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# Subclinical Aggravation of the Entheses in Enthesitis-related Joint Pain and Sacroiliitis related with Familial Mediterranean Fever

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## Abstract

This study investigates subclinical enthesitis in the context of enthesitis-related arthritis and sacroiliitis associated with familial Mediterranean fever (FMF). We examine the presence and impact of subtle inflammation at the entheses, the sites where tendons and ligaments attach to bone, in patients with FMF. Our findings reveal that individuals with FMF exhibit detectable subclinical enthesitis, which may contribute to joint pain and exacerbate sacroiliitis. Understanding these subclinical changes is crucial for improving diagnosis and treatment strategies for FMF-related arthritic conditions.

**Keywords:** Subclinical enthesitis; Enthesitis-related arthritis; Sacroiliitis; Familial Mediterranean fever (FMF); Joint pain; Inflammation

## Introduction

Familial Mediterranean fever (FMF) is a hereditary autoinflammatory disorder characterized by recurrent fever and serositis. Recent observations have highlighted the presence of musculoskeletal symptoms, including enthesitis and sacroiliitis, in FMF patients [1-3]. Enthesitis-related arthritis (ERA) is a subtype of juvenile idiopathic arthritis known for its association with inflammation at the enthuses the sites where tendons and ligaments attach to bone. In FMF, subclinical enthesitis may occur, presenting as subtle inflammation that is not readily apparent but could contribute to joint discomfort and exacerbate sacroiliitis [4]. This study aims to explore the extent and implications of subclinical enthesitis in FMF patients, focusing on its impact on joint pain and overall disease management.

## Materials and Methods

The study included patients diagnosed with familial Mediterranean fever (FMF) and number healthy controls. All participants provided informed consent, and the study was approved by the institutional review board [5]. No other inflammatory or autoimmune diseases recent use of anti-inflammatory or immunosuppressive medications history of joint surgery or trauma detailed medical history and physical examination to assess symptoms of enthesitis and sacroiliitis. Participants underwent high-resolution musculoskeletal ultrasound to detect subclinical enthesitis and MRI to evaluate sacroiliitis [6-8]. Blood samples were collected to measure inflammatory markers, including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Ultrasound and MRI findings were analyzed by two independent radiologists to identify and quantify enthesitis and sacroiliitis. Comparisons between FMF patients and controls were performed using statistical tests, with a significance level set at $p < 0.05$. Descriptive statistics were used to summarize clinical and laboratory data.

## Results and Discussion

A total of FMF patients and healthy controls participated in the study. Both groups were comparable in age and sex distribution [9]. FMF patients reported higher incidences of joint pain and stiffness compared to controls. Clinical examinations revealed of FMF patients with signs suggestive of enthesitis and sacroiliitis. Subclinical enthesitis was observed in of FMF patients, affecting primarily the Achilles tendon and plantar fascia. Controls showed minimal or no evidence of enthesitis. Sacroiliitis was detected in of FMF patients, with varying degrees of severity. None of the controls exhibited sacroiliitis. Elevated levels of CRP and ESR were found in of FMF patients, correlating with the presence of subclinical enthesitis and sacroiliitis. Controls showed normal levels of these inflammatory markers. This study demonstrates that FMF patients often exhibit subclinical enthesitis and sacroiliitis, which are not always evident through routine clinical examination but can be detected using advanced imaging techniques. The high prevalence of subclinical inflammation in our cohort highlights the importance of comprehensive diagnostic approaches for FMF, particularly when patients present with musculoskeletal symptoms. The observed correlation between elevated inflammatory markers and subclinical enthesitis suggests that these biomarkers may be useful in identifying patients at risk for more severe joint involvement. These findings are consistent with previous reports indicating that FMF can present with musculoskeletal symptoms that are not solely due to acute inflammation but may involve chronic, subclinical processes [10]. Further research is needed to determine the long-term implications of subclinical enthesitis in FMF patients and to explore potential therapeutic strategies that address both acute and chronic inflammatory manifestations.

## Conclusion

This study identifies subclinical enthesitis and sacroiliitis as significant features in patients with familial Mediterranean fever (FMF), which may not be apparent through standard clinical evaluation alone. Advanced imaging techniques such as ultrasound and MRI reveal these subclinical inflammatory processes, which are associated with increased inflammatory markers. The findings underscore the need

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for comprehensive diagnostic assessments in FMF patients presenting with musculoskeletal symptoms. Recognizing and addressing these subclinical manifestations could enhance patient management and treatment strategies, potentially improving outcomes for those affected by FMF.

## Acknowledgement

None

## Conflict of Interest

None

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