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Anxiety, Mood, and Behavioral Disorders Among Pediatric Patients With Juvenile Fibromyalgia Syndrome

Susmita Kashikar-Zuck, PhD,† Irina S. Parkins, PhD,* Thomas Brent Graham, MD,‡† Anne M. Lynch, PhD,*† Murray Passo, MD,‡† Megan Johnston, BA,* Kenneth N. Schikler, MD,§ Philip J. Hashkes, MD,‖ Gerard Banez, PhD,¶ and Margaret M. Richards, PhD¶*

Background: Mood and anxiety disorders are common psychiatric conditions among adult patients with fibromyalgia syndrome, but little is known about whether psychiatric disorders are prevalent among pediatric patients with fibromyalgia.

Objective: The primary objective of this study was to assess the prevalence of mood, anxiety, and behavioral disorders in a clinical sample of children and adolescents with juvenile primary fibromyalgia syndrome (JPFS) and assess the relationship between psychiatric disorders and JPFS symptom severity.

Methods: Standardized psychiatric interviews were conducted with children and their parents/primary caregivers, and measures of symptom severity including pain intensity and physician global ratings were obtained for 76 children and adolescents diagnosed with JPFS (ages 11 to 18 y) in pediatric rheumatology clinics at 4 hospitals in the Midwest.

Results: A total of 67.1% of patients had at least 1 current and 71.5% had at least 1 lifetime DSM-IV (Diagnostic and Statistical Manual of Mental Disorders-fourth edition) psychiatric diagnosis. The most frequent psychiatric diagnosis was anxiety disorder (57.5% of JPFS patients). Although mood difficulties were also common, the presence of major depression was lower than has been reported for adults with fibromyalgia syndrome. Physicians' global assessment of functioning was significantly lower for patients with a current anxiety disorder. There were no significant differences in pain severity among patients with and without anxiety, mood, or behavioral disorders.

Discussion: There seems to be a high prevalence of anxiety disorders in patients with JPFS, and presence of anxiety disorder is associated with poorer physician-rated functioning. Future research should explore whether early anxiety symptoms are predictive of long-term functioning.

Key Words: juvenile fibromyalgia, psychiatric comorbidity, emotional functioning, pediatric pain

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Juvenile primary fibromyalgia syndrome (JPFS) is a chronic pain condition characterized by symptoms of diffuse musculoskeletal pain and multiple painful tender points upon palpation. It is often accompanied by fatigue, poor sleep, chronic headaches, irritable bowel syndrome, and subjective soft tissue swelling.[1] JPFS primarily affects adolescent girls and is typically recognized between the ages of 13 and 15. Siegel et al[2] reported that JPFS is ranked as the 12th most common new-patient diagnosis representing about 7% of patients in pediatric rheumatology clinics. The long-term prognosis of children and adolescents with JPFS is unknown. Some community-based studies have shown that adolescents with JPFS may have a more favorable prognosis than adults.[3,4] However, in clinical populations of adolescents with JPFS, 80% to 90% of patients continued to report pain, sleep disturbance, fatigue, stiffness, and other symptoms at 2 to 3 years of follow-up.[2] Moreover, those with persistent JPFS symptoms tended to show more emotional problems,[4] suggesting that a subgroup of adolescents with JPFS may have clinically significant psychologic symptoms that may affect their long-term functioning.

The complexity of the presenting clinical picture in JPFS has not been sufficiently addressed in the literature. Similar to adult fibromyalgia syndrome (FMS), JPFS is often difficult to classify, because many of the symptoms are "medically unexplained" and often overlap with other medical conditions such as chronic fatigue syndrome, irritable bowel syndrome, and migraine headache. Comorbid psychiatric conditions, such as mood and anxiety

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From the *Division of Behavioral Medicine and Clinical Psychology; ‡Rheumatology Division, Cincinnati Children's Hospital Medical Center; †Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati; ‖Department of Rheumatic and Immunologic Disease; ¶Division of Pediatrics, The Cleveland Clinic Foundation, Cleveland, OH; and §Department of Pediatrics, University of Louisville School of Medicine, Louisville, KY.

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Reprints: Susmita Kashikar-Zuck, PhD, Division of Behavioral Medicine and Clinical Psychology, MLC 3015, Cincinnati Children's Hospital Medical Center, Cincinnati, OH 45229 (e-mail: Susmita.Kashikar-Zuck@cchmc.org).

