The Journal of Rheumatology 2022;49:489–96
doi:10.3899/jrheum.210489
First Release March 15 2022

The Journal of Rheumatology

Profiling Behavioral and Psychological Symptoms in Children Undergoing Treatment for Spondyloarthritis and Polyarthritis

Anne McHugh[1], Avis Chan[2], Carolyn Herrera[2], Jennifer M. Park[3], Imelda Balboni[2], Dana Gerstbacher[2], Joyce J. Hsu[2], Tzielan Lee[2], Margo Thienemann[4], and Jennifer Frankovich[2]

ABSTRACT. ***Objective.*** Few studies examine psychopathology in different juvenile idiopathic arthritis (JIA) subtypes and disease activity states. We aimed to (1) evaluate emotional and behavioral symptoms in children with juvenile spondyloarthritis (SpA) and polyarticular arthritis (PolyA) as compared to a national normative population using the Child Behavior Checklist (CBCL), and (2) evaluate the relationship between CBCL scores and disease activity.

Methods. Patients with JIA aged 6–17 years with SpA or PolyA were recruited from our pediatric rheumatology clinic from April 2018 to April 2019 and the CBCL and clinical Juvenile Arthritis Disease Activity Score in 10 joints (cJADAS10) were completed. Primary outcome measures were CBCL total competence, internalizing, externalizing, and total problems raw scores. We compared outcomes from each group to national CBCL normative data. To investigate the relationship between CBCL scores and disease activity, we ran a generalized linear regression model for all patients with arthritis with cJADAS10 as the main predictor.

Results. There were 111 patients and 1753 healthy controls (HCs). Compared to HCs, patients with SpA or PolyA had worse total competence and internalizing scores. Higher cJADAS10 scores were associated with worse total competence, worse internalizing, and higher total problems scores. Most of these differences reached statistical significance ($P < 0.01$). Self-harm/suicidality was almost 4-fold higher in patients with PolyA than HCs (OR 3.6, 95% CI 1.3–9.6, $P = 0.011$).

Conclusion. Our study shows that patients with SpA and PolyA with more active disease have worse psychological functioning in activities, school, and social arenas, and more internalized emotional disturbances, suggesting the need for regular mental health screening by rheumatologists.

Key Indexing Terms: behavior, pediatric rheumatology, polyarthritis, psychologic, spondyloarthritis

There is mounting evidence regarding the significant overlap between rheumatologic and mental health impairments.[1,2] However, this relationship is currently understudied in the pediatric population, including those with juvenile idiopathic arthritis (JIA), the most common chronic rheumatic disease in children, affecting 1–4 per 1000.[3] Patients with JIA have been found to have an increased risk of behavioral and mental health disorders, but research has not yet clarified the relationship between psychopathology and arthritis disease activity, nor have studies distinguished between JIA subtypes, which have different underlying mechanisms and perhaps variable risk for psychological symptoms.[4,5,6,7,8]

The overlap between rheumatologic and psychiatric disorders may be caused by both physiological and psychological factors, but the contribution of each is unknown and difficult to study. Regardless of the cause of the mental health problems, standard evidence-based approaches to identify and treat mental health impairments are important to pursue. Therefore, it is important for the rheumatology field to better understand psychological/psychiatric profiles in rheumatologic conditions to better equip clinicians with awareness and tools to properly screen patients.

Adults with psoriatic arthritis (PsA) and ankylosing spondylitis have been found to have increased rates of obsessive-compulsive disorder (OCD) symptoms, anger, hostility, paranoid ideation, somatization, anxiety, depression, and self-harm.[9,10,11,12,13,14] Patients with rheumatoid arthritis (RA)

This study was funded by the Training Program in Adult and Pediatric Rheumatology 5T32AR050942-13 and 2T32AR050942-11 grants as well as a grant from the Stanford Child Health Research Institute (Ernest and Amelia Gallo Endowed Postdoctoral Fellow).

[1]A. McHugh, MD, Division of Allergy, Immunology, and Rheumatology, Department of Pediatrics, Stanford University School of Medicine, Palo Alto, California, and Division of Rheumatology, Department of Pediatrics, Wright State University Boonshoft School of Medicine, Dayton, Ohio; [2]A. Chan, MD, MS, C. Herrera, BS, I. Balboni MD, PhD, D. Gerstbacher, MD, J.J. Hsu, MD, MS, T. Lee, MD, J. Frankovich, MD, MS, Division of Allergy, Immunology, and Rheumatology, Department of Pediatrics, Stanford University School of Medicine, Palo Alto, California; [3]J.M. Park, PhD, Rogers Behavioral Health San Francisco, Walnut Creek, California; [4]M. Thienemann, MD, Division of Child and Adolescent Psychiatry and Child Development, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Palo Alto, California, USA.

The authors have no potential conflicts of interest relevant to this article.

Address correspondence to Dr. A. McHugh, Division of Rheumatology, Dayton Children's Hospital, 1 Children's Plaza, Dayton, OH 45404, USA. Email: mchugha@childrensdayton.org.

Accepted for publication January 13, 2022.

© 2022 The Journal of Rheumatology. This is an Open Access article, which permits use, distribution, and reproduction, without modification, provided the original article is correctly cited and is not used for commercial purposes.

