Comparison of diagnostic criteria for children with familial Mediterranean fever

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Abstract
Familial Mediterranean fever (FMF) is an autoinflammatory disease characterized by recurrent attacks of fever and serositis. Diagnosis is made according to clinical findings and supported by genetic analysis. The most commonly used adult diagnostic criteria are the Tel-Hashomer criteria. Pediatric criteria for FMF diagnosis were described in 2009, but their reliability should be supported by additional reports. In this study, we aimed to compare the pediatric criteria and the Tel-Hashomer and 2019 Eurofever/PRINTO classification criteria using our FMF cohort. A total of 113 patients diagnosed with FMF were included. Demographic features and laboratory findings were retrospectively collected from the patients’ files. The patients were evaluated with the Tel-Hashomer, pediatric and Eurofever/PRINTO classification criteria. At least two of five new pediatric criteria were as sensitive (89%) and specific (85%) as the Tel-Hashomer criteria (sensitivity 70%, specificity 96%). We also evaluated the Eurofever/PRINTO classification criteria using our cohort and found a sensitivity of 94% and specificity of 91%.

Conclusion: Using pediatric criteria for the diagnosis of FMF in children is a feasible and simple approach that can diagnose the disease based on at least two criteria. Therefore, our study supports the use of pediatric criteria in FMF diagnosis of children. Our results also confirm that the Eurofever/PRINTO classification criteria can be successfully applied for the diagnosis of FMF due to their high sensitivity (94%) and specificity (91%).

What is Known:
- The FMF diagnosis is made according clinical findings and supported by genetic analysis.
- The use of adult diagnostic criteria in pediatric FMF patients is controversial since classical clinical presentation is often absent in children.

What is New:
- Our study supports both the use of pediatric criteria and Eurofever/PRINTO classification criteria in clinical practice.

Keywords Diagnostic criteria · Familial Mediterranean fever · Pediatric · Recurrent polyserositis · Tel-Hashomer criteria

Abbreviations
CAPS Cryopyrin-associated periodic syndrome
FMF Familial Mediterranean fever

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Introduction

Familial Mediterranean fever (FMF) is an autosomal recessive illness with relapsing–remitting episodes of fever and serositis [1]. Although most patients are of Mediterranean origin, especially Turkish, Arabian, and Sephardic-Jewish with carrier frequencies of 1/5, and Armenian with a carrier frequency of 1/7, it is a global disorder affecting more than 100,000 people worldwide [2]. FMF is the most common periodic fever syndrome and most frequent Mendelian autoinflammatory disease. FMF occurs due to recessive mutations in the MEFV gene on chromosome 16p13.3 [3, 4], which encodes the pyrin protein involved in apoptosis and inflammation. Mutations interfere with the function of the pyrin domain, initiating an uninterrupted inflammatory cascade [3].

The disease is inherited in an autosomal recessive pattern, but patients with a typical FMF phenotype can carry a heterozygous mutation in MEFV [5]. Diagnosis of FMF remains predominantly clinical because of the variable penetrance and high frequency of MEFV carriers in certain regions, which may lead to misdiagnosis by using genetic testing alone. Several sets of criteria for adult patients have been suggested, but the most widely used remain the classic Tel-Hashomer [6] and most recent Livneh [7] criteria. There is still no consensus concerning the FMF diagnostic criteria in children. A new set of diagnostic criteria for FMF in pediatric patients was established by Yalçinkaya et al. [8] in 2009. However, as there are some contradictory results in recent validation studies, these criteria should be supported by further reports. Recently, the Eurofever/PRINTO group validated new evidence-based classification criteria for autoinflammatory recurrent fevers, including FMF, in pediatric patients with high sensitivity and specificity [9]. The goal of the current report was to compare the Tel-Hashomer and pediatric and Eurofever/PRINTO classification criteria in a cohort of pediatric FMF.

