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ORIGINAL ARTICLES

Prevalence of juvenile fibromyalgia syndrome in Turkish patients with juvenile idiopathic arthritis: a multicenter study

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ABSTRACT

Objectives: To investigate the diagnostic prevalence of juvenile fibromyalgia syndrome (JFMS) causing widespread pain in patients with a diagnosis of juvenile idiopathic arthritis (JIA).

Methods: Patients with JIA from seven pediatric rheumatology centers in Türkiye were included. 2010 American College of Rheumatology criteria for fibromyalgia was utilized throughout a face-to-face interview. The Pain and Symptom Assessment Tool was used, and data were analyzed using the Widespread Pain Index and the Symptom Severity Scale. Patients were stratified into two groups: Group 1 (JIA with concomitant juvenile fibromyalgia) and Group 2 (JIA without juvenile fibromyalgia).

Results: A total of 313 patients with JIA were included, of whom 21 (6.7%) were found to have concomitant JFMS. In group 1, 71% (15 patients) were female and 29% (6 patients) were male, with a median age at JFMS evaluation of 16 years (range: 12.8-19). Among patients with JFMS, 62% (13 patients) were classified as having spondyloarthropathy (enthesitis-related arthritis or juvenile psoriatic arthritis), 28.5% (6 patients) as having oligoarticular JIA, and 9.5% (2 patients) as having polyarticular JIA. Seventeen patients (81%) were on medication, including five (24%) on biologics. The most common symptoms in the JFMS group were muscle pain and fatigue, followed by headache, nervousness, numbness, dizziness, acne, abdominal pain, and anorexia.

Conclusion: In JIA patients with chronic musculoskeletal pain, fatigue, headache, and irritability lasting more than three months, the possible diagnosis of JFMS should be considered in the clinical evaluation.

Keywords: Pain; Fibromyalgia; Juvenile Idiopathic Arthritis

KEY MESSAGES

- This study underscores the substantial impact of Juvenile Fibromyalgia Syndrome (JFMS) among pediatric patients, particularly in terms of pain distribution, somatic symptoms, and quality of life. It also highlights the critical role of fatigue, sleep disturbances, and cognitive issues in supporting early diagnosis.
- Patients with JIA and coexisting JFMS exhibit higher WPI and SSS scores. The structured form used for JFMS diagnosis can be easily applied in outpatient settings, aiding in the identification of difficult-to-diagnose cases that, when properly recognized, may experience improved quality of life.

INTRODUCTION

Chronic Musculoskeletal pain (CMP) is a common reason for pediatric rheumatology referrals, encompassing conditions such as arthritis, hypermobility, fibromyalgia (FM), growing pains, and complex regional pain syndrome (CRPS)[1]. Amplified Musculoskeletal pain syndrome (AMPS), including FM, CRPS, and idiopathic musculoskeletal pain exerts a heightened influence on pain signals and impairs function, manifesting in both localized (CRPS) and diffuse Juvenile Fibromyalgia Syndrome (JFMS) forms[2–4].

The diagnosis of diffuse chronic widespread pain/fibromyalgia syndrome (FMS) is a contentious matter,

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with the evaluation process relying on symptom-based assessments and the classification criteria being the subject of ongoing debate. The Yunus and Masi system, as well as the 2010 American College of Rheumatology (ACR) fibromyalgia questionnaire, are the primary tools used in this process. Limited understanding of JFMS mechanisms suggests involvement of abnormal pain processing influenced by neurologic, biochemical, inflammatory, genetic, psychosocial, and environmental factors[5,6]. The updated ACR criteria have shown high sensitivity (89.4%) and specificity (87.5%) for diagnosing JFMS in adolescent females, marking a significant diagnostic advancement[6–11].

The coexistence of JFMS with Juvenile Idiopathic Arthritis (JIA) complicates the processes of diagnosis and treatment. This is due to the involvement of distinct pathophysiological mechanisms, which may require specialized therapeutic approaches. Compared to research on fibromyalgia in adults, knowledge about the etiology and management of fibromyalgia in children remains limited [12]. Hence, the primary goal of this multicenter study was to investigate the prevalence of concomitant JFMS in patients with JIA.