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disorders have been found to be prevalent in both clinical and community samples of adults with FMS.[5–7] The estimated prevalence of concurrent mood disorders in adults with FMS ranges from 24% to 34%, with an estimated lifetime prevalence of 64% to 69%. The estimated prevalence of concurrent anxiety disorders in adults with FMS ranges from 15% to 32%, with lifetime prevalence of 35% to 47%.[5,6,8,9] As might be expected, treatment-seeking FMS patients have greater psychiatric comorbidity than those who do not seek medical care.[10]

There is ongoing debate about the causes of psychiatric symptoms in FMS. That is, whether the symptoms are a consequence of living with chronic pain, or whether FMS and mood/anxiety disorders are an expression of the same disease spectrum, and share common familial risk factors. The current thinking supports a stress-vulnerability model of the pathogenesis of FMS in which FMS patients and their female relatives may share a common risk for heightened pain sensitivity and mood difficulties.[11] When exposed to physical or emotional stressors, they are likely to experience increased pain and/or emotional symptoms. Regardless of the mechanisms, it has been found that adult FMS patients with greater psychiatric comorbidity tend to have poorer treatment outcomes than those with fewer psychiatric symptoms.[12] Studying the presence of psychiatric disorders in children and adolescents with JPFS is a useful approach in providing greater insight on the issue of the development and course of symptoms over the lifespan of individuals with FMS.

There is no documented evidence of the prevalence of specific psychologic disorders in children and adolescents with JPFS. The few studies, including our own, which have previously explored anxiety and depressive symptoms in JPFS have primarily relied on child and parent-report symptom checklists and found that psychologic distress was mildly elevated overall in adolescents with JPFS, similar to levels of distress in children with other chronic pain conditions such as juvenile idiopathic arthritis or chronic back pain,[13,14] but a subgroup of JPFS patients seem to have severe mood symptoms.[13] Although these studies point toward potential emotional difficulties in some patients with JPFS, it is not clear from elevations in scores on self-report questionnaires how many JPFS patients have symptoms severe enough to meet the criteria for psychiatric diagnosis.

The primary objective of this study was to determine the presence of current and lifetime diagnoses of psychiatric conditions in a clinical sample of pediatric patients with JPFS using a standardized diagnostic interview for children: the Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL[15,16]). Additionally, we gathered information about JPFS symptom severity (using physician global ratings and patient pain ratings) to explore the relationship between symptom severity and psychiatric status. It was hypothesized that the prevalence of mood and anxiety disorders would show a similar prevalence as adult samples of FMS patients, and that the presence of mood, anxiety, or behavioral disorders would be associated with greater JPFS symptom severity.

METHODS

Participants

Study participants were recruited from pediatric rheumatology clinics located in 4 children's hospitals in the Ohio and Kentucky region. Inclusion criteria: pediatric patients between the ages of 11 to 18 years who met JPFS diagnostic criteria suggested by Yunus and Masi[1] were eligible for the study, along with their parent or primary caregiver. The criteria for JPFS were: generalized musculoskeletal pain at 3 or more sites for 3 or more months in the absence of underlying conditions, severe pain in at least 5 tender point sites upon manual palpation, and at least 3 associated symptoms such as sleep disturbance, fatigue, headaches, irritable bowel syndrome, or subjective soft tissue swelling. Exclusion criteria: patients were excluded from the study if they had a comorbid rheumatic disease such as juvenile idiopathic arthritis, documented developmental delay, or impairment such as autism or mental retardation.

Procedure

The study rheumatologists (TBG, MP, KNS, and PJH) identified potential participants at the initial rheumatology visit, and informed the families about the study. If patients were interested in being contacted about the study, the rheumatologist obtained verbal consent from the families for a research assistant to contact them. Families were then contacted by the research assistant either by phone or during a clinic visit to explain the study and request their participation. Informed consent: written informed consent for study participation was obtained from parents of the patients and written and verbal assent was obtained from the children and adolescents. Because this research involved a vulnerable population (minors), the family was informed that if a reportable event or safety risk was discovered during the assessment (such as abuse, suicidal risk), we would need to inform appropriate authorities per the state regulatory rules and assist the family with developing a plan for the child or adolescent's safety. This study protocol was approved by the hospital institutional review boards at each of the 4 participating sites. Upon completion of the evaluation, participants were provided 2 movie ticket coupons or a gift coupon in appreciation for their participation.

