Determining Appendectomy Based on Different Mutations in Patients with Familial Mediterranean Fever Under 18 Years Old

Sandoughchian Shatrobani B. MD[*], Mahboubi L. MD[**], Shafie Dizaj L. MD[***]

Abstract:

Background and Objective: Genetic mutations in Familial Mediterranean Fever (FMF) directly cause inflammation and activation of the body's immune system. These inflammations often occur in various areas of the body, including the abdomen, and may resemble symptoms of appendicitis. In many cases, these abdominal inflammations recur, and at times, it can be challenging for physicians to determine whether the inflammation is due to appendicitis or FMF. Therefore, the present study was conducted to address this gap and aimed to determine the correlation between the type of mutations and the decision to perform appendectomy in patients under 18 years old with FMF.

Materials & Methods: This descriptive cross-sectional study was conducted at Ardabil University of Medical Sciences, involving patients with Familial Mediterranean Fever who presented to the emergency department of Kowsar Hospital in Ardabil. Data were collected from the clinical records of the patients and systematically analyzed. Between March 2023 and September 2024, 120 patients under 18 years old who visited the emergency department were included in the study. Information regarding age, gender, type of mutation, and previous surgical history was collected, and the relationships between demographic and clinical variables with treatment outcomes were assessed.

Results: Among the 120 patients with FMF, only 14 (11.67%) underwent appendectomy. The patients were divided into two groups based on whether they had undergone appendectomy or not, and the frequency of appendectomy was compared according to the type of genetic mutation. The results showed no significant difference between the two groups regarding the type of mutation (P=0.7), meaning that different mutations did not influence the decision to perform appendectomy in these patients.

Conclusion: This study concludes that in patients with Familial Mediterranean Fever, different genetic mutations do not have a significant impact on the decision to perform appendectomy. These findings highlight the importance of considering other clinical factors, such as medical history, immune status, and clinical signs, when making treatment decisions.

***Keywords:** Familial Mediterranean Fever, Appendicitis, Appendectomy, Mutation*

[*]Assistant Professor of Pediatric Hematology and Oncology, Pediatrics Department, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran
[**]Assistant Professor of Pediatric Rheumatology, Pediatric Diseases Department, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
[***]General Practitioner, Kosar Hospital, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran
Received: 12/04/2025
Accepted: 21/07/2025

Corresponding Author: Dr. Leila Mahboubi
Tel: 04135369685

E-mail: Leila_mahboobi@gmail.com

Background and Objective

Familial Mediterranean fever (FMF) is a genetic inflammatory disorder primarily observed in individuals belonging to specific ethnic groups, such as Central Asians, Armenians, Turks, Iranians, and Mediterranean Arabs.[1] This disease is caused by genetic mutations that disrupt the immune system's function, leading to episodes of fever, abdominal pain, arthritis, and other complications.[2] FMF typically begins in childhood or early adolescence, with many patients experiencing recurrent episodes of fever and inflammation in various parts of the body, particularly the abdomen, joints, and muscles.[3]

In some cases of FMF, infections may present with increased severity, which leads some patients to require surgical interventions to address their problems.[4] One such intervention is appendectomy, which is performed in patients with this disease. Appendectomy is a surgical procedure in which the appendix is removed and is usually necessary in the case of appendicitis or inflammation of this organ.[5] In this study, we aim to investigate whether performing this surgery in FMF patients under 18 years old, who visit the hospital due to abdominal problems, is influenced by the genetic mutations associated with the disease.[5]

A key point here is that FMF often causes abdominal pain that may be misdiagnosed as appendicitis.[6] Many patients with FMF experience intermittent abdominal pain, making it difficult for physicians to accurately diagnose abdominal issues in these patients.[7] In this context, identifying genetic mutations and assessing them could help improve diagnosis accuracy.[8]

The genes associated with FMF directly impact immune system function and may lead to severe inflammation in various areas of the body, including the abdomen.[9] Therefore, there is a possibility that misdiagnosis or delayed diagnosis of appendicitis may occur in these patients.[10] The aim of this study is to determine the relationship between various mutations in FMF patients under 18 years old and the need for appendectomy. This is important because it could help physicians in making more accurate diagnoses and choosing the best treatment method for FMF patients. Since this disease can present with symptoms similar to appendicitis, a more thorough and accurate examination of genetic mutations could play a significant role in the correct diagnosis and treatment of these patients.[10]

