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ORIGINAL ARTICLE

Prevalence and characteristics of juvenile fibromyalgia syndrome in pediatric rheumatic diseases: A comparative study

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ABSTRACT

Objectives: The study aimed to evaluate the frequency of juvenile fibromyalgia syndrome (JFMS) in patients diagnosed with juvenile idiopathic arthritis (JIA) and familial Mediterranean fever (FMF) with joint symptoms and compare them with a healthy control group.

Patients and methods: This retrospective study was conducted with 181 participants between January and April 2023. One hundred twenty-one patients with JIA or FMF diagnoses (71 females, 50 males; mean age: 15.6±2.1 years; range, 12 to 23 years) and 60 healthy individuals (36 females, 24 males; mean age: 14.5±1.6 years; range, 12 to 17 years) were included in the patient group and the control group, respectively. The pain and symptom assessment scale was applied for the JFMS diagnosis, and the output data were analyzed with the widespread pain index and symptom severity scale.

Results: Of the patient group, 57% (n=69) were diagnosed with FMF, and 43% (n=52) were diagnosed with JIA. When the two groups were compared with those diagnosed with JFMS, statistical significance was detected ($p<0.05$). Thirteen (87%) of those diagnosed with JFMS were female, and two (13%) were male, with a statistically significant difference.

Conclusion: In patients with JIA and FMF who complain of chronic musculoskeletal pain, tiredness, and weakness, JFMS diagnosis should always be considered in the clinical evaluation.

Keywords: Chronic pain, familial mediterranean fever, juvenile fibromyalgia syndrome, juvenile idiopatic arthritis, tiredness.

Pediatric rheumatologists often encounter patients with chronic musculoskeletal pain, which can be attributed to various inflammatory and noninflammatory conditions.[1] These conditions may include hypermobility, arthritis, fibromyalgia, growing pains, and complex regional pain syndrome.[2]

Juvenile fibromyalgia syndrome (JFMS) is a commonly encountered musculoskeletal pain disorder in children and adolescents, and its exact cause is still unknown. The condition is characterized by persistent and widespread pain throughout the body.[3] Other accompanying symptoms include sleep disturbances, fatigue, and the presence of multiple tender points upon physical examination. Chronic anxiety or tension, frequent headaches, subjective soft tissue swelling, and pain that is influenced by physical activity, weather changes, anxiety, or stress are often observed in individuals with JFMS.[4,5]

Juvenile fibromyalgia syndrome tends to persist, affecting children and adolescents' function and psychosocial development. Factors such as genetics, anatomy, sleep disturbances, and psychological distress contribute to its development.[6] Treatment should be comprehensive, involving medications for pain and sleep, as well as nonpharmacological measures, such as psychotherapy, aerobic exercise, and promoting healthy sleep habits.[7] By combining these approaches, healthcare professionals can provide holistic care for individuals with JFMS, addressing the various aspects of the condition

and working towards improving their overall well-being and quality of life.[8]

There is a lack of sufficient epidemiological data regarding the prevalence of JFMS. However, within the medical community and among other healthcare providers, there is an increasing awareness and recognition of this condition.[9,10] In the adult population, fibromyalgia is estimated to have a prevalence of approximately 3.4% among females and 0.5% among males.[11] These figures provide a reference point for understanding the prevalence of fibromyalgia in the general adult population, but specific data on JFMS in children and adolescents are limited.[12]

The terminology and diagnostic criteria for JFMS were introduced by Yunus and Masi[13] in a clinical study published in 1985. Their criteria were developed based on a cohort of 33 individuals who were 17 years of age or younger and experienced persistent pain. These criteria were designed to aid in the diagnosis of JFMS and have since been used as a reference in clinical practice and research.[14]

The new criteria offer advantages over previous ones, such as assessing symptom severity and additional somatic FM symptoms, being user-friendly and efficient, and eliminating the subjective and inconsistent tender point examination.[15] The pain and symptom assessment scale (PSAT) evaluates fibromyalgia symptoms but is not for diagnosis; instead, it monitors symptom severity over time, with diagnosis relying on criteria such as the American College of Rheumatology (ACR) classification criteria (Figure 1). The PSAT helps healthcare providers track symptom changes, treatment efficacy, and patient's overall well-being in fibromyalgia and other chronic pain conditions. In 2010, the ACR introduced updated criteria for adult fibromyalgia diagnosis, later found to be applicable to diagnosing JFMS in adolescent females with a sensitivity of 89.4% and a specificity of 87.5%, suggesting their utility in diagnosing JFMS in this population.[16,17]