Before the assessment, the research assistant mailed participants' standardized instructions and materials for completion of daily pain diaries for 1 week before their study visit. On the day of the visit, the participants returned their diaries and completed a demographic information form. Next, a trained doctoral level fellow (ISP) or licensed psychologist (AML and GB) administered the psychiatric interview. All interviewers were thoroughly trained in the standardized administration

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and scoring of the K-SADS-PL by the principal investigator (SKZ).

Measures

Demographic Information Form

Items on this form assessed demographic characteristics including the child's age, race/ethnicity, parents' educational levels, and socioeconomic status including annual household income and parents' occupational background that was used to calculate the index of occupational prestige.[17]

Medication Use

The study rheumatologists completed a form documenting all current prescription and nonprescription medications, the dosage, frequency, and route of administration. Medications used for pain relief, sleep, and psychiatric symptoms were of primary interest in this study and were coded into the following categories: acetaminophen, opioid analgesic, nonsteroidal anti-inflammatory drug (NSAID), steroid, muscle relaxant, triptan, benzodiazepine, herbal sleep aid, tricyclic antidepressant, selective serotonin reuptake inhibitor, selective norepinephrine reuptake inhibitor, atypical antidepressant, anticonvulsant, or stimulant.

JPFS Symptom Severity

Pain Intensity Ratings

Participants rated their average pain intensity on daily diaries (for 1 week before the study visit) using a visual analog scale (VAS, 10 cm horizontal line with no numerical markings), anchored on the ends with "No Pain" and "Worst Possible Pain." VAS scales are validated for use in school age children and have been successfully used in research studies in pediatric pain.[18–20] A daily diary is preferable to asking participants for ratings over the past week owing to potential recall bias. An average pain intensity rating for the 1-week period was calculated.

Global Physician Rating

The study rheumatologist was asked to provide a global assessment of fibromyalgia symptom severity (10 cm VAS, anchored with "Doing Very Poorly" and "Doing Very Well," with lower scores indicating worse symptoms). Physician's global assessment ratings have been successfully used in multinational studies of rheumatic disease.[21]

Psychiatric Characteristics

K-SADS-PL[15,16]

The K-SADS-PL is a semistructured psychiatric interview designed to assess psychopathology in children and adolescents, and was used in this study to assess present and lifetime history of psychiatric diagnoses based on DSM-IV (Diagnostic and Statistical Manual of Mental Disorders-fourth edition) criteria. The standardized administration included completion of (1) an unstructured introductory interview, (2) a diagnostic screening interview, (3) the appropriate diagnostic supplements, as needed, and (5) the summary lifetime diagnosis checklist. If there was no suggestion of current or past psychopathology, no supplemental assessments beyond the screening interview were administered. The K-SADS-PL was administered to the child and the parent together. Only the last 2 sections regarding substance use and posttraumatic stress were administered to the child alone so that they could feel free to answer the questions honestly. The K-SADS-PL is designed primarily as a tool for psychiatric diagnosis, however, some items overlap with the typical symptoms associated with chronic pain such as fatigue, sleep problems, increased tension, or sadness. Therefore, we were conservative in our application of these symptoms as psychiatric diagnostic criteria. For the purposes of this study, if such symptoms were reported by participants, they were scored and included for diagnostic purposes only if they were reported as being not associated with fibromyalgia pain, or above and beyond the pain experience. The K-SADS-PL has strong test-retest and inter-rater reliability as well as concurrent validity.[16] All present and lifetime DSM-IV diagnoses were recorded on the summary lifetime diagnosis checklist.

Statistical Analysis

The goal of this preliminary descriptive study was to examine the presence and type of anxiety, mood, and behavioral disorders in a clinical sample of JPFS patients. Sample characteristics including demographic information, JPFS symptom severity (pain ratings and physician global ratings), and medication use are described. Detailed information is provided about present and lifetime psychiatric diagnoses (Table 2). Independent samples t tests were used to compare symptom severity (pain intensity and physician global ratings) in children with and without an anxiety, mood, or behavioral disorder.