Genetic mutations in FMF directly cause inflammation and activation of the immune system. These inflammations typically occur in various parts of the body, including the abdomen, making the symptoms resemble those of appendicitis.[11] In many cases, these abdominal inflammations recur, and sometimes it is challenging for physicians to determine whether the inflammation is due to appendicitis or FMF.[12] In this study, we will explore how different genetic mutations can impact the decision-making process regarding appendectomy. This is important because providing more precise information about the cause of abdominal symptoms in FMF patients could help reduce diagnostic errors. Therefore, the results of this study could provide valuable insights for physicians in treating FMF patients. Ultimately, this study could contribute to improving the diagnosis and treatment of FMF patients, enabling physicians to make better treatment decisions based on scientific and genetic evidence. Furthermore, the results could assist researchers in proposing new methods for diagnosing and treating this disease and clarify the relationship between genetic mutations and clinical symptoms of this disorder.

Materials and Methods

Study Design

This descriptive cross-sectional study was conducted at Ardabil University of Medical Sciences and involved FMF patients visiting the emergency department of Kowsar Hospital in Ardabil, with adherence to inclusion and exclusion criteria.

Eligibility Criteria

The inclusion criteria for this study included FMF patients who were receiving treatment. Specifically, patients had to be under 18 years of age. This criterion ensures that the study only includes children and adolescents, allowing for the results to be applied to this specific age group. Additionally, patients must have been confirmed to have FMF, with the diagnosis supported by genetic and clinical tests. Furthermore, patients should have exhibited clinical symptoms resembling appendicitis, such as acute abdominal pain, fever, and nausea, to be considered for surgical intervention (appendectomy). Finally, all patients must have signed written consent to participate in the study. Additionally, patients should have been treated according to the standard care for FMF and should not have a history of severe diseases or active infections that might affect the study results. Exclusion criteria were designed to maintain data accuracy and prevent confounding factors. One such criterion was any failure to follow up or withdrawal from the study. Patients were excluded if initial evaluations revealed incorrect diagnoses or symptoms unrelated to FMF. Another exclusion criterion was the presence of any complications or medical conditions that would prevent the patient from continuing their participation. This included severe medical issues from concurrent diseases that might require immediate treatment. Third, patients who underwent significant changes in their treatment regimen, such as changes in medication or surgeries unrelated to the disease, were excluded from the study. Finally, any patient who withdrew consent to participate was excluded from the study. These measures were taken to ensure the validity and reliability of the research results.

Sampling

The study was conducted over a period of 18 months, from early Farvardin 1402 to the end of Shahrivar 1403. During this time, all children under 18 years of age visiting the emergency department of Kowsar Hospital in Ardabil were included in the study. A total of 120 participants were evaluated during this period.

Data Collection

Information regarding the patients' age, gender, type of mutation, and previous surgical history was collected. Data were systematically extracted from clinical sources and medical records and analyzed. To determine patterns related to mutation types and their impact on treatment decisions, previous surgical interventions were also considered. This information proved useful in assessing the relationships between demographic and clinical variables with treatment outcomes.

Statistical Analysis

Data were entered into SPSS software, version 25. Descriptive statistics, including frequencies, percentages, mean, and standard deviation, were used to display baseline information. The comparison of appendectomy occurrence among different mutations was performed using ANOVA. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

This study was approved by the Ethics Committee of Ardabil University of Medical Sciences (IR.ARUMS.MEDICINE.REC.1402.020). The research objectives were explained to all participants, and written informed consent was obtained from both the patient and one of the patient's parents. No additional costs were incurred by the patients, and only routine treatment costs were charged.

Findings

The initial data showed that the minimum age of the participants was 6 years, and the maximum age was 17 years; most of the participants in this study were male. The M694v mutation was the most common mutation found among the participants. A history of previous surgery was present in 25 participants (Table 1).

Table 1. Demographic data of the study participants

Variable	*Value*	
Age	*Minimum*	*6*
	Maximum	*17*
	Mean ± Standard Deviation	*12.2±3.32*
Gender	*Male*	*70(58.3%)*
	Female	*50(41.7%)*
Mutation Type	*E148Q*	*5(4.2%)*
	M690I	*2(1.7%)*
	M694v	*109(90.8%)*
	R202Q	*2(1.7%)*
	V726A	*2(1.7%)*
Previous Surgery	*Yes*	*25(20.8%)*
	No	*95(79.2%)*

In this study, during the specified period, only 14 out of 120 patients with Familial Mediterranean Fever (FMF) underwent appendectomy, meaning the frequency of appendectomy in this study was 11.67%. We divided the patients into two groups based on whether or not they underwent appendectomy and recorded the frequency of appendectomy based on each mutation type. Finally, we compared these groups, and it was found that there was no significant difference between those who had appendectomy and those who did not based on the genetic mutation type (P=0.7). In other words, the results indicated that different mutations did not play a role in the decision to perform or not perform appendectomy in patients under 18 years old with Familial Mediterranean Fever (Table 2).