Downloaded on April 9, 2024 from www.jrheum.org

with depression have poorer RA outcomes (ie, worse mortality, more comorbidities, higher pain levels).[15]

Patients with juvenile spondyloarthritis (SpA) and polyarthritis (PolyA) have worse self-reported pain, physical functioning, remission rates, and quality of life, putting them at high risk for psychopathology.[3,16,17,18,19] The relationship between these 2 JIA subtypes and mental health has not been specifically explored. While pediatric patients with SpA and PolyA have been included in some studies, the number of subjects has been low.[4,7] To address this research gap, this study evaluates behavioral and emotional symptoms in children with SpA and PolyA separately and compares them to a national normative population using the Child Behavior Checklist (CBCL).

The purpose of this study was 2-fold: (1) to report the emotional and behavioral profile in 2 common forms of chronic arthritis in children—juvenile SpA and PolyA—compared to a national normative population using the CBCL, and (2) to evaluate the relationship between CBCL scores and disease activity using the clinical Juvenile Arthritis Disease Activity Score in 10 joints (cJADAS10).

METHODS

Study design, setting, and participants. In this cross-sectional study, patients with JIA between the ages of 6–17 years were recruited from our pediatric rheumatology clinic from April 1, 2018, to March 31, 2019. Pediatric rheumatologists determined the diagnosis by history, physical examination, laboratory tests, and/or radiographic findings. Patients included in the SpA group were patients who (1) met the International League of Associations for Rheumatology (ILAR) criteria of enthesitis-related arthritis, undifferentiated arthritis, or PsA; (2) had inflammatory bowel disease (IBD)-related arthritis; or (3) met the Berlin criteria for reactive arthritis. Patients in the PolyA group included those meeting ILAR criteria for polyarticular JIA or extended oligoarticular JIA. We excluded patients with active IBD, severe psoriasis (PsO; involvement of body surface area > 10%), and severe developmental delay as determined by the provider as these features may affect their mental health beyond the arthritis and musculoskeletal conditions we examined. We did not exclude patients with mild to moderate developmental delays, or subjects who carried a diagnosis of a mental health disorder as the patients' mental health was our topic of investigation. The Stanford institutional review board approved the study protocol (#42307). Informed consent from parents and assents from children were obtained.

The national normative population (n = 1753) data provided by the Achenbach System of Empirically Based Assessment (ASEBA) came from the representative samples of 2029 American children from the National Survey of Children, Youths, and Adults. The CBCL was completed for survey participants by parents and/or guardians per the guidelines of ASEBA.[20]

Data sources and study measures. After study consent, parents completed the paper form of the CBCL for their children at the clinic or immediately after the clinic visit.[20] This was self-administered although clinicians were available for questions. The internalizing problems score is derived from the sum of the following syndrome scores: anxious/depressed, withdrawn/depressed, and somatic complaints. The externalizing problems score combines the rule-breaking and aggressive behavior syndrome scores. The total problems score is the sum of scores from 113 items rated by parents based on the following response options of "not true," "somewhat or sometimes true," and "very true or often true," that best describe the patient at present or within the past 6 months.

The primary outcome measures included the total competence score, internalizing problems score, externalizing problems score, and total problems score. Exploratory analyses (identified a priori) included OCD problem score, self-harm, and individual syndrome scores under internalizing problems and externalizing problems scores. Self-harm is a binary variable derived from question 18 (deliberately harms self or attempts suicide) and question 91 (talks about killing self) of the CBCL.

For disease activity, both clinicians and parents contributed to the cJADAS10 (range 0–30), which is a validated composite score specific to JIA measuring 3 domains: active joint count and a 10-cm visual analog scale to measure parent and physician global assessment of the child's well-being.[21] We also reviewed charts to collect demographic and clinical information and identify the presence of HLA-B27, arthritis medications, and psychiatric, developmental, and medical comorbidities. Medical comorbidities were defined as any current medical diseases through chart reviews and the CBCL questionnaire.

Statistical analysis. Demographic and clinical characteristics of patients with SpA and PolyA were examined by summary statistics. Per the ASEBA CBCL manual, *t*-scores between 65–69 (93–97th percentiles) are considered to be in the borderline clinical range whereas *t*-scores ≥ 70 (> 97th percentiles) are considered to be the clinical range. Scores in the borderline and clinical ranges significantly discriminated between children who were referred for emotional health or special education services for behavioral or emotional problems and those who were not referred.

Using generalized linear regression models and controlling for age and sex, outcome measures between patients from each group (SpA/PolyA) and controls were compared, and the relationship between primary outcome measures and disease activity (cJADAS10) were examined, with cJADAS10 as the main predictor. Raw scores were used for comparisons to account for the full-range variations. For exploratory analyses, the same models were employed to examine the secondary outcome measures (OCD scores and syndrome scores) and a logistic regression model was performed for self-harm.

All statistical tests were 2-sided, and they were considered statistically significant if $P < 0.013$ (which is 0.05 divided by 4) for the primary outcome measures to account for the multiple testing, and $P < 0.05$ for the exploratory analyses. Data were analyzed with the SAS program (SAS University Edition; SAS Institute).

RESULTS

Our study sample comprised 111 patients: 53 with SpA and 58 with PolyA. In both groups, the median age at CBCL completion was 13–14 years, and more than half of the patients were female (Table 1). The majority of patients with SpA carried a diagnosis of enthesitis-related arthritis (n = 26), PsA (n = 14), and undifferentiated arthritis (n = 6). More than 80% of patients were taking medications for arthritis at the time of administering the CBCL. More than half of the patients in each arthritis group were on aggressive medical therapy (ie, a biologic or combination of a disease-modifying antirheumatic drug [DMARD] and biologic). In the SpA group, more patients had medical comorbidities than those with PolyA.