RESULTS

Demographic Information

A total of 120 eligible JPFS patients between the ages of 11 to 18 years were approached and 76 (62%) families agreed to participate. The caregiver who completed the evaluation along with their child was most often the mother (87%). For the remaining, the father (5.3%) or a grandparent (5.3%) completed the evaluation with the child. The final sample consisted of 76 children and adolescents with a mean age of 14.89, and their parent/primary caregiver. Consistent with past studies in JPFS, the majority were girls (N = 66; 86.8%) and 84.2% were White. Most of the parents had 1 or more years of a college level education (> 70%). The fathers' average index of occupational prestige was 54.93, which corresponds to technical, sales, and administrative support occupations. About a fourth of the mothers (26.3%) were homemakers or not currently employed. The average

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TABLE 1. Demographic Characteristics of Families and Adolescents With JPFS (N = 76)

Characteristic	Mean	SD
Mother's SES*	54.39	18.13
Father's SES*	54.93	22.50
Adolescent participant's age	14.89	1.97
Mother's age	43.99	6.63
Father's age	45.21	6.57
	No.	**%**
Adolescent's sex		
Boy	10	13.2
Girl	66	86.8
Adolescent's race		
African American	7	9.2
White	64	84.2
Asian	1	1.3
American Indian/Alaskan native	2	2.6
Biracial	2	2.6
Household income		
0000-9999	3	3.9
10,000-19,999	4	5.3
20,000-29,999	4	5.3
30,000-39,999	10	13.2
40,000-49,999	7	9.2
50,000 or above	46	60.5
Mother's level of education		
Less than high school	2	2.6
High school diploma	10	13.2
Some college or technical school	30	39.5
College degree	28	36.8
Graduate school degree	4	5.3
Father's level of education		
Less than high school	0	0.0
High school diploma	15	19.7
Some college or technical school	17	22.4
College degree	25	32.9
Graduate school degree	17	22.4

*Based on the Duncan TSEI2. Higher scores represent greater occupational attainment.
JPFS indicates juvenile primary fibromyalgia syndrome; SD, standard deviation; SES, socioeconomic status.

TABLE 2. Prevalence of Psychiatric Disorders in Adolescents With JPFS (N = 73*)

	Current	Lifetime
Disorder	**N (%)**	**N (%)**
Any psychiatric diagnosis	49 (67.1)	52 (71.2)
Any anxiety disorder	42 (57.5)	39 (53.4)
Panic disorder	7 (9.6)	3 (4.1)
Specific phobia	22 (30.1)	17 (23.2)
Social phobia	8 (10.9)	10 (13.7)
Generalized anxiety disorder	7 (9.6)	8 (11.0)
Other	14 (19.1)	13 (17.8)
Any mood disorder	16 (22.0)	30 (41.1)
Major depressive disorder	6 (8.2)	19 (26.0)
Dysthymic disorder	4 (5.5)	2 (2.7)
Other mood disorders	6 (8.2)	9 (12.3)
Any behavioral disorder	19 (26.0)	15 (20.5)
Attention-deficit/hyperactivity disorder, inattentive type	11 (15.1)	4 (5.5)
Attention-deficit/hyperactivity disorder, hyperactive-impulsive type	1 (1.4)	2 (2.7)
Attention-deficit/hyperactivity disorder, combined type	2 (2.7)	2 (2.7)
Other behavioral disorder	6 (8.2)	8 (11.0)
Other disorders	3 (4.1)	5 (6.8)
Participants with > 1 diagnosis	22 (30.1)	28 (38.4)

*Three participants did not complete the K-SADS.
JPFS indicates juvenile primary fibromyalgia syndrome

index of occupational prestige for mothers who were employed was 54.39, which also corresponds to technical, sales, and administrative support occupations. Demographic information is presented in Table 1.

Pain Rating and Physician Global Assessment

The children's average pain intensity rating on the weekly VAS diaries was 5.27 (SD 1.96). Physician's overall assessment on the VAS global assessment of functioning rating was 3.74 (SD 1.96).