Discussion

In this study, we examined the relationship between the type of genetic mutations and appendectomy in patients under 18 years old with Familial Mediterranean Fever (FMF). The results of the study showed that there was no significant difference between undergoing or not undergoing appendectomy and the type of genetic mutation in these patients. These findings may be of interest due to the clinical complexities and various differences in the diagnostic and treatment pathways of this disease.

Familial Mediterranean Fever is an autoimmune genetic disorder caused by mutations in the MEFV gene and is usually associated with periodic inflammation of various organs, especially the abdomen.[13] This disease can cause various symptoms such as acute abdominal pain, fever, and nausea, which may be mistaken for conditions such as appendicitis. As a result, in some patients with Familial Mediterranean Fever, the decision to perform surgery (appendectomy) might be challenged due to the clinical similarities between these two conditions.[14] Therefore, examining the relationship between different genetic mutations and the decision to perform or not perform appendectomy is important to determine whether the genetic mutation type has any impact on treatment decisions.[15]

Table 2. Comparison of mutations among patients with and without appendectomy

Mutation Type	Study Groups (N = 120)		P Value
	Appendectomy (n = 14)	No Appendectomy (n = 106)	
E148Q	0(0%)	5(4.7%)	
M690I	0(0%)	2(1.9%)	
M694v	14(100%)	95(89.6%)	0.700
R202Q	0(0%)	2(1.9%)	
V726A	0(0%)	2(1.9%)	

The results of this study showed no significant differences between the groups who underwent appendectomy and those who did not, with regard to the type of genetic mutations. Among the various mutations studied, M694V was the only mutation found in all patients in the appendectomy group. However, despite this, this mutation alone cannot be used as a determining factor for performing appendectomy. This finding may indicate that the decision to perform surgery in patients with Familial Mediterranean Fever is more dependent on clinical criteria and the overall condition of the patient than solely on the type of genetic mutation.[15]

One possible mechanism that may explain the results is the clinical complexities of Familial Mediterranean Fever.[16] This disease can produce a wide range of symptoms, including acute abdominal pain, fever, and nausea, which might resemble symptoms of appendicitis.[17] Due to the clinical similarities, an accurate diagnosis and decision-making regarding appendectomy may be easily affected by misdiagnosis. Furthermore, in patients with Familial Mediterranean Fever, many symptoms tend to improve spontaneously, and inflammation and pain may resolve without the need for surgery.[18] Therefore, the decision to perform appendectomy in these patients is more dependent on clinical criteria and other diagnoses than on genetic mutations.[19]

Another mechanism that might explain the results is individual differences in immune responses and inflammatory reactions.[20] In Familial Mediterranean Fever, mutations in the MEFV gene lead to the production of a protein called pyrin, which plays a crucial role in regulating inflammatory responses. Typically, these responses are activated intermittently in these patients, but the intensity and duration of the inflammation can vary among individuals.[21] These differences could significantly affect how symptoms present and how patients respond to treatments. Therefore, in this study, genetic mutations might only be one factor in the clinical manifestation and the need for surgery, and other clinical and immune factors should also be considered.[22]

Moreover, the timing and method of clinical assessment of patients may have had a significant impact on the study outcomes. The decision to perform appendectomy is usually made urgently and in specific clinical circumstances, which may require a thorough and comprehensive evaluation.[23] In this study, patients with Familial Mediterranean Fever were generally treated with standard therapies, but the clinical condition of each patient may have been

uniquely different. This might be especially relevant for children under 18, as symptoms and clinical responses may differ from those in adults.[24]

Conclusion

In conclusion, this study shows that in patients with Familial Mediterranean Fever, different genetic mutations do not significantly affect the decision to perform or not perform appendectomy. These findings highlight the importance of considering other clinical factors, such as medical history, immune status, and clinical signs, when making treatment decisions. Future studies should investigate other clinical, genetic, and immune factors related to this disease and more precisely analyze the role of these factors in treatment decision-making.

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