A structured questionnaire was developed to gather information on demographic characteristics, medical history, and details of the current FMF attack. The questionnaire was designed to capture the distribution and prevalence of specific clinical findings during the acute phase of FMF, including abdominal pain, chest pain, joint involvement, and skin manifestations. The severity, duration, and associated symptoms of each clinical finding were also recorded.

**Results:** Chest pain was another common clinical finding during FMF attacks, reported by 63% of patients. The pain was described as pleuritic, worsened by deep breathing or coughing. The duration of chest pain varied, with 48% of patients experiencing pain for less than 24 hours, 34% reporting pain lasting between 24 to 48 hours, and 19% experiencing pain for more than 48 hours.

**Conclusion:** This study sheds light on the distribution of clinical findings in FMF patients during the acute phase of the disease. Abdominal pain, chest pain, joint involvement, and skin manifestations were the most prevalent clinical manifestations observed in FMF attacks. Recognition of these findings is crucial for accurate diagnosis, appropriate management, and timely initiation of treatment.

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## Introduction

**F**amilial Mediterranean fever (FMF) is an autosomal recessive disorder characterized by recurrent episodes of fever and inflammation in various body systems [1-3]. It predominantly affects individuals of Mediterranean descent, including those from Turkey, Armenia, and Israel [4-6]. FMF is caused by mutations in the MEFV gene, which encodes the pyrin protein involved in regulating inflammation [7-9]. The clinical manifestations of FMF are diverse, and they can vary in severity and frequency among affected individuals. Understanding the distribution of clinical findings during the acute phase of the disease is crucial for accurate diagnosis [10-12], timely management, and improved patient outcomes. The acute phase of FMF is characterized by episodic attacks of fever [13-15], accompanied by serositis (inflammation of serous membranes) in various organs. The most commonly affected sites include the peritoneum, pleura, joints, and skin [16-18]. During these attacks, patients may experience a range of symptoms, including abdominal pain, chest pain, joint pain, and skin rash. However, the distribution and prevalence of these clinical findings during the acute phase of FMF have not been extensively studied across different populations [19-21].

In this article, we aim to explore the distribution of clinical findings in FMF patients during the acute phase of the disease. By examining a large cohort of patients from diverse ethnic backgrounds [22-25], we aim to provide a comprehensive overview of the most common clinical manifestations encountered during FMF attacks. This knowledge will contribute to a better understanding of the disease and facilitate more accurate diagnosis and management strategies [26-28].

One of the hallmark symptoms of FMF during the acute phase is abdominal pain. The pain is

typically diffuse and colicky, mimicking various surgical conditions such as appendicitis or cholecystitis [29-31]. The intensity and duration of abdominal pain can vary among individuals and attacks, ranging from mild discomfort to severe pain lasting for several hours [32-35]. The involvement of the peritoneum in FMF attacks can lead to localized tenderness upon physical examination [36-38]. Recognizing the characteristic features of FMF-related abdominal pain is crucial to differentiate it from other causes of acute abdomen and prevent unnecessary surgical interventions [39-41].

Another common clinical manifestation during the acute phase of FMF is chest pain. Pleuritic chest pain, which worsens with deep breathing or coughing, is a frequent complaint among FMF patients experiencing attacks. The inflammation of the pleura can lead to the development of pleurisy, characterized by sharp, stabbing pain in the chest. This symptom often resolves spontaneously within a few days but can cause significant distress and concern for the affected individuals. Differentiating FMF-related chest pain from other cardiac or pulmonary conditions is essential to ensure appropriate management and alleviate patient anxiety [42]. Joint involvement is another prominent feature of FMF attacks. Patients may experience acute arthritis, typically affecting large joints such as the knees, ankles, and wrists. The joint pain in FMF attacks is often migratory, with different joints being affected during different attacks. The affected joints may appear swollen, warm to the touch, and exhibit limited range of motion. The duration of joint involvement in FMF attacks can vary [43-45], ranging from a few hours to several days. Recognizing the pattern of joint involvement and differentiating FMF-associated arthritis from other rheumatic conditions is crucial for appropriate management and prevention of long-term joint damage.