PATIENTS AND METHODS

Patient Selection and Methods

This observational study involved a retrospective review of data from 313 patients diagnosed with JIA across seven pediatric rheumatology centers. All patients were diagnosed with according to the International League of Associations for Rheumatology (ILAR) criteria[13]. A face-to-face survey was conducted to assess compliance with the American College of Rheumatology (ACR) fibromyalgia diagnostic criteria to identify patients with JFMS.

The Pain and Symptom Assessment Tool (PSAT) was used, divided into the Widespread Pain Index (WPI) and the Symptom Severity Scale (SSS). The WPI is based on the patient's self-report, indicating pain in 18 body areas over the past week. The SSS consists of two sections: the first measures symptom severity for tiredness, sleep disturbance, and cognitive problems on a 4-point Likert scale (0=no issues, 3=severe issues), with scores ranging from 0 to 9. The second section includes a checklist of 24 additional somatic symptoms, classified as 0 (no symptoms), 1 (mild or intermittent, 1-5 symptoms), 2 (moderate, 6-9 symptoms), and 3 (severe, continuous, 10 or more symptoms). The total SSS score ranges from 0 to 12, combining the severity score (0-9) and the somatic symptoms score (0-3).

Patients diagnosed with JIA were stratified into two groups for follow-up purposes: Group 1, consisting of patients with concomitant JFMS, and Group 2, comprising those without JFMS.

The study adhered to the principles of the Declaration of Helsinki (2013 revision). The study protocol received approval from the Research and Ethical Review Board of the hospital where the study was conducted (Document ID: B.10.1.TKH.4.34.H.GP.0.01/84).

Statistical analysis

Statistical analyses were conducted utilizing IBM SPSS software version 26.0 (IBM Corp., Armonk, NY, USA). Continuous data were summarized as mean ± standard deviation (SD), whereas categorical data were presented as counts and percentages. Depending on the nature of the data, various statistical methods were employed. For parametric data, independent samples t-tests were used for comparisons between two groups, while analysis of variance (ANOVA) was applied for comparisons across multiple groups. In cases of nonparametric data, two-group comparisons were conducted using the Mann-Whitney U test, and comparisons among multiple groups were performed with the Kruskal-Wallis test. Relationships between categorical variables were analyzed using the chi-square test, and correlations between variables were evaluated using Spearman's rank correlation coefficient. A p-value below 0.05 was considered indicative of statistical significance.

RESULTS

Demographic and Diagnostic Features

A total of 313 patients with JIA were included, with data compiled and analyzed from seven pediatric rheumatology centers. Of these, 21 patients (6.7%) were diagnosed with concomitant JFMS (Group 1), while the remaining 292 patients (93.3%) were classified as Group 2. The median age at JIA diagnosis was 12 years (min-max: 1-17). At the beginning of the study, JFMS was assessed in the entire patient population with a median age of 15 years (min:8, max:21). The gender distribution was 63% female (n=196) and 37% male (n=117). Statistical analysis was conducted on demographic and diagnostic features (Table-1). Among these patients, 50.2% (n=157) had oligoarticular JIA, 26.8% (n=84) had juvenile spondyloarthropathy (Enthesitis Related Arthritis and juvenile Psoriatic Arthritis) and 23.0% (n=72) had polyarticular JIA (Figure 1).

Analysis revealed that the mean Widespread Pain Index (WPI) was significantly higher in Group 1 (8.95 ± 2.33) compared to Group 2 (1.46 ± 1.79) (p = 0.0001). Similarly, the mean Symptom Severity Score (SSS) in Group 1 (7.38 ± 1.75) was significantly elevated relative to that in Group 2 (3.48 ± 2.34) (p = 0.001)

TABLE I. Demographic and Disease Parameters of Juvenile Idiopathic Arthritis (JIA) Patients

