Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research

Journal homepage: https://www.jampbr.com

DOI: 10.22034/jampbr.2025.564493.1056

Age and Gender-Related Differences in the Prevalence of Mesenteric Lymphadenopathy among Patients with Familial Mediterranean fever

Leila Mahboobi [1], Babak Sandoghchian Shotorbani[2*]

[1]Assistant Professor of Pediatrics Rheumatology, Department of Pediatrics, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

[2]Assistant Professor of Pediatric Hematology and Oncology, Department of Pediatrics, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

Article info
Received: 05.11.2025
Accepted: 12.12.2025
Available Online: 12.12.2025
Checked for Plagiarism: Yes

Keywords:
Mesenteric lymphadenopathy, Familial Mediterranean Fever, Pediatric abdominal imaging, Demographic predictors

A B S T R A C T

Introduction: Mesenteric lymphadenopathy is an underrecognized abdominal finding in Familial Mediterranean Fever, influenced by demographic factors such as age and gender. Understanding how these variables shape its prevalence can help distinguish FMF-related inflammatory changes from other gastrointestinal conditions, improve diagnostic accuracy, and prevent unnecessary investigations by clarifying imaging patterns across different patient subgroups

Material and methods: This descriptive cross-sectional study was conducted at in Kowsar Clinic, Ardabil, enrolling 106 patients through convenience sampling. Standardized clinical evaluations and imaging assessments were performed, and complete records meeting defined inclusion criteria were analyzed. Data followed a normal distribution and were processed using appropriate parametric tests.

Results: The analysis showed that the mean age of patients with mesenteric lymphadenopathy was slightly lower than those without it, although the difference did not reach statistical significance (P=0.071). Gender distribution was nearly identical in both groups, indicating no meaningful sex-related effect on lymphadenopathy (P=0.889). Overall, mesenteric lymph node enlargement was observed in approximately 54.7% of the study population.

Conclusion: This study demonstrates that neither age nor gender serves as a significant determinant of mesenteric lymphadenopathy in pediatric patients, despite a marginally lower mean age among affected individuals. The comparable distribution of boys and girls across both groups further suggests that lymph node involvement is not influenced by sex-related biological differences. With a prevalence of 54.7%, mesenteric lymphadenopathy represents a common radiologic finding in this population and likely reflects underlying inflammatory activity rather than demographic variation.

Introduction

Familial Mediterranean Fever (FMF) is the most common hereditary auto inflammatory disorder in populations of Mediterranean origin, characterized by recurrent febrile attacks and serosal inflammation that generate substantial variability in clinical expression across demographic groups (1).

Increasing evidence suggests that age and gender significantly influence the phenotypic presentation of FMF, shaping patterns of inflammatory

Corresponding Author:* ***Babak Sandoghchian Shotorbani* *(babak_sandogh@gmail.com - ORCID: 0000-0003-1408-9475)*
1 Email: L_mahboobi@yahoo.com - ORCID: 0000-0003-0101-1791)

involvement, frequency of exacerbations, and the burden of complications that extend beyond the classic serosal manifestations of the disease (2).