Using the percentile cut-off of 93%, the proportions of patients having abnormal range scores (defined by ASEBA as borderline or clinical range) in total competence, internalizing problems, externalizing problems, and total problems were 4%, 11%, 0%, 4%, respectively, in SpA and 2%, 16%, 3%, and 7%, respectively, in PolyA. Approximately 4–5% of HCs had these scores within the abnormal ranges.

On generalized linear regression, the age- and sex-adjusted score differences between HCs and patients with SpA or PolyA were small (Table 2). Both the SpA and PolyA groups had lower

Downloaded on April 9, 2024 from www.jrheum.org

Table 1. Demographic and clinical characteristics of patients with SpA or polyarthritis included in the study.

	SpA, n = 53	Polyarthritis, n = 58	*P*
Demographic characteristics			
Age at CBCL, yrs, median (IQR)	14.0 (3.0)	13.0 (6.0)	0.22
Age at diagnosis, yrs, median (IQR)	11.5 (4.1)	6.6 (6.9)	< 0.001
Disease duration since diagnosis, yrs, median (IQR)	1.8 (3.6)	6.6 (7.9)	< 0.001
Sex			0.006
Male	26 (49)	14 (24)	
Female	27 (51)	44 (76)	
Race/ethnicity[a]			0.77
Non-Hispanic White	21 (40)	26 (45)	
Non-Hispanic Black	1 (2)	0 (0)	
Non-Hispanic Asian	6 (11)	3 (6)	
Hispanic	11 (21)	17 (29)	
Other	9 (17)	6 (10)	
Unknown	5 (9)	6 (10)	
Clinical characteristics			
Taking arthritis medications[b]	44 (83)	54 (93)	0.10
NSAID alone	8 (15)	6 (10)	
DMARD ± NSAID	9 (17)	9 (16)[c]	
Biological agents alone ± NSAID	20 (38)	21 (36)	
Combination of DMARD and biologics	7 (13)	18 (31)[c]	
Medical comorbidities[d]	32 (60)	25 (43)	0.07
HLA-B27			< 0.001
Positive	18 (34)	1 (2)	
Negative	23 (43)	16 (27)	
Not done	12 (23)	41 (71)	
cJADAS10, median (IQR)	3.9 (5.7)	2.6 (6.1)	0.96
PGA	0.5 (1.8)	0.5 (1.8)	0.41
Parent global assessment	1.5 (3.2)	1.6 (2.4)	0.71
Active joint counts	0 (1.0)	0 (3.0)	0.82

Data are presented as n (%) for categorical variables and median (IQR) for continuous variables. [a] Self-reported race and ethnicity. [b] Arthritis medication includes NSAID, methotrexate, tumor necrosis factor inhibitor, sulfasalazine, tocilizumab, abatacept, leflunomide, tofacitinib, oral steroids, JAK inhibitors, and mycophenolate mofetil. [c] One of the patients in each group was taking JAK inhibitors in addition to other arthritis medication. [d] Medical comorbidities are defined as any current medical diseases through chart reviews and CBCL questionnaires, excluding psychiatric and developmental disorders. Examples include celiac disease, inflammatory bowel disease, uveitis, cataract, chronic renal disease, Raynaud phenomenon, psoriasis, migraines, asthma, and fibromyalgia. CBCL: Child Behavior Checklist; cJADAS10: clinical Juvenile Arthritis Disease Activity Score in 10 joints; DMARD: disease-modifying antirheumatic drug; JAK: Janus kinase; NSAID: nonsteroidal antiinflammatory drug; PGA: physician global assessment; SpA: spondyloarthritis.

total competence and higher internalizing problems scores (mainly driven by somatic complaints that included headaches, nausea, vomiting, abdominal pain, etc.). This was only statistically significant for patients with PolyA. Both arthritis groups had lower externalizing problems scores than HCs, indicating fewer reported problems with aggressive, hyperactive, noncompliant, and undercontrolled behaviors. Both arthritis groups were similar to the control groups with regards to the total problems score.

Patients' parents (5 in the PolyA group and 1 in the SpA group) endorsed the symptoms "talks about killing self" (n = 4) and "deliberately harms self or attempts suicide" (n = 3) on the CBCL. These patients were not statistically different than the rest of the cohort regarding use of biologics, disease duration, or cJADAS10. Endorsement of self-harm behaviors/suicidality was significantly higher in the PolyA group than the normative population (OR 3.6, 95% CI 1.3–9.6, $P = 0.011$).

Higher disease activity, as reflected by higher cJADAS10, was associated with lower total competence and higher internalizing problems and total problems scores (Table 3). However, the externalizing problems scores (including rule-breaking and aggressive behaviors) were unaffected by disease activity.

Figure 1 shows the scatter plots of composite CBCL *t*-scores against cJADAS10 in patients with SpA and PolyA. Most of our patients with arthritis had a cJADAS10 < 8. Total competence *t*-scores correlated inversely with the cJADAS10 in both groups. Internalizing problems, externalizing problems, and total problems *t*-scores correlated positively with cJADAS10 in both groups, although in the PolyA group, there was an inverse correlation when cJADAS10 was > 7.5.