	Group 1	Group 2	p-Value
Gender (Female/Male) [n, (%)]	15 (71%) / 6 (29%)	181(62%) / 111(38%)	**0.049**
Age of evaluation for JFMS [years, median; (min-max)]	16 (12.8-19)	15 (8-21)	**0.025**
Age of diagnosis for JIA [years, median; (min-max)]	13 (3-16.5)	12 (1-17)	**0.037**
Disease duration (months, mean ±standard deviation)	38.14±35.83	41.68 ± 36.12	0.665
JIA type			
Oligoarticular	6 (29%)	26 (9%)	**0.001**
Polyarticular	2 (10%)	81 (28%)	
Spondyloarthropathy (ERA & jPSA)	13 (62%)	178 (62%)	

Group 1: Patients with concomitant Juvenile Fibromyalgia; Group 2: Patients without concomitant Juvenile Fibromyalgia.
JIA: Juvenile Idiopathic Arthritis; JFMS: Juvenile Fibromyalgia Syndrome, ERA: Enthesitis Related Arthritis; jPSA: Juvenile Psoriatic Arthritis

Upon examining the subcategories of JIA, it was observed that patients in Group 1, particularly those diagnosed with juvenile spondyloarthritis, were found more frequently compared to patients diagnosed with oligoarticular and polyarticular JIA, with statistically significant differences being identified (p=0.0014) (Table I).In Group 1, the median age was 16 years (min:12.8, max:19) whereas for Group 2 was analyzed as 15 years (min:8, max:21). Statistical analysis revealed that patients in Group 1 were older on average compared to those in Group 2 and no significant difference has been noticed. (p=0.181)Statistical analysis has demonstrated a relationship between the age at evaluation and the incidence of JFM accompanying JIA; it has been determined that older patients are more susceptible to JFMS symptoms (p=0.0255). Among Group 1 patients, 71% (n=15) are female and 29% (n=6) are male. A significant female predominance has been observed in JFMS patients (p=0.0495). The age of female patients in Group 1 ranges from 12.8 to 19 years, while for male patients, it ranges from 13 to 17 yearsThe mean disease duration for JIA patients in Group 1 was 38.14±36.72 months, with no statistically significant difference in disease duration between two groups (p=0.6657). No difference was observed in the duration of JIA between the two groups, and the impact of disease duration on JFMS was not statistically significant (p>0.05), (Group 1 38.14±35.83 months vs. 41.68±36.12 months).

There was no significant difference in Body Mass Index (BMI) values between two groups (p=0.790), suggesting BMI is not a distinguishing factor for JFMS. In Group 1 patients, 19% (n=4) had a family history of rheumatologic diseases, with three having a family history of rheumatoid arthritis (RA) and one of ankylosing spondylitis (AS). No significant differences were found in rheumatological and neurological disease history between two groups (p=0.7414 and p=0.4047, respectively). Eighteen patients were on medication, with six treated with biologic agents. Additionally, 14% (n=3) of Group 1 patients had comorbid conditions, including two with migraines and one with hypothyroidism.

Clinical factors about JFMS were analyzed and examined in an additional session (Table II).

Somatic and Cognitive Symptoms

The frequency of somatic symptoms in patients were compared between two groups using the SSS (Table III). The most common symptoms in JFMS patients were muscle pain, tiredness, headache, and nervousness, followed by numbness, dizziness, acne, abdominal pain, and anorexia.

Among Group 1 patients, 95% (n=20) reported tiredness, and 90.45% (n=20) reported cognitive symptoms and waking unrefreshed. Cognitive symptoms were relatively less prevalent, with 90.45% (n=9) experiencing mild to moderate symptoms.

DISCUSSION

This multi-center study, conducted across seven pediatric rheumatology centers, evaluated 313 patients diagnosed with JIA to investigate the diagnosis and prevalence of JFMS. Our findings indicate that the prevalence of JFMS among JIA patients was 6.7%, which is