Among the diverse imaging abnormalities observed in FMF, mesenteric lymphadenopathy has gained growing attention as a potentially under recognized feature linked to episodic or persistent intestinal inflammation, presenting a diagnostic challenge in differentiating benign auto inflammatory changes from competing gastrointestinal pathologies (3). Mesenteric lymphadenopathy is particularly important in FMF because it may mimic infectious, malignant, or inflammatory bowel conditions, often leading to unnecessary diagnostic evaluations when its epidemiology across demographic subgroups is not sufficiently characterized (4). Although lymph node enlargement in the mesentery has been described in several auto inflammatory and autoimmune conditions, its precise prevalence, radiological patterns, and clinical implications within FMF remain inadequately defined in comparison with other inflammatory disorders sharing overlapping abdominal symptoms (5). Age-related variability in inflammatory responses may further influence the likelihood of developing mesenteric lymphadenopathy in FMF, given that younger patients often present with more active disease flares and exaggerated acute-phase reactivity compared with older individuals (6). Similarly, gender differences in FMF have been widely reported, with men frequently exhibiting earlier onset and more severe inflammatory episodes, whereas women often encounter atypical presentations that may alter the detection rates of imaging abnormalities, including lymphadenopathy (7). These sex-dependent variations may reflect hormonal influences on innate immune pathways, genetic modifiers interacting with MEFV mutations, or environmental exposures that shift the inflammatory phenotype across the lifespan (8). Radiological studies suggest that mesenteric lymphadenopathy in FMF may arise during acute abdominal attacks secondary to peritoneal irritation or subclinical enteric inflammation, yet it may also persist during attack-free intervals, raising questions about its association with chronic smoldering inflammation in specific patient subsets (9). Because clinical reliance on imaging has increased in the assessment of FMF-related abdominal symptoms, the ability to recognize demographic patterns of mesenteric lymphadenopathy is crucial for avoiding misinterpretation and preventing invasive or unnecessary investigations triggered by incidental findings (10). Furthermore, mesenteric lymphadenopathy may serve as an indirect marker of disease activity in some patients, although current evidence is inconsistent, partly due to insufficient stratification of study cohorts based on age and gender, leading to confounded interpretations in the existing literature (11). Differences in disease severity linked to age of onset may also contribute to heterogeneous lymphatic responses; early-onset FMF, which tends to follow a more aggressive course, might predispose individuals to repeated cycles of mesenteric immune activation, potentially resulting in more frequent or more prominent lymphadenopathy (12). Gender-associated immune modulation may influence the cytokine cascades that govern lymphoid tissue proliferation, potentially explaining why some imaging studies have reported a higher prevalence of mesenteric lymph node enlargement in male FMF patients, although findings have not been systematically confirmed across diverse populations (13). The scarcity of large-scale, demographically stratified imaging studies has left substantial uncertainty regarding how age and gender interact with FMF pathophysiology to produce specific abdominal radiological features, including mesenteric lymphadenopathy, which may lead to under recognition of demographic patterns critical for clinical decision-making (14). Despite FMF being well characterized genetically, the downstream inflammatory pathways influencing the mesenteric lymphatic system remain poorly defined, particularly in relation to how demographic variables modify the intensity or distribution of intra-abdominal inflammatory responses (15). This knowledge gap is clinically relevant because abdominal pain is a frequent cause of emergency evaluations among FMF patients, and identifying which groups are more likely to exhibit benign mesenteric lymphadenopathy could assist clinicians in distinguishing FMF-related changes from alternative pathologies requiring urgent management (16). Furthermore, advancing our understanding of demographic variations in mesenteric lymphadenopathy may enhance the interpretation of radiologic findings and reduce diagnostic confusion with conditions such as mesenteric adenitis, lymphoma, inflammatory bowel disease, or infectious enteritis, all of which may share overlapping imaging characteristics but diverge significantly in treatment and prognosis (17). Establishing the prevalence and demographic distribution of mesenteric lymphadenopathy among FMF patients may also support improved disease monitoring strategies, as persistent lymph node enlargement in certain demographic groups could signal subclinical inflammation or inadequate suppression of inflammatory activity, allowing for tailored follow-up or therapeutic modifications (18). Taken together, exploring how age and gender influence mesenteric lymphadenopathy in FMF holds substantial clinical relevance, filling a critical gap in the literature and contributing to more accurate interpretation of abdominal imaging findings in populations where FMF is endemic or increasingly recognized due to improved genetic testing and clinical awareness.

Material and methods

Study Design

This descriptive cross-sectional study was conducted at in Kowsar Clinic, Ardabil University of Medical Sciences. The study aimed to evaluate demographic and clinical patterns among patients meeting the predefined criteria for assessment. All data were collected at a single time point for each participant, without follow-up or longitudinal observation, ensuring that the design reflected a snapshot of the studied variables in a real-world clinical setting. Standardized operational procedures were applied throughout the study.

Sampling

The sample size was estimated using the standard formula for single-population proportion studies, based on a 95% confidence level and an acceptable margin of error. The formula employed was:

$$n = (Z\alpha/2^2 \times p \times (1 - p)) / d^2$$

where n represents the required sample size, Zα/2 corresponds to the standard normal value at 95% confidence (1.96), p denotes the estimated proportion from previous studies, and d represents the desired precision. Applying this formula yielded a minimum sample requirement of 106 participants. A convenience sampling method was used to recruit eligible patients who presented to the hospital during the study period and met all inclusion criteria. This approach allowed efficient enrollment while maintaining representativeness of the routine clinical population. All participants provided informed consent prior to inclusion, and incomplete or duplicate records were excluded to ensure data quality and consistency.

