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High Rates of Symptoms of Major Depressive Disorder and Panic Disorder in a Canadian Sample of Adolescents With Juvenile Idiopathic Arthritis

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ABSTRACT. ***Objective.*** We aimed to evaluate the rate of depressive and/or anxiety symptoms in adolescents with juvenile idiopathic arthritis (JIA) and to explore the association with demographic and disease activity measures.

Methods. Depressive and anxiety symptoms were assessed in adolescents with JIA aged 12 to 18 years at a Canadian tertiary care hospital, using the Revised Child Anxiety and Depression Scale (RCADS). The RCADS includes 6 subscales: separation anxiety, social phobia, generalized anxiety, panic disorder, obsessive-compulsive, and major depressive disorder. Scores above clinical threshold on the RCADS subscales indicate that an individual's responses reflect symptoms similar to those diagnosed with the corresponding mental health disorder. Fisher exact test and Mann-Whitney *U* test were used to compare demographic and disease-related variables between participants who scored above and below clinical threshold on each of the subscales.

Results. There were 32/80 (40%) of participants who scored above clinical threshold on at least 1 subscale. Scores above clinical threshold were most frequent for major depressive disorder (23.8%) and panic disorder (22.5%) subscales. Social phobia and separation anxiety followed with 16.3% and 13.8%, respectively. Females were more likely to have scores above clinical threshold on the panic disorder subscale. Participants with higher self-reported disease activity were more likely to have scores above clinical threshold for all anxiety subscales except separation anxiety.

Conclusion. We report high rates of symptoms of depression and anxiety (panic in particular) in adolescents with JIA. This highlights the ongoing need for mental health screening protocols and services. The relationships between concomitant mental health disorders, disease activity, and patient-reported outcomes requires further research.

Key Indexing Terms: adolescent, anxiety, depression, juvenile arthritis

Adolescence is a period of heightened risk for the onset of mental health disorders, with approximately half of all psychiatric disorders starting between late adolescence and early adulthood.[1] In recent years, emphasis has been placed on understanding the prevalence and effect of mental health conditions in patients with pediatric-onset rheumatic diseases.[2] In 2019, a systematic review examining the prevalence of depression and anxiety in patients with juvenile idiopathic arthritis (JIA) found that 7% to 36% of children with JIA experience clinically significant depressive symptoms and 7% to 64% experience anxiety.[3] Fawole et al found an even higher prevalence estimate of 75% of patients with rheumatic disease (aged 14-24 yrs, the majority with JIA) reporting a clinician-diagnosed disorder and/or self-diagnosed mental health symptoms via an online survey.[4] Limitations to this study included the potential for self-selection bias and lack of a validated tool to measure mental health symptoms. In contrast, lower estimates were reported in a recent clinic-based study that used a standardized measure, wherein 33% and 30% of children and adolescents with JIA scored above threshold for depression and anxiety, respectively.[5] The variability reported in the literature likely reflects several factors, including study design, population(s) studied (eg, age, disease, geographic region), and measure(s) used to ascertain the presence or absence of mental health conditions. Collectively, however, the prevalence of mental health challenges in children and youth with rheumatic disease appears significant.

There is a pressing need to further understand the effect of the complex relationship between mental health and rheumatic

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disease on clinical care and measuring outcomes. This encompasses a wide range of disease-related factors, including underlying immunologic processes, disease activity, and patient-reported outcomes (PROs). For example, in adult inflammatory arthritis, evidence of a bidirectional relationship between mental health and disease activity exists, where targeting common inflammatory pathways shared between rheumatoid arthritis (RA) and depression may improve mental health outcomes.[6] There is also evidence that baseline depression or anxiety is associated with poorer health outcomes and reduced likelihood of response to treatment in RA and psoriatic arthritis (PsA).[7,8] There is emerging evidence that similar relationships exist in JIA. A systematic review by Treemarcki et al reviewed the impact of mental health on disease-related outcomes in pediatric rheumatic disease.[9] Multiple outcomes including disease activity, pain, disability, health-related quality of life, and peer relationships appear to be negatively associated with the presence of depression and anxiety in children and youth with JIA. A more recent report found an association between depressive and anxiety symptoms with pain and stress in adolescents with JIA but no association with measures of disease activity.[5]

At our institution, mental health screening of adolescents is routinely performed by members of the rheumatology multidisciplinary team comprising physicians, nurses, and other allied health professionals. Specifically, in early adolescence (age 12-13 yrs) a transition care pathway checklist, which includes inquiring about mood, is implemented in routine clinical care and the transition clinic.[10] In our clinic setting, concomitant mental health challenges appear to represent a high burden and contribute significantly to morbidity across this age spectrum. This study aimed to evaluate rates of depressive and/or anxiety symptoms in a clinic sample of adolescents with JIA and to explore the association with demographic and disease activity measures.