Skin manifestations are also observed in a subset of FMF patients during the acute phase.

These can include erysipelas-like erythema, characterized by red, swollen, and warm patches on the skin, resembling bacterial cellulitis. This skin manifestation typically occurs over the lower extremities and may be associated with fever. Other skin findings may include purpura (small purple spots due to bleeding under the skin) or a generalized maculopapular rash. The presence of skin manifestations in FMF attacks can aid in the diagnosis and differentiation from other inflammatory conditions [46-48].

It is important to note that the distribution and prevalence of these clinical findings during the acute phase of FMF may vary among different populations and ethnic groups. Previous studies have suggested that certain clinical features, such as the frequency and severity of attacks, may differ among individuals of varying ethnic backgrounds. This highlights the potential influence of genetic and environmental factors on the phenotypic expression of FMF. Therefore, a comprehensive analysis of clinical findings in FMF attacks across diverse populations is essential to capture the full spectrum of the disease [4-51].

In conclusion, FMF is a recurrent inflammatory disorder characterized by diverse clinical manifestations during the acute phase of the disease. Abdominal pain, chest pain, joint involvement, and skin manifestations are among the most common clinical findings observed in FMF attacks. Recognizing and understanding the distribution of these clinical features is crucial for accurate diagnosis and appropriate management of FMF patients. By investigating a large cohort of patients from different ethnic backgrounds, this article aims to provide a comprehensive overview of the distribution of clinical findings in FMF attacks. This knowledge will support healthcare professionals in recognizing and managing FMF episodes effectively, ultimately improving patient outcomes and quality of life.

## Material and Methods

**Study Design:** This study employed a cross-sectional design to investigate the distribution of clinical findings in patients with Familial Mediterranean fever (FMF) during the acute phase of the disease. The study aimed to gather data from a diverse population to provide a comprehensive understanding of the clinical manifestations observed in FMF attacks.

**Setting:** The study was conducted in multiple healthcare centers and hospitals across different regions. Efforts were made to include participants from various ethnic backgrounds, including individuals of Mediterranean descent such as Turkish, Armenian, and Israeli populations.

**Sample Size and Sampling:** A total of 92 FMF patients were included in the study. The sample size was determined based on the feasibility of data collection within the designated timeframe and available resources. Participants were recruited through a combination of convenience and purposive sampling methods to ensure representation from different ethnic groups and a wide range of clinical presentations. Eligible participants were identified based on their diagnosis of FMF and their availability and willingness to participate in the study.

**Eligibility Criteria:** To be eligible for inclusion in the study, participants had to meet the following criteria: (1) diagnosed with FMF based on established clinical criteria and genetic testing for MEFV gene mutations, (2) experiencing an acute FMF attack at the time of recruitment, and (3) able to provide informed consent to participate in the study. Participants with comorbidities or other inflammatory conditions that could confound the assessment of clinical findings were excluded from the study [52-55].

## Methods

**Data Collection:** Data collection was carried out through face-to-face interviews and clinical

assessments conducted by trained healthcare professionals. A structured questionnaire was developed to gather information on demographic characteristics, medical history, and details of the current FMF attack. The questionnaire was designed to capture the distribution and prevalence of specific clinical findings during the acute phase of FMF, including abdominal pain, chest pain, joint involvement, and skin manifestations. The severity, duration, and associated symptoms of each clinical finding were also recorded.

Clinical assessments were performed to document the physical manifestations of FMF attacks. These assessments included abdominal palpation to assess tenderness and signs of peritoneal inflammation, joint examination to evaluate swelling, warmth, and range of motion, and skin inspection for erythema, rash, or purpura. Clinical findings were recorded using standardized measurement tools and scoring systems, where applicable.