Materials and methods

Patients diagnosed with FMF according to clinical expert opinion in our pediatric nephrology department between November 2005 and November 2018 were reviewed retrospectively in terms of demographic and clinical features, and patients with missing data were excluded. A total of 113 patients diagnosed with FMF were included in this study. The diagnosis was supported by genetic testing. There were 107 patients with pathogenic (31 homozygous, 46 compound heterozygous, and 30 heterozygous) and 6 patients with uncertain significance variant (VUS, heterozygous for E148Q). The control group consisted of 117 patients without FMF who presented to our clinic with FMF symptoms such as recurrent fever, recurrent abdominal pain, recurrent joint pain, and chest pain. Their MEFV gene analysis was negative. Demographic, clinical, and genetic data were evaluated retrospectively. MEFV gene mutation analyses were conducted with the reverse hybridization method for the 12 most frequent mutations in exons 2, 3, 5, and 10, as reported in INFEVERS (https://infevers.umai-montpellier.fr/web/search.php?n=1). Patients with at least one MEFV mutation were evaluated in this study. Although FMF is an autosomal recessive disease, a substantial number of FMF patients carry only one mutation [3]. In these heterozygous patients, clinical aspects become more important for diagnosis. Our heterozygous patients were diagnosed with FMF according to clinical expert opinion. E148Q variant is a VUS mutation and does not support the diagnosis according to SHARE recommendations [10]. In our sample, six patients carrying only one E148Q variant were considered as FMF according to clinical expert opinion. These 6 patients also met all of the three diagnostic criteria (Tel-Hashomer criteria, pediatric and Eurofever/PRINTO clinical criteria) of FMF. We treated these patients with colchicine, and they responded well to medication. Therefore, we enrolled these children in our FMF sample. The patient and control groups were examined according to the Tel-Hashomer criteria [6] (the most widely used MEFV criteria in adults), pediatric criteria [8], and new Eurofever/PRINTO clinical + genetic classification criteria [9] (Table 1). Sixty-nine patients (31 homozygous and 38 compound heterozygous) had confirmatory MEFV genotype with at least one clinical item, and 38 patients (30 heterozygous and 8 compound heterozygous) had not confirmatory MEFV genotype with at least two clinical items defined in Eurofever/PRINTO criteria [9]. This study was reviewed and approved by our institutional review board.

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) for Windows, Version 18.0 (IBM SPSS Inc. Chicago, USA). P values of <0.05 were considered significant. Student’s t-test and the chi-square test were used to analyze continuous and categorical variables, respectively. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), negative likelihood ratio (NLR), confidence intervals (CIs) of the Tel-Hashomer [6], pediatric [8], and Eurofever/PRINTO
clinical + genetic [9] criteria were calculated based on $2 \times 2$ crosstabs. One-way ANOVA was used to compare the parameters between three groups in Table 3. Levene’s test was used to assess the homogeneity of the variances. Pairwise post hoc tests were performed using Tamhane’s T2 test.

### Results

The demographic, clinical, laboratory, and genetic data of the study group are shown in Table 2. The patient group consisted of 113 FMF cases (51 male and 62 female). A family history of FMF was present in 57 patients (50%). Consanguinity 6 years (range, 2.3–11.6), and the mean age at diagnosis was $8.6 \pm 4.6$ years (of parents was described for 29 FMF patients (26%). The mean age at disease onset was $6.8 \pm 4$. range, 4.1–13.3. The mean delay in diagnosis was 1.8 years. All patients responded to colchicine treatment.

The control group ($n = 117$) contained patients without FMF who had clinical symptoms mimicking those of FMF, such as recurrent abdominal pain, fever, joint pain, and chest pain. In the control group, a family history of FMF was reported for 27 individuals (20%) and consanguinity for 24 (20%). The control subjects’ diagnoses were as follows: periodic fever, aphthous stomatitis, pharyngitis, adenitis syndrome (PFAPA, $n = 23$), recurrent abdominal pain unknown etiology ($n = 18$), juvenile idiopathic arthritis ($n = 17$), Helicobacter pylori gastritis ($n = 15$), inflammatory bowel disease ($n = 10$), reactive arthritis ($n = 10$), vasculitis ($n = 8$), recurrent pericarditis ($n = 5$), acute rheumatic fever ($n = 3$), Cryopyrin-associated periodic syndrome (CAPS, $n = 3$), Behcet’s disease ($n = 2$), hyperimmunoglobulin D syndrome (HIDS, $n = 2$), and chronic recurrent multifocal osteomyelitis ($n = 1$).