In childhood rheumatic diseases such as juvenile idiopathic arthritis (JIA) and familial Mediterranean fever (FMF), distinguishing between their symptoms and those of JFMS, particularly widespread joint pain and morning stiffness, can be challenging. The cooccurrence of JPFM further complicates the diagnosis and treatment process, as it may involve different underlying mechanisms and require specialized therapeutic approaches.[18]

This study was conducted within a tertiary pediatric rheumatology clinic, where these patients were being regularly monitored and treated. By assessing the prevalence of JFMS in this specific group of patients, we aimed to shed light on the coexistence of JFMS with JIA and FMF, as well as the potential impact of these overlapping conditions on symptom presentation, disease course, and management strategies. The objective was to contribute to a better understanding of JFMS in the context of JIA and FMF, ultimately improving the diagnosis and management of these complex musculoskeletal conditions in pediatric patients.

PATIENTS AND METHODS

The retrospective study was conducted with 181 participants in two groups: the patient group and the control group. The patient group included 121 individuals (71 females, 50 males; mean age: 15.6±2.1 years; range, 12 to 23 years) with JIA diagnosed according to the International League of Associations for Rheumatology or FMF diagnosed according to the new set of criteria for the diagnosis of

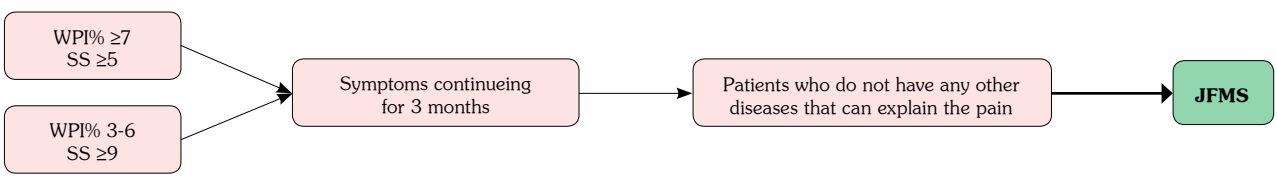

Figure 1. The flowchart of Fibromyalgia according to 2010 American College of Rheumatology Criteria.
WPI: Widespread pain index; SS: Symptom severity; JFMS: Juvenile fibromyalgia syndrome.

FMF in childhood (the 2008 Ankara criteria) who presented to the pediatric rheumatology clinic of the Ümraniye Training and Research Hospital between January and April 2023.[19,20] Sixty healthy individuals (36 females, 24 males; mean age: 14.5±1.6 years; range, 12 to 17 years) who visited the general pediatrics clinic on the same dates constituted the control group.

Fibromyalgia was evaluated with the PSAT. PSAT consists of two parts: the first is the widespread pain index (WPI), which is based on the patient's self-report, and the other is the symptom severity scale (SSS). Participants were asked to indicate which of the 18 body areas they experienced pain in over the past week for the WPI.[21] The SSS comprises two sections, with the first measuring symptom severity based on a 4-point Likert scale (0=no issues, 3=severe, pervasive, continuous, life-disturbing issue) for tiredness, sleep disturbance, and cognitive problems (range, 0-9). The second section is a checklist of 24 additional somatic symptoms. To classify the magnitude of somatic symptoms, the number of symptoms was grouped as follows: 0=no symptoms, 1=mild or intermittent (range, 1-5), 2=moderate or considerable (range, 6-9), or 3=severe, continuous (≥10). The total SSS score (range, 0-12) was created by adding the severity score (0-9) and the magnitude of somatic symptoms (0-3). The reliability of the scale in this sample was alpha=0.79 (WPI) and alpha=0.78 (SSS) (Table 1).

Statistical analysis

Statistical analyses were performed using IBM SPSS version 26.0 vesion (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation (SD), and categorical variables were expressed as frequency and percentage. A diverse set of statistical tests was employed to address different characteristics of the data. For parametric data, differences between groups were assessed using independent samples t-tests for two groups and analysis of variance for multiple groups. Nonparametric variables were analyzed using the Mann-Whitney U test and the Kruskal-Wallis test for comparisons among various groups. Additionally, the chi-square test was applied to examine associations between categorical variables. The correlation between variables was explored using Spearman's rank correlation coefficient. A p-value <0.05 was considered statistically significant.