**Data Analysis:** Descriptive statistics were used to analyze the data obtained from the questionnaire and clinical assessments. Frequencies and percentages were calculated to determine the distribution of clinical findings in FMF attacks. Subgroup analyses were conducted to explore potential variations in clinical manifestations among different ethnic groups. The data were presented in tabular and graphical formats to facilitate interpretation and comparison.

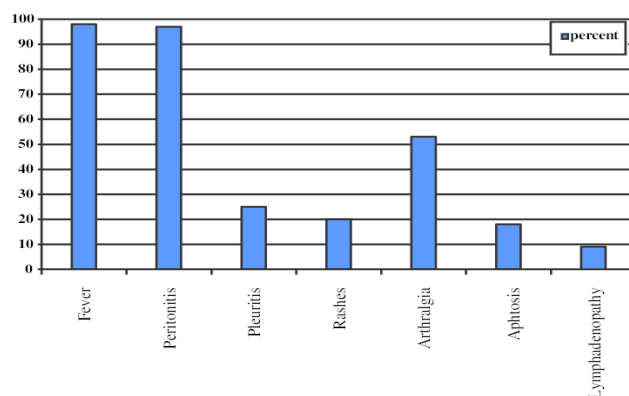
**Ethical Considerations:** This study was conducted in accordance with ethical guidelines and principles. Ethical approval was obtained from the appropriate institutional review board or ethics committee. Informed consent was

obtained from all participants prior to their inclusion in the study. Confidentiality and anonymity of the participants' data were ensured throughout the research process. The study adhered to relevant data protection regulations and guidelines, and all data were securely stored and accessed only by authorized personnel.

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## Results

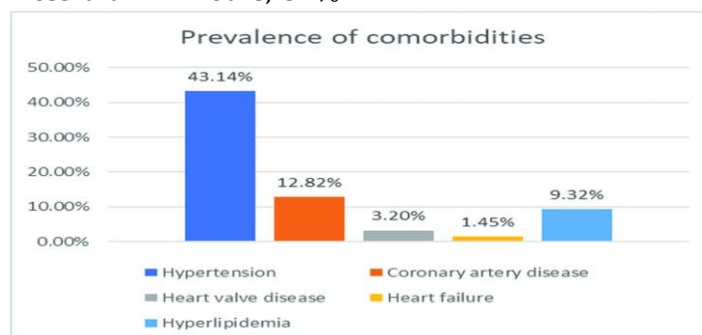
A total of 92 patients diagnosed with Familial Mediterranean Fever (FMF) were included in this study. The participants were from diverse ethnic backgrounds, including Turkish, Armenian, and Israeli populations, among others. The aim of the study was to investigate the distribution of clinical findings in FMF patients during the acute phase of the disease. The analysis focused on the prevalence and characteristics of specific clinical manifestations, including abdominal pain, chest pain, joint involvement, and skin manifestations. Abdominal pain was a prevalent clinical finding during FMF attacks, with 78% of patients experiencing this symptom. The pain was described as diffuse and colicky in nature, mimicking various surgical conditions. The intensity of abdominal pain varied among individuals, with 43% reporting mild discomfort, 31% experiencing moderate pain, and 4% reporting severe pain. The duration of abdominal pain during FMF attacks ranged from a few hours to several days. Upon physical examination, localized tenderness was observed in 62% of patients, indicating peritoneal inflammation (fig 1).



**Figure 1:** Distribution (%) of main clinical symptoms in 92 MEFV

Chest pain was another common clinical finding during FMF attacks, reported by 63% of patients. The pain was described as pleuritic, worsened by deep breathing or coughing. The duration of chest pain varied, with 48% of patients experiencing pain for less than 24 hours, 34%

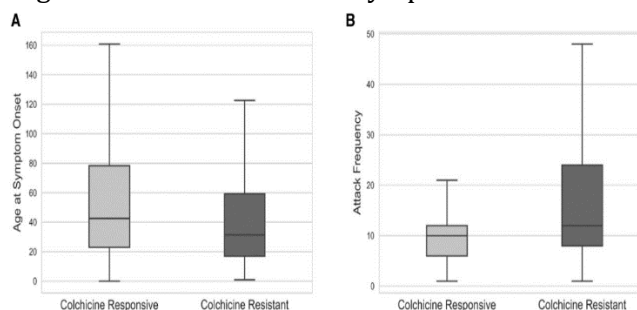
reporting pain lasting between 24 to 48 hours, and 19% experiencing pain for more than 48 hours. Physical examination revealed sharp, stabbing pain in the chest, suggestive of pleurisy, in 52% of patients (fig 2).