Downloaded on April 9, 2024 from www.jrheum.org

Table 2. Age- and sex-adjusted differences in CBCL raw scores[a] between patients with SpA or polyarthritis and healthy controls.

	SpA, n = 53		Polyarthritis, n = 58	
	Adjusted Difference[b]	*P*	Adjusted Difference[b]	*P*
Total competence	**−1.5 (−2.7 to −0.3)**	**0.018**	**−1.6 (−2.8 to −0.5)**	**0.006***
Internalizing problems	**1.5 (0.0 to 2.9)**	**0.047**	**1.9 (0.5 to 3.3)**	**0.007***
Anxious/depressed	0.0 (−0.8 to 0.7)	0.92	0.6 (−0.2 to 1.3)	0.14
Withdrawn/depressed	0.4 (−0.2 to 0.9)	0.21	0.2 (−3.1 to 0.7)	0.44
Somatic complaints	1.2 (0.7 to 1.7)	< 0.001*	1.2 (0.7 to 1.6)	< 0.001*
Externalizing problems	**−2.7 (−4.5 to −0.9)**	**0.004***	**−1.9 (−3.7 to −0.2)**	**0.033**
Rule-breaking behavior	−1.1 (−1.8 to −0.3)	0.004*	−1.1 (−1.8 to −0.4)	0.002*
Aggressive behavior	−1.6 (−2.8 to−0.4)	0.012*	−0.8 (−2.0 to 0.4)	0.19
Total problems	**−3.3 (−8.1 to 1.6)**	**0.19**	**−0.3 (−5.0 to 4.4)**	**0.91**
OCD problems	−0.1 (−0.6 to 0.4)	0.68	0.4 (0.0 to 0.8)	0.08
Self-harm[c]	0.8 (0.1 to 5.9)[b]	0.82	3.6 (1.3 to 9.6)[b]	0.011*

Data are presented as point estimates (95% CI). Scores in bold are primary outcome measures; all other scores are subscales (exploratory analyses). [a] Raw scores are used to account for the full-range variation. [b] Age- and sex-adjusted; with reference to controls. [c] Logistic regression model for a binary outcome derived from CBCL problem question 18 (deliberately harms self or attempts suicide) and question 91 (talks about killing self); result is presented as odds ratio (95% CI). * Statistically significant *P* values with the level of significance set at 0.013, which is equal to 0.05 divided by 4 to account for multiple comparisons within the primary categories (ie, primary outcomes, in bold), and 0.05 for exploratory/subcategory measures. CBCL: Child Behavior Checklist; OCD: obsessive-compulsive disorder; SpA: spondyloarthritis.

Table 3. Adjusted differences in CBCL raw scores[a] by cJADAS10 in patients with SpA or polyarthritis.

	SpA, n = 53		Polyarthritis, n = 58	
	Adjusted Difference[b]	*P*	Adjusted Difference[b]	*P*
Total competence	**−0.4 (−0.6 to −0.1)**	**0.009***	**−0.3 (−0.5 to −0.1)**	**< 0.001***
Internalizing problems	**0.5 (0.1 to 0.9)**	**0.007***	**0.3 (0.0 to 0.7)**	**0.09**
Anxious/depressed	0.3 (0.1 to 0.5)	0.004*	0.1 (−0.1 to 0.3)	0.48
Withdrawn/depressed	0.1 (−0.1 to 0.3)	0.18	0.1 (0.0 to 0.2)	0.05*
Somatic complaints	0.1 (−0.2 to 0.3)	0.17	0.1 (0.0 to 0.2)	0.04
Externalizing problems	**0.0 (−0.2 to 0.3)**	**0.71**	**0.0 (−0.2 to 0.3)**	**0.77**
Rule-breaking behavior	0.0 (−0.1 to 0.1)	0.84	0.1 (0.0 to 0.2)	0.09
Aggressive behavior	0.1 (−0.1 to 0.3)	0.53	0.0 (−0.2 to 0.2)	0.74
Total problems	**1.0 (0.1 to 1.8)**	**0.023**	**0.6 (−0.4 to 1.5)**	**0.22**

Data are presented as point estimates (95% CI). Scores in bold are primary outcome measures; all other scores are subscales (exploratory analyses). [a] Raw scores are used to account for the full-range variation. [b] Adjusted difference by each point increase in cJADAS10, adjusted for JADAS, age, sex, and medical comorbidities. * Statistically significant *P* values with the level of significance set at 0.013 which is 0.05 divided by 4 for outcome measures in bold, and 0.05 for other measures. CBCL: Child Behavior Checklist; cJADAS10: clinical Juvenile Arthritis Disease Activity Score in 10 joints; SpA: spondyloarthritis.

We performed a sensitivity analysis by excluding 20 patients with arthritis with attention deficit hyperactivity disorder, autism, depression, anxiety, avoidant restrictive food intake disorder, and OCD. The directions of change were consistent with the primary analysis, but the only analyses that were statistically significant were the externalizing problems scores, which were lower when compared to HCs (Supplementary Table 1, available with the online version of this article).