RESULTS

The sex distribution across the two groups was identical. Of the patient group, 57% (n=69) were diagnosed with FMF, and 43% (n=52) were diagnosed with JIA. Among the patients diagnosed with JIA, 53.8% (n=28) were oligoarticular, 7.7% (n=4) were polyarticular, and 38.5% (n=20) were enthesitis-related arthritis. According to PSAT measurements, 12% (n=14) of the patient group (JIA and FMF combined) were diagnosed with JFM, while only 2% (n=1) of the control group had the diagnosis. There was a statistically significant difference (p=0.022) between the patient group and the control group in terms of JFM diagnosis. In the patient group, 19% (n=10) of patients with JIA and 5% (n=4) of patients with FMF were diagnosed with JFMS. Of the JIA patients diagnosed with JFMS, 40% were in the oligoarticular JIA group, and 60% were in the class of enthesitis-related arthritis (Figure 2).

The mean age of patients diagnosed with JFMS was 13.6±1.7 years, and 87% (n=12) were female, while 13% (n=2) were male. The age of the female FJMS patients ranged from 12 to 19 years, whereas in males, the range was 15 to 19 years. A significant female predominance was observed in patients diagnosed with JFMS, and a statistically significant difference was found (p=0.023).

The duration of the disease in the patient group had a median of four years (range, 1 to 16 years). In the patient group, a statistically significant difference was observed between the duration of the disease and the diagnosis of JFMS (p<0.05), indicating that the duration of the disease may influence the likelihood of being diagnosed with JFMS.

The mean duration of disease was 2.8±1.8 years (range, 1 to 6 years) among patients diagnosed with JFMS, while it was 4.2 years among those who were not diagnosed with JFMS. This indicates that, on average, patients diagnosed with JFMS had a shorter duration of disease compared to those who did not receive a JFMS diagnosis.