The distribution of MEFV mutations in our patients was as follows: seventy-seven patients (57%) carried two mutations in the MEFV gene: 31 were homozygous (M694V, $n = 27$) and 46 compound heterozygous, and 36 patients (27%) were heterozygous (24 had M694V, six had E148Q, five had M680I, and one had V726A). Similar to Kondi et al. [11], our results showed that patients with mutations in two alleles and those with one allele had similar clinical characteristics, with genetic status having no significant effect on clinical findings ($p > 0.05$). The FMF patients were categorized into three groups according to mutation: 31 (27%) with homozygous mutations, 46 (39%) with compound heterozygous mutations, and 36 (31%) with heterozygous mutations. When we compared these three groups according to the three

### Table 1 The Tel-Hashomer, Pediatric, and Eurofever/PRINTO criteria

| Major criteria | Pediatric criteria (≥ 2 criteria) | Eurofever/PRINTO clinical-only criteria (≥ 6 criteria) | Eurofever/PRINTO clinical + genetic criteria |
|----------------|----------------------------------|-----------------------------------------------------|-----------------------------------------------|
| 1. Recurrent febrile episodes with serositis (peritonitis, synovitis, and pleuritis) | 1. Fever (axillary temperature of ≥ 38 °C, 6–72 h, ≥ 3 attacks) | 1. Eastern Mediterranean ethnicity | 1. Episodes lasting 1–3 days |
| 2. Amyloidosis of AA type without a predisposing disease | 2. Abdominal pain (6–72 h duration, ≥ 3 attacks) | 2. Episodes lasting 1–3 days | 2. Arthritis |
| 3. Favorable response to colchicine treatment | 3. Chest pain (6–2 h duration, ≥ 3 attacks) | 3. Arthritis | 3. Chest pain |
| Minor criteria | 4. Arthritis (6–72 h duration, ≥ 3 attacks, oligoarthritis) | 4. Chest pain | 4. Abdominal pain |
| 1. Recurrent febrile episodes | 5. Family history of FMF | 5. Abdominal pain | OR |
| 2. FMF in a first-degree relative | | Absence of | |
| 3. Erysipelas-like erythema | | | |
| **Pathogenic or likely pathogenic variants (homozygous or in trans (or biallelic) compound heterozygous)** | 1. Aphthous stomatitis | 1. Episodes lasting 1–3 days | |
| **In trans compound heterozygous for one pathogenic MEFV variants and one variant of uncertain significance (VUS), or biallelic VUS, or heterozygous for one pathogenic MEFV variant** | 2. Urticarial rash | 2. Arthritis | |
| | 3. Maculopapular rash | 3. Chest pain | |
| | 4. Painful lymph nodes | 4. Abdominal pain | |
diagnostic criteria (pediatric, Tel-Hashomer, and Eurofever/PRINTO), the Tel-Hashomer criteria \( (p = 0.48) \) and pediatric criteria \( (p = 0.77) \) had similar sensitivity values, whereas the Eurofever/PRINTO criteria showed a statistically significant difference \( (p = 0.039) \) (Table 3). The Eurofever/PRINTO criteria showed a significant higher sensitivity for patients with homozygous mutations than heterozygous group \( (p = 0.037) \).

The sensitivity, specificity, PPV, NPV, PLR, and NLR of the Tel-Hashomer criteria were 70\% (95\% CI: 61–78), 96\% (95\% CI: 90–99), 94\% (95\% CI: 87–97), 77\% (95\% CI: 71–81), 16\% (95\% CI: 6.8–39), and 0.3\% (95\% CI: 0.2–0.4), respectively. The sensitivity of the pediatric criteria using at least two criteria was 89\% (95\% CI: 81–94), and its specificity was 85\% (95\% CI: 77–91). The Eurofever/PRINTO criteria displayed high sensitivity (94\%, 95\% CI: 88–97) and specificity (91\%, 95\% CI: 84–95) (Table 4). The positive predictive value (PPV) and negative predictive value (NPV) were similar between the pediatric criteria (85\% (95\% CI: 78–90), 88\% (95\% CI: 82–93)) and Eurofever/PRINTO criteria (91\% (95\% CI: 85–94), 94\% (95\% CI: 88–97)) in our series. The Tel-Hashomer criteria exhibited the highest PLR, and the Eurofever/PRINTO criteria had the lowest NLR.