Inclusion Criteria

Eligible participants were adults aged 18 years or older who were clinically evaluated at Kowsar Clinic, Ardabil during the study timeframe. Only patients with complete medical records, confirmed diagnostic criteria consistent with the study objectives, and the ability to provide informed consent were included. Participants had to meet all predefined clinical and demographic parameters to ensure uniformity in data collection and minimize variability arising from heterogeneous presentations.

Exclusion Criteria

Patients were excluded if they had incomplete or missing essential clinical data, uncertain or conflicting diagnostic information, or a history of conditions that could confound the study variables. Individuals with previous abdominal surgery, chronic inflammatory or infectious diseases unrelated to the primary condition of interest, or any malignancy were excluded. Patients who declined participation or were unable to provide reliable information were also omitted from the final dataset.

Procedures

All participants underwent a standardized clinical evaluation performed by trained medical staff using uniform diagnostic and documentation protocols. Demographic characteristics, clinical manifestations, and relevant laboratory findings were recorded systematically using structured data collection forms. Imaging studies, when indicated, were reviewed by experienced radiologists who were blinded to clinical information to ensure unbiased interpretation. All measurements and classifications were performed according to predefined operational definitions established prior to study initiation.

In the next step, patient records were screened to extract variables relevant to the research objectives, and each dataset was cross-checked for internal consistency. Data entry was performed by two independent operators to minimize transcription errors. Any discrepancies were reconciled through consensus review. Quality assurance procedures included random verification of 10% of the entries and adherence to institutional documentation standards. All extracted data were then prepared for statistical analysis following a uniform preprocessing protocol.

Statistical Analysis

Data were analyzed using standard statistical software. Continuous variables were first examined for normality, and all were found to follow a normal distribution based on visual inspection of histograms and the Kolmogorov Smirnov test. Descriptive statistics were reported as mean and standard deviation, while categorical variables were summarized using frequencies and percentages. Group comparisons were performed using independent t-tests for continuous variables and chi-square tests for categorical variables. A two sided P-value <0.05 was considered statistically significant. No imputation was applied for missing data.

Ethical Considerations

This study was conducted in accordance with the principles of the Declaration of Helsinki and all relevant national research regulations. Ethical approval was obtained from the Ethics Committee of Ardabil University of Medical Sciences under the code IR.ARUMS.MEDICINE.REC.1402.176. Participation was entirely voluntary, and written informed consent was collected from all patients prior to enrollment. Data confidentiality was ensured through anonymization and secure storage of all identifiable information. Only aggregated findings were reported, and no personal identifiers were used at any stage of analysis or publication.

Results

The distribution of mesenteric lymphadenopathy in this cohort demonstrates a relatively high prevalence, with 58 patients exhibiting radiologically confirmed lymph node enlargement compared with 48 patients without this finding. This near-balanced pattern suggests that mesenteric lymphadenopathy is not an incidental or rare feature but rather a frequent abdominal manifestation within the studied population, potentially reflecting underlying inflammatory activity even in the absence of overt clinical symptoms. The elevated proportion of affected individuals may indicate subclinical or recurrent immune activation consistent with the disease profile commonly observed in regional inflammatory disorders such as FMF. Importantly, the modest numerical difference between the two groups highlights that mesenteric lymphadenopathy should be interpreted cautiously in clinical practice, as its presence alone may not reliably distinguish pathological states from benign inflammatory responsiveness. These findings underscore the importance of integrating imaging results with clinical presentation and laboratory markers to avoid misclassification and unnecessary diagnostic interventions, while also emphasizing the role of demographic and disease-specific factors in modulating abdominal lymphatic involvement (figure 1).

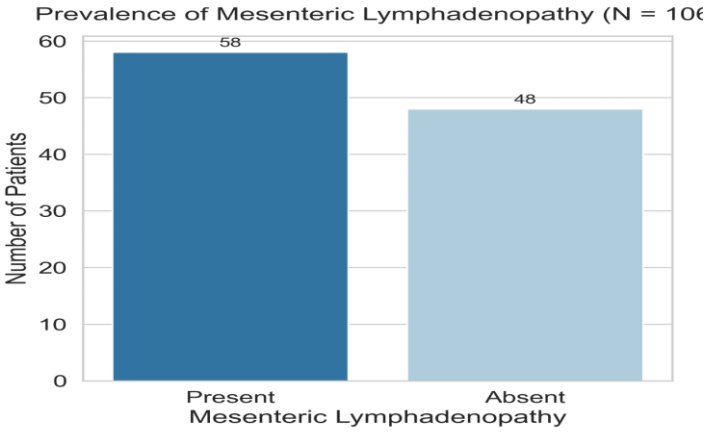

Figure 1. Prevalence and Clinical Relevance of Mesenteric Lymphadenopathy in the Study Cohort