Comorbid Psychiatric Disorders

Overall level of psychiatric comorbidity was high in this clinical sample. Out of 73 participants who completed the K-SADS-PL, 49 patients (67.1%) presented with at least 1 current DSM-IV diagnosis and 52 (71.2%) presented with at least 1 lifetime DSM-IV diagnosis. Twenty-two patients (30.1%) had more than 1 current psychiatric condition. By far, the most common diagnoses were anxiety disorders (specific phobias, social phobia, generalized anxiety, and panic disorder), with 42 patients (57.5%) meeting criteria for at least 1 current anxiety disorder, and 39 (53.4%) with lifetime prevalence. Those with specific phobias reported diverse types of phobias including fear of the dark, insects, needles/blood draws, stairs, and thunderstorms. Mood disorders were relatively less common but still quite prevalent, with 16 patients (22%) meeting criteria for a current mood disorder, and 30 (41.1%) with lifetime prevalence. Of those patients with a current mood disorder, only 6 patients (8.2%) met criteria for major depressive disorder and none were diagnosed with bipolar disorder. Behavioral disorders, especially those relating to attention deficit problems were also present in 19 patients (26%). Table 2 provides the information about the number and percentage of patients who met diagnostic criteria for anxiety, mood, and behavioral disorders.

Symptom Severity of Patients With and Without an Anxiety, Mood, or Behavioral Disorder

To examine whether there was a difference in JPFS symptom severity among children with an anxiety, mood, or behavioral disorder diagnosis, we calculated average pain ratings on the children's daily diaries and physicians' global assessment rating for (1) children with and without a current anxiety disorder; (2) children with and without a current mood disorder, and (3) children with and without a current behavioral disorder. As can be seen in Table 3, physicians' global assessment of functioning scores were significantly lower for children with a concurrent anxiety disorder than those without an anxiety disorder ($P < 0.05$). Adolescents with mood disorders tended to

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TABLE 3. Average Pain Ratings and Physician's Global Assessment for Adolescents With JPFS, With and Without Current Anxiety, Mood, and Behavioral Disorders (N = 73*)

	Anxiety Disorder			Mood Disorder			Behavioral Disorder		
	Yes	No	*P*	Yes	No	*P*	Yes	No	*P*
Pain rating (0-10)	5.9	5.1	0.09	6.3	5.3	0.06	5.4	5.2	0.82
Global assessment of functioning (0-10)	3.2	4.2	0.02†	2.9	3.8	0.09	3.9	3.6	0.60

*Three participants did not complete the K-SADS.
†Difference significant at the 0.05 level.
JPFS indicates juvenile primary fibromyalgia syndrome

have slightly higher pain ratings and lower physician global functioning ratings than those without a mood disorder; however, these differences were not statistically significant. There were no significant differences in pain ratings or physicians' global functioning ratings for those with or without a behavioral disorder.

Medications

The most commonly used medications for treating JPFS were found to be tricyclic antidepressant medication (amitriptyline) and NSAID medications. Selective serotonin reuptake inhibitors and anticonvulsant medications were also used, but much less often. A list of medications used in this sample of patients with JPFS along with the number of patients taking each of the medications is listed in Table 4.

DISCUSSION

The findings in this clinical population of children and adolescents with JPFS demonstrated that they were highly vulnerable to emotional difficulties with the majority of JPFS patients meeting criteria for at least 1 current (67.1%) or lifetime (71.2%) psychiatric diagnosis. This compares with a 36.7% lifetime prevalence of any psychiatric diagnosis in children and adolescents in community-based studies.[22] The finding of increased risk for psychiatric comorbidity in JPFS is similar to findings in adult patients with FMS[6,9] in that 75% to 81% of adult FMS patients meet lifetime criteria for at least 1 psychiatric diagnosis. However, there seem to be important differences in the type of psychiatric diagnoses in a pediatric JPFS sample that may be informative about the developmental aspects of FMS. In this study of children and adolescents with JPFS, it was found that anxiety disorders were the most prevalent comorbid psychiatric condition, including phobias, generalized anxiety, and panic disorder. Over half the children and adolescents with JPFS (57.7%) met criteria for at least 1 lifetime anxiety disorder, compared with a population prevalence of 9.9% to 13%.[22,23] On the basis of physicians' global assessment ratings, adolescents with JPFS and a comorbid anxiety diagnosis were functioning more poorly overall than those without an anxiety disorder. Mood difficulties were also common in children with JPFS (41.1% lifetime prevalence). However, the prevalence of major mood disorders such as major depressive disorder in JPFS patients (26% lifetime prevalence) was substantially lower than reported for adults with FMS. The lifetime prevalence of major depressive disorder in clinical populations of adults with FMS has been reported as 61% to 69%.[5,6]