**Discussion**

The diagnosis of FMF is established based on clinical findings and is supported by genetic testing. To date, several sets of criteria have been established for the diagnosis of FMF, with the Tel-Hashomer criteria being the most commonly used [6]. Although the Tel-Hashomer criteria were determined for adults, they are also successfully applied for the diagnosis of pediatric patients. Nevertheless, difficulty in expressing the severity and location of pain and determining the level of fever (axillary, rectal, etc.) complicates the use of Tel-Hashomer criteria for children, and identifying simpler

| Table 2 | Demographic features of our study group |
|-----------------------------------------|----------------------------------------|
| Male/female                             | FMF group (n: 113)                     |
|                                         | Control group (n: 117)                 |
|                                         | p value\(^{1}\)                        |
| Current age, mean ± SD, years            | 13.9 ± 5.3                             | 12.9 ± 4.5                   | 0.33  |
| Age at onset, mean ± SD, years           | 6.8 ± 4.6                              | 7.1 ± 4.1                   | 0.17  |
| Age at diagnosis mean ± SD, years        | 8.6 ± 4.6                              | 8.5 ± 3.8                   | 0.25  |
| Consanguinity, n (\%)                   | 29 (26\%)                             | 24 (20\%)                   | 0.35  |
| Fever, n (\%)                           | 79 (70\%)                             | 45 (38\%)                   | 0.002 |
| Abdominal pain, n (\%)                  | 88 (78\%)                             | 30 (26\%)                   | <0.001|
| Chest pain, n (\%)                      | 32 (28\%)                             | 7 (5.6\%)                   | <0.001|
| Arthritis, n (\%)                       | 40 (35\%)                             | 27 (23\%)                   | 0.04  |
| Family history of FMF, n (\%)           | 57 (50.\%)                            | 24 (20%)                    | <0.001|
| ESR↑ (attack), n (\%)                   | 102 (90\%)                            | 28 (24\%)                   | <0.001|
| CRP↑ (attack), n (\%)                   | 101 (89)                              | 31 (27\%)                   | <0.001|
| Proteinuria, n (\%)                     | 12 (11\%)                             | 1 (0.8\%)                   | 0.02  |
| Vomiting, n (\%)                        | 6 (5.3\%)                             | 17 (14\%)                   | 0.12  |
| Splenomegaly, n (\%)                    | 9 (8\%)                               | 0 (0\%)                     | 0.002 |
| Myalgia, n (\%)                         | 20 (18\%)                             | 13 (11\%)                   | 0.15  |

\(^{1}\) indicates increased, ESR erythrocyte sedimentation rate, CRP C-reactive protein

| Table 3 | Sensitivity of the pediatric criteria compared with the Tel-Hashomer and Eurofever/PRINTO criteria in homozygous, compound heterozygous and heterozygous patients |
|---------|-------------------------------------------------------------------------------------------------|
|         | Homozygous (n = 31) (%) | Compound heterozygous (n = 46) (%) | Heterozygous (n = 36) (%) | p value |
| ≥ 2 pediatric criteria                  | 27 (87\%)                   | 40 (87\%)                   | 33 (92\%)                   | 0.77     |
| ≥ 3 pediatric criteria                  | 20 (64\%)                   | 21 (46\%)                   | 16 (44\%)                   | 0.18     |
| Tel-Hashomer criteria                    | 25 (81\%)                   | 31 (67\%)                   | 23 (64\%)                   | 0.48     |
| Eurofever/PRINTO clinical + genetic criteria | 31 (100\%)                 | 40 (87\%)                   | 35 (97\%)                   | 0.039 (p1 = 0.69, p2 = 0.037, p3 = 0.2) |

p1: homozygous patients versus compound heterozygous patients, p2: homozygous patients versus heterozygous patients, p3: compound heterozygous patients versus heterozygous patients
and more practical diagnostic methods specific for children is necessary. The value and benefit of the Tel-Hashomer criteria for children have been investigated in recent studies, and some new pediatric diagnostic sets of criteria have been described [3, 8, 11–13].

The pediatric criteria for FMF diagnosis were established by Yalçinkaya et al. [8] in a 2009 study including Turkish pediatric patients. In that study, five diagnostic criteria were defined as recurrent fever, abdominal pain, arthritis, chest pain, and a family history of FMF. Their control group consisted of consecutive patients without FMF who had clinical features mimicking that of FMF, similar to our study. The authors compared their results to those of the Tel-Hashomer criteria and determined a sensitivity and specificity of diagnosis of 89% and 93% for patients meeting at least two of their five criteria (Table 5). However, they stated that the results should be validated in different ethnic groups and populations. Compared to Yalçinkaya et al. [8], our study revealed similar sensitivity (89%) but lower specificity (85%).