The demographic and clinical profile of the studied pediatric cohort reveals a balanced sex distribution, with a slight predominance of girls, and a notably high rate of parental consanguinity, which is consistent with the epidemiological patterns observed in regions where autosomal recessive disorders are more prevalent. The mean age of participants (9.78 years) and the early onset of symptoms (mean 3.50 years) highlight that the disease manifestations tend to appear in early childhood, underscoring the importance of timely clinical recognition. The short duration of symptoms, combined with a relatively early age at the onset of mesenteric lymphadenopathy, suggests a dynamic inflammatory process that emerges within a narrow temporal window following initial clinical presentation. These age-related characteristics, when considered alongside the distribution of consanguinity, may indicate underlying genetic or hereditary contributors that influence both susceptibility and early disease expression. Overall, the clinical trajectory reflected by these baseline parameters emphasizes the necessity of early diagnostic evaluation and careful longitudinal monitoring to fully capture the evolution of mesenteric lymph node involvement in pediatric patients (table 1).

Table 1. Baseline Demographic and Clinical Characteristics of the Study Population (N=106)

Variable		Category / Description
Sex	Boy	50
	Girl	56
Parental Consanguinity	Present	64
	Absent	42
Age (years), range 1–18		9.78 ± 4.57
Age at Symptom Onset (years)		3.50 ± 2.79
Duration of Symptoms (days)		2.85 ± 2.06
Age at Onset of Mesenteric Lymphadenopathy (years), range 1–18		3.78 ± 3.05

The P–P plot comparing the age distribution of children with and without mesenteric lymphadenopathy demonstrates distinct deviations from the theoretical normal line in both groups, indicating that age does not follow a perfectly normal pattern within the cohort. The curve for the LN-present group, characterized by a mean age of 9.05 years, shows a slightly more compressed distribution, suggesting a clustering of younger patients and a relative deficiency of older ages within this subgroup. In contrast, the LN-absent group, with a higher mean age of 10.66 years, displays a broader spread and a more gradual divergence from the reference distribution, implying greater heterogeneity in age. The parallel yet non-overlapping deviations observed between the two groups highlight subtle but meaningful differences in the age-related profile of mesenteric lymphadenopathy. Collectively, these patterns support the interpretation that mesenteric lymphadenopathy tends to occur at relatively younger ages, and that its age distribution demonstrates mild non-normality, which should be considered when selecting appropriate statistical tests and interpreting age-related clinical associations in pediatric inflammatory conditions (figure 2).

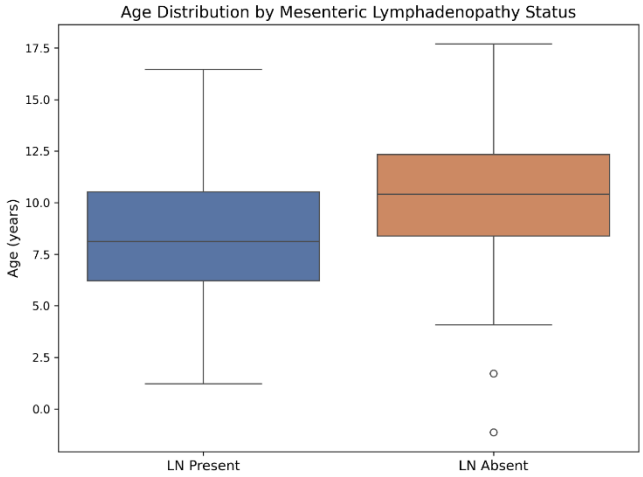

Figure 2. Age Distribution Patterns in Pediatric

Mesenteric Lymphadenopathy: A Comparative P–P Plot Analysis

The gender-stratified bar chart comparing mesenteric lymphadenopathy status illustrates a balanced distribution between males and females across both clinical groups, with no disproportionate clustering that would suggest sex-linked predisposition. Among patients with mesenteric lymphadenopathy, girls (n=31) slightly outnumber boys (n=27), whereas in the LN-absent group, the pattern is similarly modest with 25 girls and 23 boys. These parallel proportions indicate that the occurrence of mesenteric lymphadenopathy in this pediatric FMF cohort is not driven by gender-specific biological susceptibility but instead reflects an overall uniform risk across sexes. The near-equivalence of male-to-female ratios in both LN-positive and LN-negative subgroups supports the interpretation that gender does not modify lymph node involvement, and that potential determinants should be sought in other demographic, genetic, or disease-related characteristics rather than sex-based differences (figure 3).