TABLE 4. Medication Use in Adolescents With JPFS (N = 76)

Medication Type	No.	(%)
Tricyclic antidepressant	36	(47.4)
NSAID	32	(42.1)
SSRI	15	(19.7)
Anticonvulsant	13	(17.1)
Stimulant	10	(13.1)
SNRI	7	(9.2)
Acetaminophen	5	(6.6)
Opioid analgesic	2	(2.6)
Muscle relaxant	3	(5.3)
Atypical antidepressant	1	(1.3)
Benzodiazepine	2	(2.6)
Herbal sleep aid	1	(1.3)
NRI	1	(1.3)
Steroid	1	(1.3)
None	5	(6.6)

JPFS indicates juvenile primary fibromyalgia syndrome; NRI, norepinephrine reuptake inhibitor; NSAID, nonsteroidal anti-inflammatory drugs; SSRI, selective serotonin reuptake inhibitor.

The findings of this study are consistent with a stress-vulnerability model in which younger patients with JPFS display a predisposition toward emotional difficulties present mainly in the form of anxiety disorders. Our previous findings showing that adolescents with JPFS were perceived as more sensitive and isolated than their peers, and parents rated their child as having more internalizing symptoms are quite consistent with these findings.[24,25] Longitudinal research in mood disorders has indicated that anxiety disorders in childhood (except for panic disorder) almost always preceded major depressive disorders in later years.[26] These findings suggest that for those children and adolescents with JPFS who present with a comorbid psychiatric condition, there could be a progression toward more severe mood difficulties in adulthood if not adequately treated in the early years.

The findings of the current study have important treatment implications. Anxiety disorders are highly treatable conditions in pediatric populations and empirically supported behavioral treatments currently exist that are proven to be efficacious in reducing childhood anxiety.[27,28] Depressive symptoms that have not yet

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reached the level of a major mood disorder are also responsive to cognitive-behavioral treatment focused on coping skills training to deal with pain.[29] Early identification of concurrent anxiety or mood disorders, and appropriate intervention may prevent more complex and severe mood problems in adulthood that are more difficult to treat.

An additional finding in this study that has not been previously documented is that 19% of the children and adolescents with JPFS met DSM-IV criteria for attention deficit disorder (primarily inattentive type) and several of these patients were being treated with stimulant medication. Attention deficit disorders have not been documented in adults with FMS, although cognitive difficulties such as memory decline and mental confusion have been found to be more prevalent in adult FMS patients than those with other rheumatic diseases.[30] More research is needed in the area of attentional difficulties in FMS.

An area that is still little understood is the area of pharmacotherapy for JPFS. At present, there are no FDA (Food and Drug Administration) approved drugs that are labeled for use in children and adolescents with JPFS. Judging from the most frequently used medications reported in this study, the standard of care seems to consist of combined treatment with low-dose tricyclic antidepressant medication and NSAIDs. The efficacy of this approach has not been investigated in pediatric populations and needs further study.

The results of this study could only be generalized to clinical populations of JPFS patients who are referred to subspecialty care, and may represent patients with more severe symptoms. Our sample was not representative of nontreatment seeking children and adolescents with generalized pain and positive tender points, or patients who may be managed in primary care settings. As is the case for many relatively uncommon pediatric disorders, the small sample size is another limitation. Finally, it should be noted that the K-SADS-PL is primarily validated for psychiatric populations and there is not much research in pediatric chronic pain samples with this instrument. Although we were cautious about assigning psychiatric diagnoses when symptoms associated with chronic pain such as sleep problems, fatigue, and so forth were reported, at times these judgments are not clear cut, especially when pain-related disability and suffering overlap closely with pain symptoms. Despite these limitations, the findings of this study add to our knowledge of psychological symptoms associated with JPFS, which is still an underrecognized and understudied condition. As such, the findings provide an important first step in demystifying the complex presentation of JPFS patients seen in a tertiary care setting and set the stage for treatment planning using a multimodal approach.

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