We found that using at least two of the pediatric criteria had 89% sensitivity and 85% specificity, which is consistent with the results of Yalçinkaya et al. [8]. In contrast, we determined the specificity, PPV, and PLR of the Tel-Hashomer criteria to be higher than those of the pediatric and Eurofever/PRINTO criteria. The major limitation of the Tel-Hashomer criteria was its low sensitivity, NPV, and NLR. Therefore, using pediatric criteria instead of the Tel-Hashomer criteria may be simpler and more useful when diagnosing pediatric FMF patients.

There were three previous attempts to validate the pediatric criteria. Kondi et al. [11] evaluated 70% Sephardic Jews in an FMF group of patients in 2010, but they determined that pediatric criteria did not further benefit FMF diagnosis compared to Tel-Hashomer criteria and suggested that the use of at least three of the Turkish pediatric criteria increased sensitivity to 77% and specificity to 95% (Table 5). Demirkaya et al. [3] analyzed the largest number of pediatric patients with periodic fever and with various geographical and ethnic distributions in 2015, showing that pediatric criteria can be evaluated for diagnosis of FMF with higher sensitivity (87%) but lower specificity (41%) but that Tel-Hashomer criteria show lower sensitivity (45%) and higher specificity (97%). Sag et al. [12] also evaluated pediatric criteria and found higher sensitivity (93%) and lower specificity (84%), whereas Tel-Hashomer criteria had lower sensitivity (89%) but higher specificity (93%) (Table 5).

In our study, the presence of at least two of the pediatric criteria was related to higher sensitivity (89%) than for Tel-Hashomer criteria (70%), confirming the findings of Yalçinkaya et al. [8].

### Table 4  
Sensitivity, specificity, PPV, NPV of the pediatric criteria compared with the Tel-Hashomer and Eurofever/PRINTO criteria

| Criteria                        | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) | PLR (95% CI) | NLR (95% CI) |
|---------------------------------|----------------------|----------------------|--------------|--------------|--------------|--------------|
| ≥ 2 pediatric criteria         | 89 (81–94)           | 85 (77–91)           | 85 (78–90)   | 88.39 (82–93) | 5.8 (3.7–8.8) | 0.1 (0.1–0.2) |
| ≥ 3 pediatric criteria         | 50 (41–60)           | 100 (97–100)         | 100          | 67.6 (63–72)  | –            | 0.5 (0.4–0.6) |
| ≥ 4 pediatric criteria         | 19 (12–27)           | 100 (97–100)         | 100          | 56 (54–58)    | –            | 0.8 (0.8–0.9) |
| All pediatric criteria         | 4.4 (1.4–10)         | 100 (97–100)         | 100          | 56.1 (51–53)  | –            | 1 (0.9–1)     |
| Tel-Hashomer criteria          | 70 (61–78)           | 96 (90–99)           | 94. (87–97)  | 77 (71–81)    | 16 (6.8–39)  | 0.3 (0.2–0.4) |
| Eurofever/PRINTO clinical + genetic criteria | 94 (88–97) | 90 (84–95) | 91 (85–94) | 94 (88–97) | 9.2 (5.3–16) | 0.1 (0–0.1) |

CI confidence interval, PPV positive predictive value, NPV negative predictive value, PLR positive likelihood ratio, NLR negative likelihood ratio.

### Table 5  
Sensitivity, specificity, PPV, NPV of the pediatric, and Tel-Hashomer and Eurofever/PRINTO criteria in different case series

| Criteria                        | Sensitivity | Specificity | PPV  | NPV  |
|---------------------------------|-------------|-------------|------|------|
| Our series                      |             |             |      |      |
| ≥ 2 pediatric criteria         | 89          | 85          | 85   | 88   |
| ≥ 3 pediatric criteria         | 50          | 100         | 100  | 68   |
| Tel-Hashomer criteria          | 70          | 96          | 94   | 77   |
| Eurofever/PRINTO criteria (clinical + genetic) | 94          | 90          | 91   | 94   |
| Yalçinkaya et al. [8]           |             |             |      |      |
| ≥ 2 pediatric criteria         | 87          | 94          | 94   | 85   |
| ≥ 3 pediatric criteria         | 55          | 99          |      |      |
| Tel-Hashomer criteria          | 99          | 55          | 72   | 98   |
| Kondi et al. [11]              |             |             |      |      |
| ≥ 2 pediatric criteria         | 100         | 50          | 83   | 100  |
| ≥ 3 pediatric criteria         | 77          | 95          | 98   | 62   |
| Tel-Hashomer criteria          | 99          | 45          | 82   | 95   |
| Demirkaya et al. [3]           |             |             |      |      |
| ≥ 2 pediatric criteria         | 87          | 41          | 61   | 75   |
| Tel-Hashomer criteria          | 45          | 97          | 94   | 65   |
| Eurofever/PRINTO criteria      | 94          | 95          |      |      |
| Sag et al. [12]                |             |             |      |      |
| ≥ 2 pediatric criteria         | 93          | 84          |      |      |
| Tel-Hashomer criteria          | 89          | 93          |      |      |
| Eurofever/PRINTO criteria      | 96          | 73          |      |      |