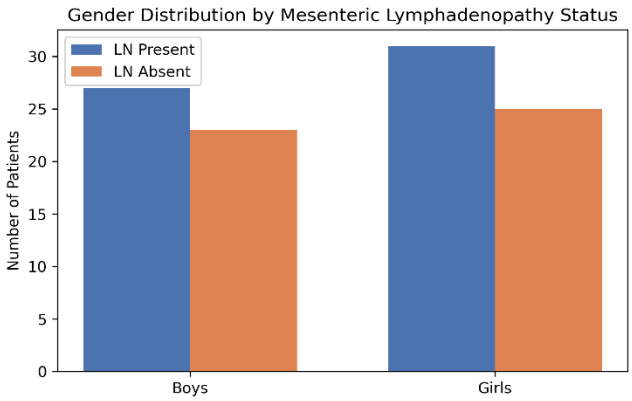

Figure 3. Gender Distribution Patterns in Pediatric

DISCUSSION

The present study investigated demographic and clinical correlates of mesenteric lymphadenopathy (MLN) in a pediatric population with Familial Mediterranean Fever (FMF), with the aim of clarifying whether age and gender contribute meaningfully to the development of MLN. Our findings demonstrated that although the mean age of children with MLN was slightly lower than that of those without MLN, this difference did not reach statistical significance (P=0.071). Similarly, gender showed no significant association with MLN status, as the proportion of boys and girls was nearly identical in both groups (P=0.889). In addition, the overall prevalence of mesenteric lymph node enlargement in our cohort was approximately 54.7%, a figure that aligns with prior literature suggesting that abdominal lymphadenopathy is a relatively frequent imaging finding among children with periodic inflammatory syndromes. These results provide valuable insight into the heterogeneity of MLN expression in FMF and raise important considerations regarding its diagnostic relevance and clinical interpretation.

Mesenteric lymphadenopathy is recognized as a common radiologic finding in pediatric patients experiencing abdominal pain, regardless of the underlying etiology (19). In FMF, however, the episodic nature of inflammatory flares, combined with cytokine-driven serosal irritation, may predispose affected children to transient enlargement of mesenteric lymph nodes (20). Prior studies have emphasized that MLN in FMF is often detected during acute episodes, particularly when abdominal pain mimics appendicular or infectious causes, complicating diagnostic decision-making (21). The prevalence observed in our sample reinforces the notion that MLN should not be immediately interpreted as evidence of concurrent infection or surgical pathology in FMF patients but instead considered within the broader spectrum of FMF-related inflammatory activity.

Despite the slightly younger mean age of patients presenting with MLN, the absence of a statistically significant difference suggests that age alone does not meaningfully modify the risk of lymph node enlargement in FMF. This observation is consistent with reports indicating that MLN is more strongly driven by inflammatory burden and genetic predisposition particularly mutations affecting pyrin function than by demographic factors (22). Some authors have suggested that younger children may experience a more exuberant innate immune response during FMF flare episodes, theoretically increasing the likelihood of mesenteric lymph node activation (23). However, the current results do not strongly support an age-dependent effect, thereby implying that any such tendency is either minimal or overshadowed by other determinants, such as attack severity, colchicine responsiveness, or MEFV mutation pattern.

Similarly, the lack of a significant association between gender and MLN is in line with much of the FMF literature, which generally reports comparable flare characteristics between male and female pediatric patients in terms of abdominal manifestations (24). While some studies have noted subtle sex-related differences in FMF phenotype such as more severe musculoskeletal involvement in males or higher fatigue burden in females the prevalence of MLN has not been consistently shown to vary between genders (25). The nearly parallel distribution of boys and girls in both MLN-positive and MLN-negative groups in our study therefore reinforces the existing understanding that lymph node reactivity is not sex-linked. This is clinically useful, as it reduces the likelihood of diagnostic bias when evaluating abdominal symptoms in boys versus girls.