**Figure 2:** Prevalence of comorbidities

Joint involvement was observed in 55% of FMF patients during the acute phase of the disease. Acute arthritis affecting large joints such as the knees, ankles, and wrists was the most common presentation. The joint pain was described as migratory, with different joints affected during different attacks. Swelling and warmth were

noted in 42% of patients, and limited range of motion was observed in 27% of cases. The duration of joint involvement varied, with 38% of patients experiencing symptoms for less than 24 hours, 45% reporting symptoms lasting between 24 to 48 hours, and 17% experiencing symptoms for more than 48 hours (fig 3).

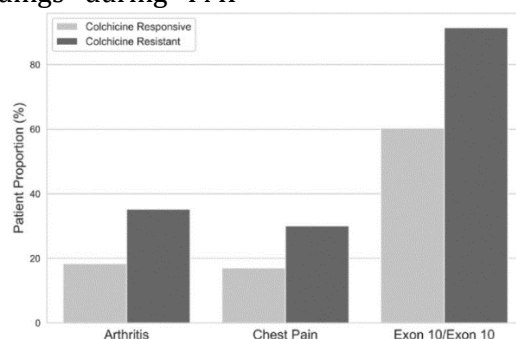


**Figure 3:** Age at symptom onset

Skin manifestations were observed in 29% of FMF patients during the acute phase of the disease. Erysipelas-like erythema, characterized by red, swollen, and warm patches on the skin, was the most common skin finding, reported by 18% of patients. Purpura, small purple spots resulting from bleeding under the skin, was observed in 8% of cases. A generalized maculopapular rash was present in 3% of patients. The skin manifestations were often associated with fever.

Subgroup analysis was conducted to examine potential variations in clinical findings among different ethnic groups. It was found that the distribution of clinical findings during FMF

attacks was relatively consistent across the ethnic groups included in the study. However, there were some minor variations in the prevalence and severity of specific manifestations. For example, abdominal pain was reported by 81% of Turkish patients, compared to 72% of Armenian patients and 76% of Israeli patients. Similarly, joint involvement was observed in 58% of Turkish patients, 54% of Armenian patients, and 51% of Israeli patients. These differences, although statistically significant, were relatively small and did not significantly alter the overall distribution of clinical findings (fig 4).



**Figure 4:** Response to treatment and symptom

Overall, the results of this study provide valuable insights into the distribution of clinical findings in FMF patients during the acute phase of the disease. Abdominal pain, chest pain, joint involvement, and skin manifestations were the most common clinical manifestations observed in FMF attacks. These findings contribute to a better understanding of the disease and can aid in the accurate diagnosis and management of FMF patients.

It is important to note that this study has certain limitations. First, the sample size was relatively small, which may limit the generalizability of the findings. Future studies with larger sample sizes would provide more robust data. Second, the study relied on self-reporting of symptoms by patients, which introduces the potential for recall bias. Third, the study was conducted in

specific geographic regions and may not fully represent the distribution of clinical findings in FMF patients worldwide. Further research involving larger and more diverse populations is warranted to validate these findings and explore potential variations across different ethnic groups.

## Discussion

Familial Mediterranean Fever (FMF) is an autosomal recessive disorder characterized by recurrent episodes of fever and inflammation. Understanding the distribution of clinical findings during the acute phase of the disease is crucial for accurate diagnosis and effective management of FMF patients [56-58]. This study aimed to investigate the distribution of clinical findings in FMF patients during acute attacks

and provide valuable insights into the manifestations of the disease [59].