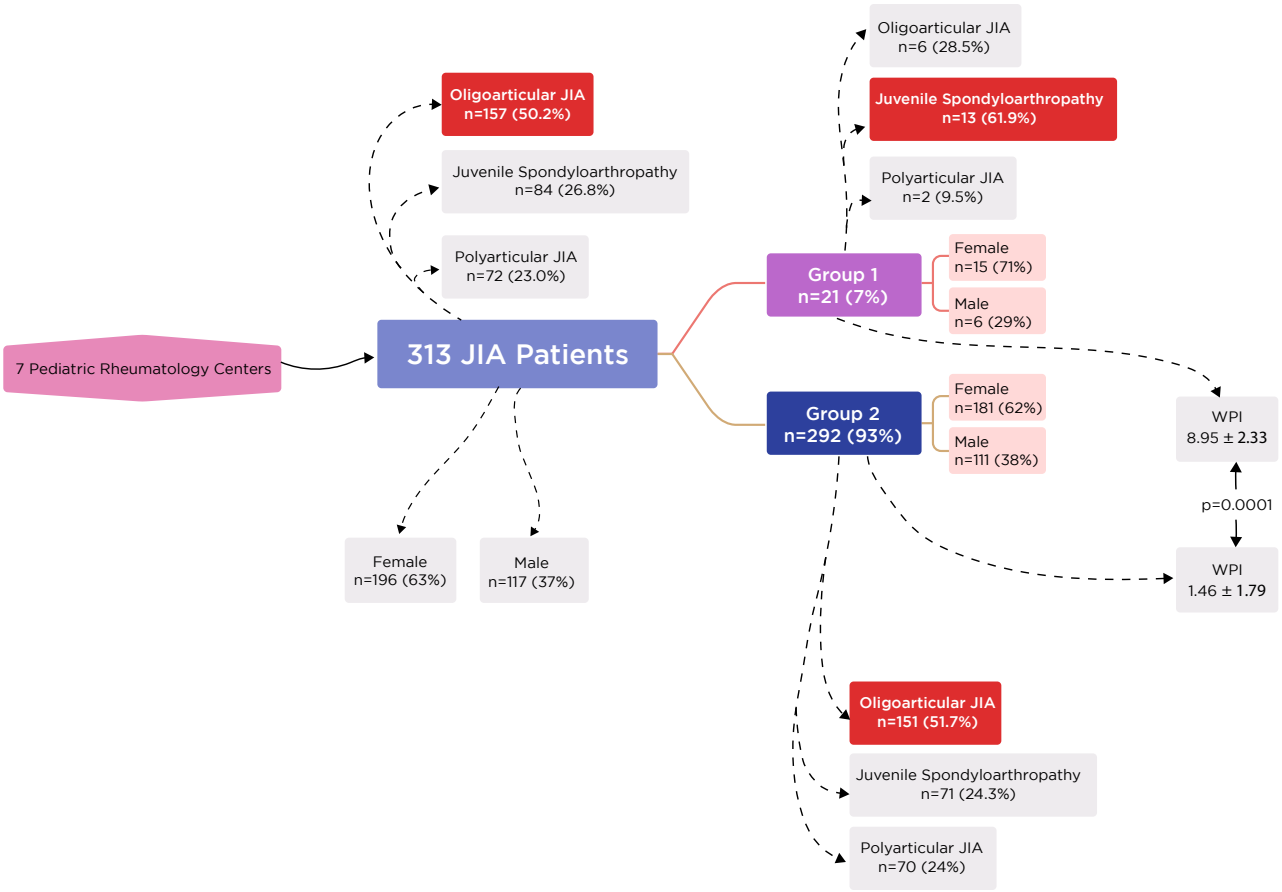

Figure 1. Schematization of the study across JIA types accompanied with/without JFMS.

lower than the reported prevalence in adult rheumatology patients. JFMS is recognized as the third most common reason for pediatric rheumatology outpatient visits, highlighting its clinical significance in this population[14]. A comparison of fibromyalgia prevalence in rheumatology outpatient clinics and the general population reveals a substantially higher frequency in clinical settings (11–30% vs. 2–7%), emphasizing its importance in differential diagnosis[15]. Previous studies have reported JFMS prevalence rates ranging between 12% and 17%, with Wolfe and Michaud identifying a prevalence rate of 17.1% in adult populations[15]. The relatively lower prevalence observed in our cohort suggests that JFMS, while common in pediatric rheumatology clinics, may be underdiagnosed in JIA patients or may manifest differently in this population.