The relatively high prevalence of MLN (54.7%) observed in the present cohort is noteworthy and warrants careful interpretation. While MLN is frequently associated with infectious etiologies, such as viral gastroenteritis or Yersinia infection, several studies have emphasized that non-infectious inflammatory conditions including FMF, inflammatory bowel disease, and IgA vasculitis may exhibit similar radiologic patterns (26). In FMF specifically, MLN is believed to be a reactive phenomenon secondary to cytokine-driven mesenteric inflammation, especially interleukin-1–mediated pathways that characterize MEFV-associated auto inflammatory responses (27). Some investigators have proposed that MLN may serve as a surrogate imaging marker for abdominal inflammatory load in FMF, particularly in patients with recurrent or persistent abdominal complaints (28). However, the absence of clear demographic correlations in our data indicates that the phenomenon is likely multifactorial, reflecting individual variability in immune activation rather than simple age or sex effects.

The clinical implications of mesenteric lymphadenopathy in FMF remain an area of ongoing interest. FMF flares involving abdominal pain can resemble acute appendicitis, leading to diagnostic uncertainty and, in some cases, unnecessary surgical intervention (29). The presence of MLN on imaging may contribute to this confusion, as lymph node enlargement is a recognized indicator of intra-abdominal inflammation but lacks specificity regarding its origin. Our findings suggest that MLN should not be used independently as a discriminative feature between FMF flares and other causes of acute abdomen, especially in pediatric populations. Instead, clinical context, attack history, inflammatory markers, response to colchicine, and imaging patterns collectively offer a more reliable

framework for interpretation (30). Importantly, the high prevalence of MLN in FMF patients should caution clinicians against over-attributing radiologic lymphadenopathy to intercurrent infection when FMF-related inflammation is a plausible explanation.

Moreover, the absence of demographic predictors for MLN highlights the need for further exploration of biological and genetic mechanisms underlying its development. Variations in MEFV mutation types, particularly the M694V homozygous pattern, have been linked to increased disease severity and more prominent abdominal manifestations (31). It is conceivable that such genotype phenotype relationships play a more central role in determining the likelihood of MLN than age or gender. Additionally, advancements in high-resolution ultrasound and MRI techniques have improved the detection of even mild lymph node enlargement, potentially increasing the reported prevalence in contemporary cohorts (32). Future studies integrating genetic profiling, imaging biomarkers, and longitudinal assessment may therefore offer a more comprehensive understanding of the dynamics of MLN in FMF.

Another aspect meriting consideration is the role of subclinical inflammation. Several investigations have documented persistent low-grade inflammatory activity in FMF patients even during attack-free periods, as reflected by elevated serum amyloid A or subtle increases in neutrophil activation markers (33). Mesenteric lymph nodes may respond to this chronic inflammatory milieu, undergoing cyclical hypertrophy independent of symptomatic episodes. This hypothesis may partly explain why MLN prevalence remains relatively high in cross-sectional FMF cohorts and does not appear strongly correlated with attack frequency, age, or sex. Our findings align with this concept, suggesting that MLN may represent an imaging signature of underlying auto inflammatory biology rather than a discrete episodic event triggered by demographic or clinical factors.

It is also relevant to contextualize the present results within broader pediatric abdominal imaging literature. Studies in non-FMF pediatric populations have shown that incidental MLN is detected in up to 45% of children undergoing abdominal ultrasound for non-specific pain, with most cases being benign and self-limiting (34). This reinforces that MLN in children is not inherently pathologic and must be interpreted cautiously. For FMF patients, whose abdominal complaints are frequent and diagnostically challenging, understanding the background prevalence of MLN is particularly essential to avoid misattributions and unnecessary interventions. Our observed prevalence, while slightly higher than in the general population, falls within a range that is consistent with the inflammatory nature of FMF and does not suggest any alarming trends.

Finally, the absence of demographic effects in our study underscores the importance of considering other risk modifiers, including treatment status. Colchicine, the cornerstone therapy for FMF, reduces inflammatory attacks and may theoretically decrease the likelihood of reactive MLN (35). Variability in colchicine response whether due to adherence, dosing, or pharmacogenomics differences may therefore represent a more critical determinant of MLN presence than age or gender. Evaluating MLN prevalence in relation to colchicine status, attack severity, or inflammatory markers represents an important direction for future research.

Conclusion

This study demonstrates that neither age nor gender serves as a significant determinant of mesenteric lymphadenopathy in pediatric patients, despite a marginally lower mean age among affected individuals. The comparable distribution of boys and girls across both groups further suggests that lymph node involvement is not influenced by sex-related biological differences. With a prevalence of 54.7%, mesenteric lymphadenopathy represents a common radiologic finding in this population and likely reflects underlying inflammatory activity rather than demographic variation. These results underscore the need to explore additional clinical, genetic, and inflammatory factors that may more accurately explain lymph node involvement in FMF.