DISCUSSION

Our study evaluated behavioral symptoms in patients with SpA and PolyA using the CBCL. The CBCL is one of the most widely validated instruments for evaluation of emotional and behavioral symptoms in children and has been used in thousands of studies.[22] It generates 8 syndrome scores: anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behavior, and aggressive behavior. It then summarizes these syndrome scores into composite scores to estimate the child's total competence score (functional performance), internalizing problems score, externalizing problems score, and total problems score.[20,23]

Downloaded on April 9, 2024 from www.jrheum.org

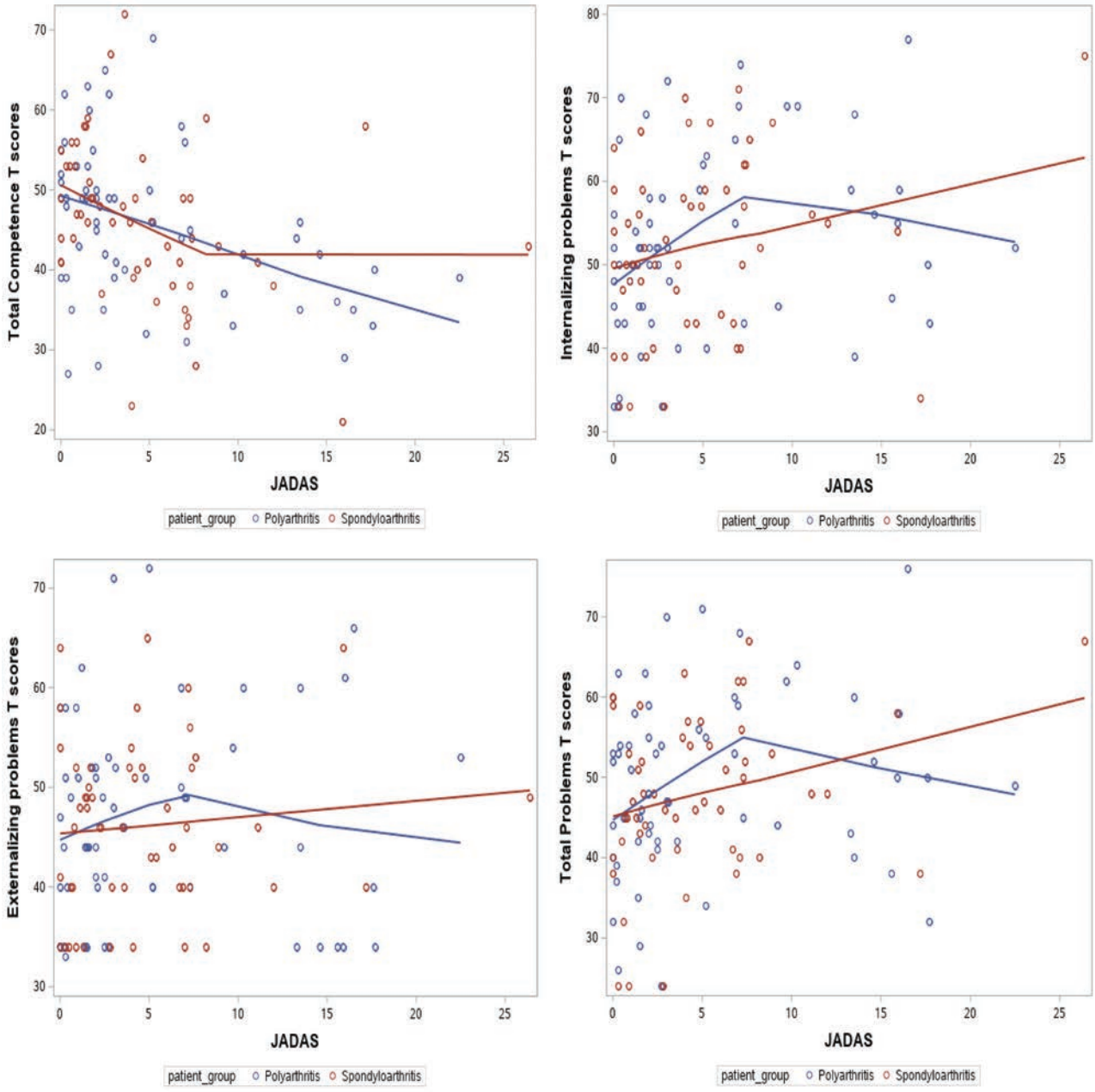

Figure 1. Variations of the Child Behavior Checklist total competence, internalizing problems, externalizing problems and total problems *t*-scores with clinical Juvenile Arthritis Disease Activity Score in 10 joints (JADAS).

We found that a higher proportion of patients with SpA and PolyA in our study (11% and 16%, respectively) had borderline or clinical range of abnormalities in internalizing symptoms when compared to HCs (5%). However, on generalized linear regression, the age- and sex-adjusted score differences between patients and HCs were small. When compared with HCs, patients with arthritis had lower total competence (ie, functional psychological impairments) and higher internalizing problems scores (anxious/depressed, withdrawn/depressed, somatic complaints). Importantly, higher disease activity was associated with lower total competence and higher internalizing and total problems scores. These findings underscore the importance for clinicians to screen children with arthritis for social, school, and activity competencies and internalized emotional disturbances, especially during periods of higher disease activity.