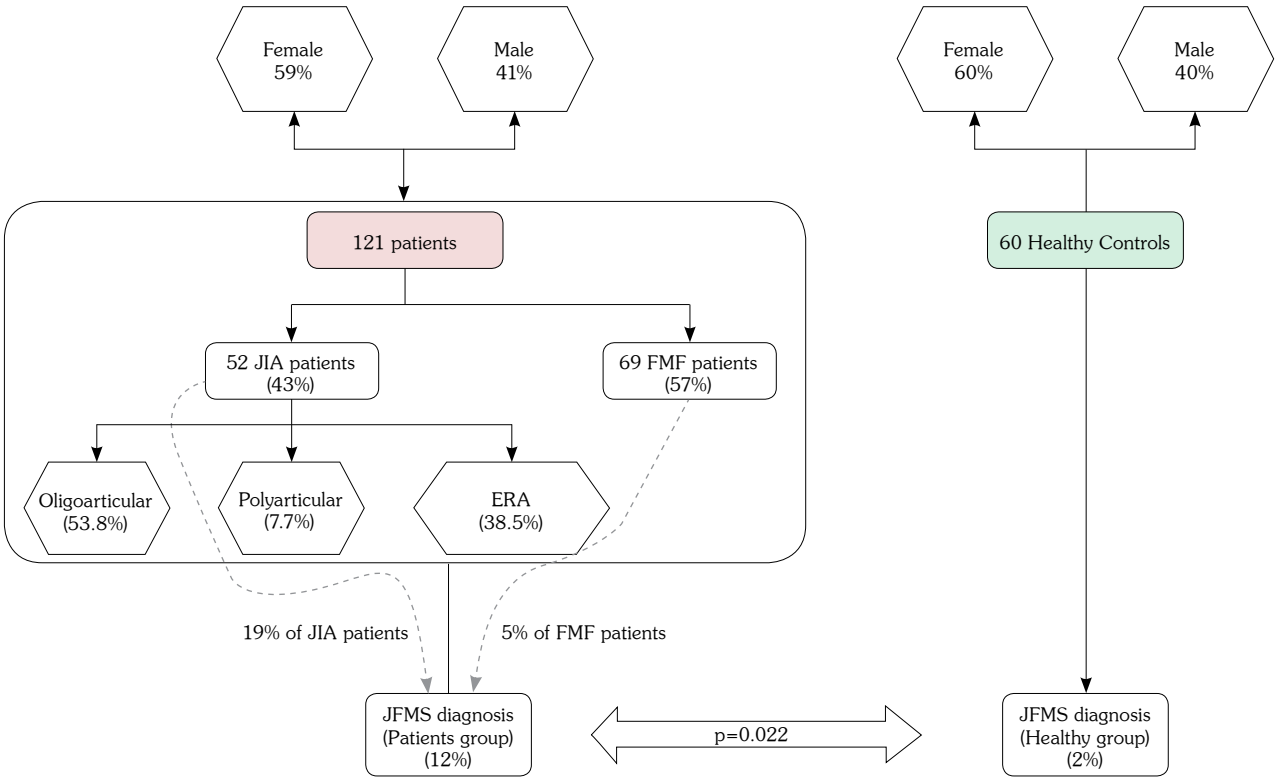

Figure 2. Diagram for the distribution of individuals forming the scope of the study.
JIA: Juvenile idiopathic arthritis; FMF: Familial Mediterranean fever; JFMS: Juvenile fibromyalgia syndrome; ERA: Enthesitis related arthiritis.

Table 1. The 2010 ACR criteria for fibromyalgia[16]

Criteria	Definition
Widespread pain index (WPI)	The WPI score is determined by counting the number of areas on the body where the patient has experienced pain over the past week. A score of 0-19 is possible.
Symptom severity (SS) scale	The SSS score is determined by asking the patient to rate the severity of their tiredness, waking unrefreshed, and cognitive symptoms over the past week on a scale of 0-3 (0: No problem, 3: Severe problem). A score of 0-12 is possible.
Classification criteria	A patient meets the classification criteria for fibromyalgia if the following two conditions are met WPI ≥7 and SSS score ≥5, or WPI: 3-6 and SSS score ≥9.
WPI tender point count (optional)	In addition to the WPI score, the number of tender points on the body can also be assessed. A score of 0-18 is possible.
Other possible diagnoses that should be excluded first:	A thorough history and physical examination should be performed to exclude other possible diagnoses that could explain the patient's symptoms. These may include rheumatic and autoimmune diseases.

Table 2. Somatic symptoms of the patient group diagnosed with JFMS

	Existence/nonexistence	
	n	%
Muscle pain	11/4	73.3
Tiredness	10/5	66.7
Muscle weakness	8/7	53.3
Headache	8/7	53.3
Nervousness	8/7	53.3
Depression	6/9	40.0
Abdominal pain	5/10	33.3
Numbness and tingling	5/10	33.3
Acne	5/10	33.3

JFMS: Juvenile fibromyalgia syndrome.

The mean WPI value (7.8±2.5) was significantly higher in individuals diagnosed with JFMS compared to those without a JFMS diagnosis [1.8]. A statistically significant difference was observed between the presence or absence of a JFMS diagnosis and the scores on WPI and SSS ($p<0.05$).

The most common symptoms observed in patients diagnosed with JFMS are muscle pain, tiredness, muscle weakness, and headache. These were followed by depression, abdominal pain, numbness, and tingling (Table 2). No statistically significant difference was found between body mass index values in those diagnosed with JFMS ($p>0.05$). The study did not find a statistically significant difference between having a family history of rheumatologic or neurologic diseases and being diagnosed with JFMS ($p>0.05$).

The results showed that tiredness 87% (n=13) and waking unrefreshed 80% (n=12) were present in varying degrees in all patients, with the majority experiencing moderate to severe symptoms. Cognitive symptoms were relatively less prevalent, with 60% (n=9), compared to other SSS compounds among patients experiencing mild to moderate symptoms (Table 3).

DISCUSSION

The findings of this study revealed important information about the prevalence and characteristics of JFMS in pediatric patients with JIA and FMF. A total of 121 patients were included in the analysis. To our knowledge, this is the first study in the literature to evaluate JFMS in rheumatological patients in the adolescent age group.[11]

Compared to studies on fibromyalgia in adults, there is limited knowledge about the underlying causes and treatment of fibromyalgia in children.[22] However, as communication and collaboration between medical units improve, awareness of juvenile fibromyalgia is increasing among healthcare providers.

While the prevalence of fibromyalgia in the general population in adult studies was between 2 and 7%,[23-32] the incidence in rheumatological diseases was found to be between 11 and 30%.