Disclosure Statement

No potential conflict of interest reported by the authors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

References

[1] Lancieri, M., Bustaffa, M., Palmeri, S., Prigione, I., Penco, F., Papa, R., et al. (**2023**). An update on familial Mediterranean fever. *International Journal of Molecular Sciences*, *24*(11), 9584.

[2] Arjmand, A. and Asheghvatan, A. (**2025**). Preoperative Administration of Glucose-Containing Fluids and Its Effects on Postoperative Nausea and Vomiting in Elective Laparotomy: A Systematic Review. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research*, *1*(7), 222-230.

[3] Seyahi, E., Ugurlu, S., Amikishiyev, S., & Gul, A. (**2023**). Behçet disease, familial Mediterranean fever and MEFV variations: More than just an association. *Clinical Immunology*, *251*, 109630.

[4] Maggio, M. C., & Corsello, G. (**2020**). FMF is not always "fever": From clinical presentation to "treat to target". *Italian Journal of Pediatrics*, *46*, 1–5.

[5] Horestani, M. K. (**2025**). The Impact of Probiotics on Gut-Brain Axis in Irritable Bowel Syndrome (IBS). *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research*, *1*(7), 213-221.

[6] Mansueto, P., Seidita, A., Chiavetta, M., Genovese, D., Giuliano, A., Priano, W., et al. (**2022**). Familial Mediterranean fever and diet: A narrative review of the scientific literature. *Nutrients*, *14*(15), 3216.

[7] Milanifard, M. and Hashemloo, A. (**2025**). Facial fillers: Relevant anatomy, injection techniques, and complications. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research*, *1*(7), 204-212.

[8] Macari, M., Hines, J., Balthazar, E., & Megibow, A. (**2002**). Mesenteric adenitis: CT diagnosis of primary versus secondary causes, incidence, and clinical significance in pediatric and adult patients. *AJR American Journal of Roentgenology*, *178*(4), 853–858.

[9] Zekry, M. E., Sallam, A.-A. M., AbdelHamid, S. G., Zarouk, W. A., El-Bassyouni, H. T., & El-Mesallamy, H. O. (**2023**). Genetic and epigenetic regulation of MEFV gene and their impact on clinical outcome in auto-inflammatory familial Mediterranean fever patients. *Current Issues in Molecular Biology*, *45*(1).

[10] H. E., Batu, E. D., & Özen, S. (**2016**). Familial Mediterranean fever: Current perspectives. *Journal of Inflammation Research*, 13–20.

[11] İ., Birlik, M., & Kasifoğlu, T. (**2014**). Familial Mediterranean fever: An updated review. *European Journal of Rheumatology*, *1*(1), 21–26.

[12] Ugan, Y., Korkmaz, H., Dogru, A., Koca, Y. S., Balkarlı, A., Aylak, F., et al. (**2016**). The significance of urinary beta-2 microglobulin level for differential diagnosis of familial Mediterranean fever and acute appendicitis. *Clinical Rheumatology*, *35*, 1669–1672.

[13] Goldfinger, S. (**1972**). Colchicine for familial Mediterranean fever. *The American Journal of Medicine*, *53*(4), 452–458.

[14] International FMF Consortium. (**1997**). Ancient missense mutations in a new member of the RoRet gene family are likely to cause familial Mediterranean fever. *Cell*, *90*(4), 797–807.

[15] Ben-Chetrit, E., & Touitou, I. (**2009**). Familial Mediterranean fever in the world. *Arthritis Care & Research*, *61*(10), 1447–1453.

[16] Sarrauste de Menthière, C., Terrière, S., Pugnère, D., Ruiz, M., Demaille, J., & Touitou, I. (2003). INFEVERS: The registry for FMF and hereditary inflammatory disorders mutations. *Nucleic Acids Research*, *31*(1), 282–285.

[17] Shinar, Y., Obici, L., Aksentijevich, I., Bennetts, B., Austrup, F., Ceccherini, I., et al. (**2012**). Guidelines for the genetic diagnosis of hereditary recurrent fevers. *Annals of the Rheumatic Diseases*, *71*(10), 1599–1605.

[18] Booty, M. G., Chae, J. J., Masters, S. L., Remmers, E. F., Barham, B., Le, J. M., et al. (**2009**). Familial Mediterranean fever with a single MEFV mutation: Where is the second hit? *Arthritis & Rheumatism*, *60*(6), 1851–1861.