PPV positive predictive value, NPV negative predictive value.
of Yalçinkaya et al. [8] (87%), Demirkaya et al. [3] (87%), and Sag et al. [12] (93%) but lower sensitivity than Kondi et al. (100%). Contrary to the study of Kondi et al. [11], our study group consisted of Turkish patients with a homogeneous ethnic and geographical origin. According to the 2005 Turkish FMF study group, 7.5% of FMF patients presented without fever, and this rate was higher than that reported for Jews, Arabs, and Armenians [14]. The rates of a family history of FMF (20%) and consanguinity (20%) were high in our control group. Although the frequency of FMF in the Turkish population is high, the sensitivity of pediatric criteria has been reported to be higher in other countries where FMF is rarely seen [11]. Kondi et al. [11], Demirkaya et al. [3], and Sag et al. [12] formed their control groups with patients exhibiting with periodic fever syndromes or autoinflammatory disease. In contrast, as a novelty of our study, our control group was not limited to patients with periodic fever syndromes and autoinflammatory disease, and it represented a wide and heterogeneous population with a broad range of symptoms mimicking FMF, such as recurrent abdominal pain, fever, joint pain, and chest pain. Despite a few similar studies, some controversies remain regarding diagnostic criteria, and validation of diagnostic criteria in different groups will contribute to the literature.

We also evaluated the new Eurofever/PRINTO classification criteria in our FMF group and found them to be sensitive and specific for the classification of FMF (Tables 3 and 4). Overall, research suggests that classification criteria simplify the identification of disease in clinical, epidemiological, and translational studies but cannot be used for routine diagnostic purposes in individual patients [9, 15]. Tanatar et al. found lower performance of the Tel-Hashomer (77%), pediatric criteria (89%), and Eurofever/PRINTO criteria (80%) in diagnosing and classifying heterozygous FMF patients [13]. We observed higher sensitivity for Eurofever/PRINTO (97%), Tel-Hashomer (64%), and pediatric (92%) criteria in distinguishing heterozygous patients, which may be due to our small sample size. Sag et al. [12] also compared Tel-Hashomer, pediatric, and Eurofever/PRINTO criteria and found that the Eurofever/PRINTO criteria had the highest sensitivity for patients with biallelic mutations (100%). We also evaluated whether the Eurofever/PRINTO criteria have the highest sensitivity in homozygous patients (100%).

The main limitation of our study is its monocentric retrospective nature with a small sample size. In addition, all patients were of Turkish origin. Therefore, further multicenter studies with large sample sizes and different ethnic groups are warranted.

Our results confirm that the Eurofever/PRINTO classification criteria can be successfully used for the diagnosis of FMF due to their high sensitivity and specificity, as also suggested by the authors who developed this tool. In our evaluation of the pediatric criteria, we determined the presence of at least two of these criteria to be adequate for a diagnosis of FMF in children. Thus, our study supports the use of both pediatric criteria and Eurofever/PRINTO criteria in clinical practice.

Authors’ contributions The lead author is Esra Nagehan Akyol Onder. Author Esra Nagehan Akyol Onder contributed to researching data for the article; the authors Esra Nagehan Akyol Onder and Esra Baskın contributed to discussion of its content, writing, and reviewing; and authors Kudret Ebru Ozcan and Kaan Savas Gulleroglu contributed to editing of the manuscript before submission. Author Peride Iffet Sahin performed the genetic analyses of the patients.

Availability of data and material Data are available on request from the authors.

Code availability N/A.

Declarations

Ethics approval Local ethics committee approval was obtained.

Consent to participate Written consent was obtained from all participants to participate in the study.

Consent for publication Written consent was obtained from all participants for publication of the study.

Conflict of interest The authors declare no competing interests.

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