Table 3. Frequency of the symptoms designated in SSS (tiredness, waking unrefreshed, and cognitive symptoms) among pediatric patients diagnosed with JFMS

	Symptom scale*							
	No symptom		Mild or intermittent		Moderate considerable		Severe, continuous	
	n	%	n	%	n	%	n	%
Tiredness	0	0	2	13.3	7	46.7	6	40
Waking unrefreshed	0	0	3	20	5	33.3	7	46.7
Cognitive symptoms	1	6.7	5	33.3	3	20	6	40

SSS: Symptom severity scale; JFMS: Juvenile fibromyalgia syndrome; * The data is presented as the count (percentage) of cardinal symptoms, which are assessed through the SSS of the PSAT. The scale measures symptoms as follows: "no symptom," "mild or intermittent," "moderate or considerable," and "severe, continuous."

According to the 2010 ACR diagnostic criteria, the prevalence of fibromyalgia in RA patients in the literature is 12 to 15.4%.[33-36] While the frequency of fibromyalgia in RA patients was between 12 and 17% in the study of Pollard et al.,[34] it was found to be 17.1% in the study of Wolfe and Michaud[36]

Similar to findings on adults, we observed a prevalence of 19% for JFMS among patients with JIA. However, a comprehensive analysis of adults with FMF was not feasible due to the insufficient number of patients available for the study. In a pediatric study by Kasapçopur et al.,[37] fibromyalgia was identified in 1.8% of 108 FMF patients, a rate not statistically distinct from that of fibromyalgia in healthy children. In our study, JFMS was diagnosed in a slightly higher proportion, accounting for 6% (n=4) of individuals with an existing FMF diagnosis; however, this difference did not reach statistical significance.

It is important to note that a statistically significant difference was found between patients who presented to the pediatric rheumatology outpatient clinic and the healthy control group when comparing the diagnosis of JFMS. This suggests that JFMS is more prevalent among patients seeking care in the pediatric rheumatology setting compared to the general population. The findings support the notion that children and adolescents with musculoskeletal pain and related symptoms are more likely to seek medical attention and receive a diagnosis of JFMS when evaluated in a specialized rheumatology clinic. Further research and investigations can help shed light on the reasons behind this difference and contribute to the understanding and management of JFMS in the pediatric population.

The findings from our study regarding the prevalence and demographic characteristics of JFMS align with existing literature.[13,16] JFMS is indeed more commonly observed in children and adolescents, particularly in female patients. The higher prevalence of JFMS in females during adulthood is also consistent with our findings. The significantly higher proportion of females diagnosed with JFM (87%) compared to males further supports the sex predilection observed in JFMS in Kashikar-Zuck et al.'s study.[3,38]

The age distribution of JFMS in the 13 to 15 age group aligns with previous research, indicating that this age range is frequently affected by the condition. The mean age at diagnosis in our study (13.6±1.7) is in line with the reported age of onset in the literature.[39]

These findings reinforce the understanding that JFMS predominantly affects adolescent females, with similar prevalence rates to those observed in adult studies. The consistency of these findings across different studies strengthens our knowledge of the demographic characteristics of JFMS and provides valuable insights for further research and clinical management of the condition.

In our study, the mean duration of disease was 2.8±1.8 years (range, 1 to 6 years; median: 2.5 years) among patients diagnosed with JFMS, whereas in the study of Gedalia et al.,[40] it was indicated as 18.3 months.

Based on available data, JFMS is a common condition in pediatric rheumatology outpatient clinics. The Penta Group Registry of Rheumatology Clinics in the Ohio, Indiana, and Kentucky regions has 231 diagnosed cases of JFMS.[39] Recent studies indicate that the number of diagnosed cases of JFMS is increasing, with reports of an increasing proportion of new patient diagnoses in pediatric rheumatology clinics. According to a 1996 report by Bowyer and Roettcher,[41] JFMS accounted for 2.1% of new patient diagnoses in a pediatric rheumatology clinic disease registry in the USA. This figure rose to 7.65% in the same disease registry by 1998. Siegel et al.[39] reported that JFMS ranked third among new patient diagnoses at their pediatric rheumatology clinic. However, these figures do not include patients seen at pediatric care clinics. Population-based studies in Israel, Finland, and Mexico have also provided additional information on the prevalence of JFMS.[27] Mikkelsson et al.[42] discovered that 7.5% of 1,756 Finnish schoolchildren reported experiencing widespread musculoskeletal pain similar to JFMS. However, this estimate was solely based on self-reported pain and did not involve physical examination of tender points. Meanwhile, an Israeli study conducted by Buskila et al.[28] revealed that 6.2% of schoolchildren met the 1990 ACR criteria for JFMS.