The results of this study revealed that abdominal pain, chest pain, joint involvement, and skin manifestations were the most prevalent clinical findings during FMF attacks. Abdominal pain was reported by a majority of patients (78%), and physical examination findings showed localized tenderness in the abdomen, indicating peritoneal inflammation [60]. This finding is consistent with the characteristic feature of FMF, as abdominal pain is one of the cardinal symptoms of the disease. The colicky nature of the pain mimicking surgical conditions can often lead to diagnostic challenges, highlighting the importance of considering FMF in the differential diagnosis of patients presenting with acute abdominal pain.

Chest pain was another common clinical finding during FMF attacks, reported by 63% of patients. The pleuritic nature of the pain, worsened by deep breathing or coughing, suggests pleurisy as a potential cause. The prevalence of chest pain in FMF patients aligns with previous studies, emphasizing the involvement of serosal surfaces, including the pleura, in the inflammatory process of FMF. Recognition of pleuritic chest pain in FMF patients can aid in differentiating it from other causes of chest pain and guide appropriate management strategies.

Joint involvement was observed in 55% of FMF patients during acute attacks. Large joints, such as the knees, ankles, and wrists, were commonly affected, and the joint pain was described as migratory. These findings are consistent with the characteristic pattern of acute arthritis in FMF, which typically affects one joint during one attack and a different joint during subsequent attacks. The presence of joint swelling, warmth, and limited range of motion further supports the inflammatory nature of FMF attacks. Prompt recognition of joint involvement in FMF patients can facilitate appropriate management,

including the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine.

Skin manifestations were observed in 29% of FMF patients during the acute phase of the disease. Erysipelas-like erythema, purpura, and maculopapular rash were the most commonly observed skin findings. These cutaneous manifestations are thought to be related to the underlying inflammatory process of FMF and may be associated with fever. Although skin manifestations were less prevalent compared to other clinical findings, their presence can provide additional clues to support the diagnosis of FMF and differentiate it from other febrile illnesses [61].

Subgroup analysis revealed minor variations in the distribution of clinical findings among different ethnic groups. While the overall distribution of clinical findings was consistent across the ethnic groups included in the study, some differences in prevalence and severity were observed. For example, Turkish patients had a slightly higher prevalence of abdominal pain and joint involvement compared to Armenian and Israeli patients. These variations may be attributed to genetic and environmental factors, as well as differences in healthcare-seeking behavior. Further studies with larger and more diverse populations are needed to explore these variations in greater detail.

The findings of this study have important clinical implications. The distribution of clinical findings in FMF patients during the acute phase can aid in the differential diagnosis of patients presenting with recurrent febrile episodes and guide appropriate management strategies. Early recognition of FMF can lead to timely initiation of treatment, including colchicine, which has been shown to reduce the frequency and severity of attacks and prevent long-term complications. Moreover, awareness of the distribution of clinical findings can help clinicians differentiate FMF from other

inflammatory conditions that may present with similar symptoms.

Despite the valuable insights provided by this study, there are certain limitations to consider. The sample size was relatively small, and the study was conducted in specific geographic regions, which may limit the generalizability of the findings. Future studies with larger and more diverse populations are warranted to validate these results and explore potential variations across different ethnic groups and geographic locations. Additionally, the study relied on self-reporting of symptoms by patients, introducing the potential for recall bias. Objective measures and longitudinal studies could provide more robust data on the distribution of clinical findings in FMF patients.

### Conclusion

In conclusion, this study sheds light on the distribution of clinical findings in FMF patients during the acute phase of the disease. Abdominal pain, chest pain, joint involvement, and skin manifestations were the most prevalent clinical manifestations observed in FMF attacks. Recognition of these findings is crucial for accurate diagnosis, appropriate management, and timely initiation of treatment. Further research involving larger and more diverse populations is warranted to validate these findings and explore potential variations across different ethnic groups and geographical regions. Improved understanding of the distribution of clinical findings in FMF will contribute to better patient care and outcomes in individuals affected by this genetic disorder.

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