Kashikar-Zuck *et al.* emphasized that epidemiological data on JFMS remain limited, although awareness of the condition has been increasing[8]. While the prevalence of fibromyalgia in adults is approximately 3.4% in women and 0.5% in men, data on its occurrence in childhood remain scarce. However, it is well recognized that JFMS is more frequently diagnosed among adolescent girls, particularly between the ages of 13 and 15[8].

Although pediatric data on fibromyalgia remains limited compared to adult populations, awareness among healthcare professionals has been growing. Notably, during the treatment and follow-up of JIA, the persistence of pain despite successful control of inflammation has necessitated further investigation, bringing JFMS into focus as a potential comorbid condition. Distinguishing JIA from JFMS presents a significant clinical challenge due to overlapping symptoms, such as joint pain and morning stiffness. Moreover, the coexistence of these conditions complicates both diagnosis and management, requiring a specialized approach to optimize patient care.

Given these complexities, clinicians should maintain a high index of suspicion for JFMS in JIA patients, particularly those presenting with persistent pain beyond the expected inflammatory disease course. Comprehensive patient assessment, including evaluation of sleep disturbances, fatigue, and cognitive symptoms, may aid in early recognition and appropriate management.

TABLE II. Diagnostic Parameters Related to Juvenile Fibromyalgia Syndrome

	Group 1	Group 2	p-Value
WPI Score [mean ± standard deviation]	8.95 ± 2.33	1.46 ± 1.79	**0.000**
Symptom Severity Scale [mean ± standard deviation]	7.38 ± 1.75	3.48 ± 2.34	**0.001**
BMI [mean ± standard deviation]	21.51±4.47	20.66 ± 4.30	0.790
Family History of Neurological Diseases [n, (%)]	0 (0%)	49 (17%)	0.405
Family History of Rheumatological Diseases [n, (%)]	4 (19%)	99 (34%)	0.741

WPI: Widespread Pain Index; BMI: Body Mass Index

TABLE III. Frequencies and Somatic Symptoms

Somatic Symptoms	Group 1	Group 2
Muscle Pain	90.0%	27.0%
Fatigue	81.0%	35.0%
Headache	71.0%	24.0%
Dizziness	62.0%	15.0%
Irritability	62.0%	26.0%
Numbness	57.0%	8.0%
Acne	52.0%	18.0%
Muscle Weakness	48.0%	14.0%
Abdominal Pain	48.0%	10.0%
Loss of Appetite	48.0%	13.0%
Insomnia	43.0%	16.0%
Depression	33.0%	5.0%
Stomach Pain	33.0%	8.0%
Chest Pain	33.0%	7.0%
Memory Problems	29.0%	11.0%
Dry Mouth	29.0%	5.0%
Itching	29.0%	6.0%
Gastroesophageal Reflux	29.0%	5.0%
Shortness of Breath	29.0%	6.0%
Bruising	24.0%	3.0%
Irritable Bowel Syndrome	19.0%	2.0%
Diarrhea	19.0%	4.0%
Runny Nose	19.0%	8.0%
Blurred Vision	19.0%	7.0%
Vomiting	19.0%	2.0%
Constipation	14.0%	4.0%
Raynaud's	14.0%	2.0%
Tinnitus	14.0%	5.0%
Aphthous stomatitis	14.0%	4.0%
Deafness	10.0%	3.0%
Rash	10.0%	6.0%
Fever	5.0%	1.0%
Tastelessness	5.0%	1.0%
Wheezing	0.0%	2.0%
Seizure	0.0%	0.0%
Hearing Loss	0.0%	2.0%

Future prospective studies are warranted to further elucidate the prevalence and impact of JFMS in pediatric rheumatology and to develop targeted strategies for improving patient outcomes.

Data from the Penta Group Rheumatology Clinics, including the Ohio, Indiana, and Kentucky regions, documented a total of 231 JFMS cases[14]. Bowyer and Roettcher's 1996 study reported that JFMS accounted for 2.1% of new diagnoses in a U.S. pediatric rheumatology patient registry, increasing to 7.65% in 1998, demonstrating a rising trend in JFMS diagnoses [16]. This trend suggests improved awareness and recognition of the condition[14,16]. Similarly, it indicated that JFMS ranked as the third most common new diagnosis in their pediatric rheumatology clinic [14].