In our study, tiredness (86.7%) and waking unrefreshed (80%), assessed with SSS, were the most significant concerns of JFMS patients and were observed in all patients. Cognitive symptoms (60%) on the same scale were less prevalent, and some of the patients did not show these types of symptoms. In studies, 90% of fibromyalgia patients have tiredness, and 80% have sleep disorders.[31] In the study of Bennet et al.,[43] it was mentioned that the most common problems were morning stiffness, fatigue, nonrestorative sleep, pain, concentration, and memory.

These findings suggest that tiredness and poor sleep quality are significant concerns for pediatric patients with JFMS and should be taken into consideration when developing treatment plans. Further research is needed to explore the underlying mechanisms and effective interventions for these symptoms in this patient population.

The findings from our study and the study by Ting et al.[17] demonstrate that individuals diagnosed with JFMS exhibit higher levels of pain location and somatic symptoms compared to control groups or individuals without a JFMS diagnosis.

In the study of Lynch-Jordan et al.,[21] patients with JFMS had significantly greater body mass index values (a mean of 24.2 *vs.* 21.2), whereas in our study, no statistically significant difference was found between body mass indexes in those diagnosed with JFMS.

The higher scores in the WPI and SSS among those diagnosed with JFMS in our study suggest a greater distribution of pain throughout the body and a higher number of somatic symptoms experienced by these individuals compared to those without a JFMS diagnosis. These findings are in line with the characteristic features of JFMS, which include widespread pain, tenderness, and the presence of multiple somatic symptoms. Assessing pain location and somatic symptoms is an important aspect of diagnosing and monitoring JFMS, as it helps differentiate the condition from other rheumatic or musculoskeletal disorders. By highlighting the differences in pain location and somatic symptoms between individuals with JFMS and control groups, these studies contribute to our understanding of the clinical presentation and symptomatology of JFMS. They provide valuable insights for healthcare professionals in diagnosing and managing the condition effectively.[21] This supports the idea that there may be a genetic or familial predisposition to JFMS, as suggested by the higher prevalence of family history of fibromyalgia or autoimmune diseases in these patients in previous studies. However, there was no statistically significant difference in the reported family history of neurologic or rheumatologic diseases among JFMS patients in our study.

This study was limited by its sample size, requiring caution in generalizing the findings. A broader population could enhance the study's robustness. The use of form-based measurements and subjective patient reports introduced potential biases, given the inherent subjectivity. Moreover, overlapping symptoms in JIA, FMF, and fibromyalgia necessitate careful consideration when interpreting results.

In conclusion, we observed a significant difference in the diagnosis of JFMS between the patient group and the control group, indicating a higher prevalence of JFMS among children and adolescents with rheumatic diseases. This highlights the importance of considering and evaluating JFMS as a potential comorbidity in this population. Furthermore, the duration of the disease was found to be associated with the diagnosis of JFMS, with a shorter median duration observed in those diagnosed with JFMS compared to those without the diagnosis. This suggests that JFMS may manifest earlier in the disease course and emphasizes the need for early recognition and intervention to improve outcomes and quality of life for these patients. Overall, this study contributes to the growing body of literature on JFMS in pediatric rheumatic populations and emphasizes the importance of early recognition, diagnosis, and management of this condition. Further research is needed to elucidate the underlying etiology, risk factors, and optimal treatment approaches for JFMS, with the goal of improving outcomes and enhancing the quality of life for affected children and adolescents.

Ethics Committee Approval: The study protocol was approved by the Umraniye Training and Research Hospital Clinical Research Ethics Committee (date: 22.12.2022, no: B.10.1.TKH.4.34.H.GP.0.01). The study

was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from the patients and/or parents of the patients.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Study Conception and design was performed, final approval of the verison of the article to be published was performed, analysis and interpreteation of data was performed: G.Ö.B., B.S.; Acquisition of data was performed: G.Ö.B., D.K., S.A.; Drafting the article or revising it critically for important intellectual content was performed: G.Ö.B., D.K., B.S.

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