Our findings are consistent with existing literature that children with JIA are at risk for internalizing symptoms and functional impairment.[7,24,25,26] Internalizing scores in both patients with SpA and PolyA were driven mainly by somatic symptoms (and not by anxiety, depression, or social withdrawal). Both arthritis and the side effects of medication can contribute to somatic symptoms (eg, headaches, nausea, vomiting, abdominal pain, etc.) as was found in a study by Noll et al.[27] In our study, when we controlled for disease activity,

Downloaded on April 9, 2024 from www.jrheum.org

the internalizing problems score was no longer being driven by somatic complaints but rather by anxious/depressed and withdrawn/depressed scores.

The absolute CBCL score differences between our study patients and HCs were small after controlling for age, sex, and medical comorbidities. It is important to note that the majority of these patients with JIA were on aggressive immunomodulatory therapies and had low cJADAS10 scores, indicating minimal disease activity. This finding coupled with that of psychopathology being worse with higher arthritis activity may be another justification for treating JIA aggressively beyond the goal of joint and physical function preservation.

Interestingly, we saw a plateau and even improvement of CBCL scores in patients with PolyA with a cJADAS10 > 7.5 (Figure 1). This finding of inversely correlating scores (when cJADAS10 > 7.5) in patients with PolyA may warrant further exploration since one might speculate that those patients with higher cJADAS10 had either a different treatment path or different immunogenetic profile that somehow correlates to better CBCL scores. Importantly, this finding needs to be interpreted with caution since there were few patients with PolyA and cJADAS10 > 7.5.

Not surprisingly, existing evidence regarding the relationship between psychiatric symptoms and arthritis disease activity varies, likely reflecting the heterogeneity of these arthritis cohorts with regards to arthritis subtype, treatment status, and study design.[4,5,6,7] In a previous study of patients with JIA, psychiatric symptoms correlated more with physical disability than the physician-rated disease activity score or the number of active joints on physical examination.[5] Another group of researchers found that in adolescents with newly diagnosed JIA, depression was associated with active disease, pain, and disability; but after 1 year, depression remained associated with pain and disability, but not disease activity.[6] While our study shows an association between disease activity and psychiatric symptoms and functioning, we did not assess physical disability formally nor did we study physician-rated disease as a separate variable, but rather used the cJADAS10, which is a composite index that incorporates the physician assessment with a parent/patient assessment and an active joint count. When looking further at the relationship between disease severity and mental health in our exploratory analyses, we found that higher cJADAS10 was associated with increased anxious/depressed and withdrawn/depressed scores (syndrome scores within the internalizing problems score), but not with somatic complaints (Table 3).

Medical comorbidities, such as celiac disease, IBD, uveitis, cataracts, chronic renal disease, Raynaud phenomenon, PsO, migraines, and asthma, were common in our patients (60% in patients with SpA and 43% in patients with PolyA). Surprisingly, a comorbid pain syndrome such as fibromyalgia was uncommon in our cohort (< 1% of patients). Although it is not possible to fully know the effect of these disorders on mental health in our cohort, we did control for medical comorbidities in our multivariate analysis. We also did a sensitivity analysis whereby we excluded patients with preexisting mental health problems or developmental delays. This analysis did not alter the primary study results, as the direction of change on composite scores remained consistent.

As with our study, a metaanalysis by LeBovidge showed more internalizing symptoms and fewer externalizing symptoms in patients with JIA (SpA, systemic JIA, oligoarticular JIA, etc.) compared to controls.[7] The authors also found that somatic complaints were a primary driver of internalizing symptoms in multiple studies. We question whether these somatic symptoms could simultaneously be dampening externalizing symptoms. However, we recognize that externalizing behaviors are the result of a complex interplay between social, familial, and physical factors and this is beyond the scope of this project to assess.

A number of mechanisms are likely involved in the relationship between disease activity and mental health: arthritis-associated physical disability, pain, fear, stress of having a medical diagnosis, and also the possibility of inflammation directly affecting brain functioning, which is emerging as a major field of research.[6,25,28,29,30,31] More than 80% of the cohort we studied were treated with medications and almost 50% were on combination therapy with a DMARD and biologic. Continued work on understanding mental health in rheumatologic conditions will help us better understand how to best treat these diseases and their overlapping psychological/psychiatric problems. In the meantime, most data point toward better outcomes in patients who are treated aggressively.[32]

Parents of patients with SpA and PolyA (6/111, 5%) gave positive answers on history of self-harm, suicidal ideation, and/or suicide attempts, and endorsement of these behaviors was significantly higher in the PolyA group compared to the normative population. Suicide is the second leading cause of death among youth, and children with chronic medical conditions are twice as likely to present with suicide risk than HCs.[33,34] The American Academy of Pediatrics have published guidelines for primary care providers for the identification, assessment, and initial management of adolescents with depression.[35] They recommend universal screening of youth aged ≥ 12 years at their annual health maintenance visits. The guidelines also encourage providers to use screening tools that ask suicide questions and recommend that providers develop a safety plan for those who screen positive for depression given their increased risk for suicidality.[35] Patients with depression could be missed, though, if seeing their primary care provider only once a year, whereas patients with arthritis see their rheumatologist every few months. Therefore, screening in the rheumatology clinic could lead to earlier identification and intervention. Interestingly, a survey of pediatric rheumatology providers showed that only 2% performed universal screenings with a standardized instrument for depression, anxiety, and suicidal risk,[36] despite the fact that patients of specialty clinics could be equally or at greater risk of parasuicidal symptoms.[37] Our study has confirmed the same finding and reinforces the need for depression and suicide screening, especially for youth with PolyA.