Population-based studies conducted in Finland, Mexico and Israel provided significant insights into the prevalence of JFMS. Buskila *et al.* found that 6.2% of school children in Israel met the 1990 ACR criteria for JFMS[17]. Mikkelsson *et al.* reported that 7.5% of 1.756 Finnish school children experienced widespread musculoskeletal pain, although their study relied on self-reported symptoms without physical examinations to assess tender points[18]. Such community-based research highlights the prevalence of JFMS among children[19].

JFMS appears to be particularly prevalent among females, as evidenced by our study where 87% of the patients were female, aligning with findings by Kashikar-Zuck *et al.* [20,21], and further emphasizing that JFMS predominantly affects juvenile females[14]. Gender might play a role in the diagnosis of JFMS, with females showing a higher frequency of diagnosis compared to males.

The age distribution within the 13 to 15 age group aligns with previous research, indicating this age range is commonly affected by the condition[14]. The age of evaluation for JFMS in our cohort aligns with earlier reports indicating that this age group is most affected. As indicated in Table I, age at the time of JIA evaluation may be associated with the likelihood of meeting criteria for a JFMS diagnosis. This might imply that certain age groups are more susceptible to conditions that meet the criteria for JFMS, or that symptoms become more

discernible or severe at certain ages.

The higher age at JIA diagnosis in Group 1 compared to Group 2 suggests that there may be critical periods during which JFMS symptoms become more apparent or its diagnosis is more likely. This finding highlights the importance of considering age as a factor when evaluating symptoms and diagnosing JFMS, potentially aiding clinicians in earlier recognition and management.

In our study, the average disease duration for Group 1 was higher than the 18.3 months reported by Gedalia et al. [22]. These variations highlight the importance of further research into JFMS's clinical and demographic characteristics.

The BMI of JFMS patients in our cohort aligned with the range of 21.2–24.2 reported by Lynch-Jordan *et al.* [23]. However, no significant BMI difference was observed between diagnosed and undiagnosed patients.

Additionally, research indicates that 90% of fibromyalgia patients experience fatigue, while 80% report sleep disturbances[24]. Consistent with the literature, 95% of our JFMS patients reported fatigue, and 90.45% experienced cognitive symptoms. While fatigue and poor sleep quality were common and often severe, cognitive symptoms tended to be milder, with 90.45% of patients reporting mild to moderate cognitive difficulties.

These findings underscore the importance of early diagnosis and intervention in improving outcomes and quality of life for patients with JFMS. Early recognition, diagnosis, and management of JFMS are critical in pediatric rheumatology clinics. Additionally, data from the Penta Group indicate that 231 JFMS cases were recorded in the Ohio, Indiana, and Kentucky regions[14], reflecting the increasing recognition of this condition. Bowyer and Roettcher's[16] findings from the same registry support this increase, highlighting improved awareness over time.

In conclusion, JFMS is a condition that primarily affects adolescent females with a diagnosis of JIA and is characterized by pronounced fatigue, poor sleep quality, and cognitive impairments. These symptoms, combined with varying disease durations and associated BMI findings. Early diagnosis is crucial for ensuring timely identification of these patients, facilitating appropriate therapeutic approaches, and improving their quality of life. Future studies are needed to better understand the underlying causes and risk factors of JFMS. These studies will provide valuable insights into effective treatment strategies.

We concluded that JFMS can co-occur in patients with JIA, particularly during adolescence. When assessing treatment response, including pain evaluation and morning stiffness, consideration of JFMS may contribute to a more comprehensive patient follow-up. We suggest that before determining remission or flare in adolescents with JIA, JFMS should be considered as a potential source of pain and appropriately evaluated.

Limitations of the Study

The primary limitation of this study is its retrospective design, which precluded the assessment of not only the prevalence of JFMS but also its impact on disease outcomes. A prospective design would have allowed for a more comprehensive evaluation, including the influence of JFMS on disease progression and patient outcomes.

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