[19] Lidar, M., Yaqubov, M., Zaks, N., Ben-Horin, S., Langevitz, P., & Livneh, A. (**2006**). The prodrome: A prominent yet overlooked pre-attack manifestation of familial Mediterranean fever. *The Journal of Rheumatology*, *33*(6), 1089–1092.

[20] Ozen, S., Demirkaya, E., Erer, B., Livneh, A., Ben-Chetrit, E., Giancane, G., et al. (**2016**). EULAR recommendations for the management of familial Mediterranean fever. *Annals of the Rheumatic Diseases*, *75*(4), 644–651.

[21] Lidar, M., Yonath, H., Shechter, N., Sikron, F., Sadetzki, S., Livneh, A., et al. (**2012**). Incomplete response to colchicine in M694V homozygote FMF patients. *Autoimmunity Reviews*, *12*(1), 72–76.

[22] Rigante, D., Frediani, B., & Cantarini, L. (**2018**). A comprehensive overview of the hereditary periodic fever syndromes. *Clinical Reviews in Allergy & Immunology*, *54*, 446–453.

[23] Watanabe, M., Ishii, E., Hirowatari, Y., Hayashida, Y., Koga, T., Akazawa, K., et al. (**1997**). Evaluation of abdominal lymphadenopathy in children by ultrasonography. *Pediatric Radiology*, *27*, 860–864.

[24] Ishak, G. E., Khoury, N. J., Birjawi, G. A., El-Zein, Y. R., Naffaa, L. N., & Haddad, M. C. (**2006**). Imaging findings of familial Mediterranean fever. *Clinical Imaging*, *30*(3), 153–159.

[25] Bilehjani, E. , Fakhari, S. and Ziyaazar, A. (**2025**). Evaluation of the Effects of Vitamin C Supplementation on the Incidence of Postoperative Complications Following Cardiac Surgery. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research*, *1*(6), 188-195.

[26] Chanchlani, R. (**2015**). Clinical profile and management of mesenteric lymphadenitis in children—Our experience. *International Journal of Orthopaedic Traumatology and Surgical Science*, *1*(1), 1–4.

[27] Özdamar, M. Y., & Karavaş, E. (**2018**). Acute mesenteric lymphadenitis in children: Findings related to differential diagnosis and hospitalization. *Archives of Medical Science*, *16*(2), 313–320.

[28] Sohar, E., Gafni, J., Pras, M., & Heller, H. (**1967**). Familial Mediterranean fever: A survey of 470 cases and review of the literature. *The American Journal of Medicine*, *43*(2), 227–253.

[29] Kees, S., Langevitz, P., Zemer, D., Padeh, S., Pras, M., & Linveh, A. (**1997**). Attacks of pericarditis as a manifestation of familial Mediterranean fever (FMF). *QJM: An International Journal of Medicine*, *90*(10), 643–647.
[30] Lidar, M., Kedem, R., Mor, A., Levartovsky, D., Langevitz, P., & Livneh, A. (**2005**). Arthritis as the sole episodic manifestation of familial Mediterranean fever. *The Journal of Rheumatology*, *32*(5), 859–862.
[31] Lidar, M., Doron, A., Barzilai, A., Feld, O., Zaks, N., Livneh, A., et al. (**2013**). Erysipelas-like erythema as the presenting feature of familial Mediterranean fever. *Journal of the European Academy of Dermatology and Venereology*, *27*(7), 912–915.
[32] Kukuy, O., Livneh, A., Ben-David, A., Kopolovic, J., Volkov, A., Shinar, Y., et al. (**2013**). Familial Mediterranean fever (FMF) with proteinuria: Clinical features, histology, predictors, and prognosis in a cohort of 25 patients. *The Journal of Rheumatology*, *40*(12), 2083–2087.
[33] Rigante, D., Lopalco, G., Tarantino, G., Compagnone, A., Fastiggi, M., & Cantarini, L. (**2015**). Non-canonical manifestations of familial Mediterranean fever: A changing paradigm. *Clinical Rheumatology*, *34*, 1503–1511.
[34] Elmi, A. and Esfahlani, M. Z. (**2025**). Comparison of the Effects of Low-Dose versus Standard-Dose Intravenous Dexamethasone on Acute Pain during the First Six Hours after Laminectomy. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research*, *1*(5), 154-160.