To the best of our knowledge, our study is the first to examine behavior and mental health in the specific JIA populations of SpA and PolyA. CBCL forms were completed at or shortly

Downloaded on April 9, 2024 from www.jrheum.org

after the cJADAS10 assessment to align psychological scores with arthritis scores. We thought that we would discover new patterns by separating the JIA subtypes; unfortunately, we did not discover anything new using this approach and our findings parallel prior studies.[4,7]

Our study has important limitations. First, the majority of our patients were on arthritis medications and had low disease activity scores, which limits the generalizability of our results to relatively quiescent arthritis. Future studies should aim to enroll newly diagnosed patients prior to treatment as this may provide more information about mental health during a period of higher inflammation. Another important limitation is that CBCL reports are completed by parents. This may lead to an underestimation of symptoms by parents, especially in light of the finding of high internalizing symptoms. It will be important for future studies to include surveys completed by the patients to better understand the scope and frequency of these internalizing symptoms.[24,38,39] Additionally, the socioeconomic status data were poorly completed by our study participants, so we were not able to adequately control for confounding in this study. Last, as a result of this being a cross-sectional study, we cannot determine a causal relationship between arthritis disease activity and psychopathology.

This study adds to the growing body of literature indicating that children with arthritis may be at increased risk for psychiatric problems. Specifically, this study indicates pediatric patients with SpA and PolyA have functional impairments and more internalizing symptoms, especially those with higher cJADAS10 scores. Externalizing symptoms are less frequent than that found in the healthy population and do not appear to be influenced by disease activity. Since these patients with SpA and PolyA have more internalizing symptoms and less overt (ie, externalizing) symptoms, this poses a challenge for clinicians to identify mental health problems without formal screening procedures. Of particular concern is the increased risk of self-harm/suicidality among patients with PolyA. These results emphasize the importance of mental health screening in pediatric patients with arthritis, especially when their disease is active, and it highlights the need for further studies into the mechanisms driving this psychopathology to better identify and treat psychiatric comorbidities.

ACKNOWLEDGMENT

We would like to thank Collin Leibold for his help with initiating this study as well as Laurie Columbo for assisting with methodology.

ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

REFERENCES

1. Knight A, Vickery M, Faust L, et al. Gaps in mental health care for youth with rheumatologic conditions: a mixed methods study of perspectives from behavioral health providers. Arthritis Care Res 2019;71:591-601.
2. Taylor PC, Jain R. The Odd Couple?—Hardly. Rheumatology 2018;57:1313-15.
3. Weiss P, Beukelman T, Schanberg LE, Kimura Y, Colbert R., CARRA Registry Investigators. Enthesitis-related arthritis is associated with higher pain intensity and poorer health status in comparison with other categories of juvenile idiopathic arthritis: the Childhood Arthritis and Rheumatology Research Alliance Registry. J Rheumatol 2012;39:2341-51.
4. Fair DC, Rodriquez M, Knight AM, Rubinstein TB. Depression and anxiety in patients with juvenile idiopathic arthritis: current insights and impact on quality of life, a systematic review. Open Access Rheumatol 2019;11:237-52.
5. Ding T, Hall A, Jacobs K, David J. Psychological functioning of children and adolescents with juvenile idiopathic arthritis is related to physical disability but not to disease status. Rheumatology 2008;47:660-4.
6. Hanns L, Cordingley L, Galloway J, et al. Depressive symptoms, pain and disability for adolescent patients with juvenile idiopathic arthritis: results from the Childhood Arthritis Prospective Study. Rheumatology 2018;57:1381-9.
7. LeBovidge JS, Lavigne JV, Donenberg GR, Miller ML. Psychological adjustment of children and adolescents with chronic arthritis: a meta-analytic review. J Pediatr Psychol 2003;28:29-39.
8. Memari AH, Chamanara E, Ziaee V, Kordi R, Raeeskarami SR. Behavioral problems in juvenile idiopathic arthritis: a controlled study to examine the risk of psychopathology in a chronic pediatric disorder. Int J Chronic Dis 2016;2016:5726236.
9. Durmus D, Sarisoy G, Alayli G, et al. Psychiatric symptoms in ankylosing spondylitis: their relationship with disease activity, functional capacity, pain and fatigue. Compr Psychiatry 2015;62:170-7.
10. Baysal O, Durmuş B, Ersoy Y, et al. Relationship between psychological status and disease activity and quality of life in ankylosing spondylitis. Rheumatol Int 2011;31:795-800.
11. Hyphantis T, Kotsis K, Tsifetaki N, et al. The relationship between depressive symptoms, illness perceptions and quality of life in ankylosing spondylitis in comparison to rheumatoid arthritis. Clin Rheumatol 2013;32:635-44.
12. Meesters JJ, Bremander A, Bergman S, Petersson IF, Turkiewicz A, Englund M. The risk for depression in patients with ankylosing spondylitis: a population-based cohort study. Arthritis Res Ther 2014;16:418.
13. Kuriya B, Vigod S, Luo J, Widdifield J, Haroon N. The risk of deliberate self-harm following a diagnosis of rheumatoid arthritis or ankylosing spondylitis: a population-based cohort study. PLoS One 2020;15:e0229273.
14. Rodríguez N, Morer A, González-Navarro EA, et al. Altered frequencies of Th17 and Treg cells in children and adolescents with obsessive-compulsive disorder. Brain Behav Immun 2019;81:608-16.
15. Matcham F, Rayner L, Steer S, Hotopf M. The prevalence of depression in rheumatoid arthritis: a systematic review and meta-analysis. Rheumatology 2013;52:2136-48.
16. Taxter AJ, Wileyto EP, Behrens EM, Weiss PF. Patient-reported outcomes across categories of juvenile idiopathic arthritis. J Rheumatol 2015;42:1914-21.
17. Chen HA, Chen CH, Liao HT, et al. Clinical, functional, and radiographic differences among juvenile-onset, adult-onset, and late-onset ankylosing spondylitis. J Rheumatol 2012;39:1013-8.
18. Ringold S, Seidel KD, Koepsell TD, Wallace CA. Inactive disease in polyarticular juvenile idiopathic arthritis: current patterns and associations. Rheumatology 2009;48:972-7.
19. Wallace CA, Huang B, Bandeira M, Ravelli A, Giannini EH. Patterns of clinical remission in select categories of juvenile idiopathic arthritis. Arthritis Rheum 2005;52:3554-62.
20. Achenbach TM, Rescorla L. Manual for the ASEBA school-age forms & profiles: an integrated system of multi-informant assessment. Burlington: University of Vermont, Research Center for Children, Youth and Families; 2001.

Downloaded on April 9, 2024 from www.jrheum.org

21. Consolaro A, Ruperto N, Bazso A, et al. Development and validation of a composite disease activity score for juvenile idiopathic arthritis. Arthritis Rheum 2009;61:658-66.
22. Althoff RR, Ayer LA, Rettew DC, Hudziak JJ. Assessment of dysregulated children using the Child Behavior Checklist: a receiver operating characteristic curve analysis. Psychol Assess 2010; 22:609-17.
23. Achenbach TM, Ruffle TM. The Child Behavior Checklist and related forms for assessing behavioral/emotional problems and competencies. Pediatr Rev 2000;21:265-71.
24. Bomba M, Meini A, Molinaro A, et al. Body experiences, emotional competence, and psychosocial functioning in juvenile idiopathic arthritis. Rheumatol Int 2013;33:2045-52.
25. Margetić B, Aukst-Margetić B, Bilić E, Jelusić M, Tambić Bukovac L. Depression, anxiety and pain in children with juvenile idiopathic arthritis (JIA). Eur Psychiatry 2005;20:274-6.
26. Krause ML, Zamora-Legoff JA, Crowson CS, Muskardin TW, Mason T, Matteson EL. Population-based study of outcomes of patients with juvenile idiopathic arthritis (JIA) compared to non-JIA subjects. Semin Arthritis Rheum 2017;46:439-43.
27. Noll RB, Kozlowski K, Gerhardt C, Vannatta K, Taylor J, Passo M. Social, emotional, and behavioral functioning of children with juvenile rheumatoid arthritis. Arthritis Rheum 2000;43:1387-96.
28. Shaw KL, Southwood TR, Duffy CM, McDonagh JE. Health-related quality of life in adolescents with juvenile idiopathic arthritis. Arthritis Rheum 2006;55:199-207.
29. Pape K, Tamouza R, Leboyer M, Zipp F. Immunoneuropsychiatry - novel perspectives on brain disorders. Nat Rev Neurol 2019; 15:317-28.
30. Nerurkar L, Siebert S, McInnes IB, Cavanagh J. Rheumatoid arthritis and depression: an inflammatory perspective. Lancet Psychiatry 2019;6:164-73.
31. Lotrich FE, El-Gabalawy H, Guenther LC, Ware CF. The role of inflammation in the pathophysiology of depression: different treatments and their effects. J Rheumatol Suppl 2011;88:48-54.
32. Wallace CA, Giannini EH, Spalding SJ, et al. Clinically inactive disease in a cohort of children with new-onset polyarticular juvenile idiopathic arthritis treated with early aggressive therapy: time to achievement, total duration, and predictors. J Rheumatol 2014;41:1163-70.
33. Shain B, Committee on Adolescence. Suicide and suicide attempts in adolescents. Pediatrics 2016;138:e20161420.
34. Lois BH, Urban TH, Wong C, et al. Integrating suicide risk screening into pediatric ambulatory subspecialty care. Pediatr Qual Saf. 2020;5:e310.
35. Zuckerbrot RA, Cheung A, Jensen PS, Stein REK, Laraque D; GLAD-PC Steering Group. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): Part I. Practice preparation, identification, assessment, and initial management. Pediatrics 2018;141:e20174081.
36. Knight AM, Vickery ME, Muscal E, et al. Identifying targets for improving mental healthcare of adolescents with systemic lupus erythematosus: perspectives from pediatric rheumatology clinicians in the United States and Canada. J Rheumatol 2016;43:1136-45.
37. Horowitz L, Tipton MV, Pao M. Primary and secondary prevention of youth suicide. Pediatrics 2020;145 Suppl 2:S195-203.
38. Shaw KL, Southwood TR, McDonagh JE. Growing up and moving on in rheumatology: parents as proxies of adolescents with juvenile idiopathic arthritis. Arthritis Rheum 2006;55:189-98.
39. Lal SD, McDonagh J, Baildam E, et al. Agreement between proxy and adolescent assessment of disability, pain, and well-being in juvenile idiopathic arthritis. J Pediatr 2011;158:307-12.

Downloaded on April 9, 2024 from www.jrheum.org