METHODS

English-speaking adolescents (aged 12-18 yrs) with a diagnosis of JIA for at least 6 months were eligible for this cross-sectional study performed at IWK Health, a Canadian tertiary care pediatric hospital in Eastern Canada. During regularly scheduled rheumatology clinic appointments, over a 3-month period (July-September 2019), eligible patients were consecutively approached to participate in an anonymous survey about their mental health. Written informed consent was obtained from all participants and informed assent was obtained from parents/guardians where appropriate. This study was approved by the IWK Research Ethics Board (file no. 1024594).

The rates of depression and anxiety symptoms were assessed using the Revised Child Anxiety and Depression Scale (RCADS). RCADS is a validated 47-item youth self-report questionnaire with acceptable reliability and 6 subscales: separation anxiety disorder, social phobia, generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, and major depressive disorder, as well as a total anxiety scale (sum of the 5 anxiety subscales) and a total internalizing scale (sum of all 6 subscales).[11] The RCADS subscales align with anxiety and depression diagnosis criteria in the Diagnostic and Statistical Manual IV (DSM-IV).[12] Each questionnaire item was rated by the participants on a scale of 0 to 4, based on frequency, with the numbers corresponding to "never," "sometimes," "often," and "always," respectively.[11] Raw scores were converted to *t*-scores with scores ≥ 65 indicating borderline clinical threshold for the subscale and ≥ 70 being positive for above clinical threshold. A *t*-score above clinical threshold on a subscale indicates that an individual's responses reflect anxiety and depression-related symptoms similar to those of individuals who meet the diagnostic criteria for the corresponding disorder.[11]

The RCADS questionnaire was input into REDCap (Research Electronic Data Capture), a secure web application for building and managing electronic surveys, allowing the participant to complete all questionnaire items on a tablet. Participants completed the questionnaire in the waiting room or clinic room prior to their appointment with the rheumatologist. As a safety measure, the attending rheumatologists were made aware that the patient consented to the study and they screened participants for any distress caused by completing the survey during the clinic visit so that this could be addressed if present.

In addition to completing the RCADS, participants also rated their present disease activity on a 0- to 10-cm visual analog scale (VAS; 0 = very well; 10 = very poorly). Other variables were collected by review of the health record including age, sex, school grade, date of JIA diagnosis, time since JIA diagnosis, JIA subtype (systemic, oligoarticular, polyarthritis rheumatoid factor [RF]-positive/negative, PsA, enthesitis-related arthritis [ERA], or undifferentiated), current medication use as defined by medications recorded on the day of study visit (including joint injections performed on day of study visit), active joint and enthesitis count, physician-reported presence/absence of widespread pain, and physician global assessment of disease activity (PGA; 10-cm VAS).

Clinical characteristics and RCADS subscale results were reported as median (range) or n (%) as applicable. Univariate statistical tests were used, specifically Fisher exact test (to compare proportions in small sample sizes) and Mann-Whitney *U* test (to compare independent samples in nonnormally distributed data). Demographic and disease-related variables (sex, age, self-reported disease activity and PGA, active joint count, enthesitis count, and absence or presence of widespread pain) were compared between participants with RCADS scale/subscale *t*-scores < 70 (below clinical threshold) and ≥ 70 (above clinical threshold). Two variables each had 1 missing value that was excluded from the analysis. The statistical software package R 4.1.3 with RStudio was used for the statistical analysis.[13,14]

RESULTS

Of the 82 consecutively approached patients, 80 (98%) consented to participate in the study. The study population, comprising 58 (73%) female and 22 (28%) male participants, had a median age of 15 years. The most frequent JIA subtypes were psoriatic (28%), oligoarticular JIA (20%), RF-polyarticular JIA (19%), and ERA (19%). Demographic and disease characteristics of the participants are shown in Table 1.

Forty percent of subjects scored higher than threshold in at least one of the individual subscales. The highest frequency of participants scoring above clinical threshold was on the major depressive disorder subscale (19 participants, 23.8%). Panic disorder, social phobia, and separation anxiety disorder followed, with 18 (22.5%), 13 (16.3%) and 11 (13.8%) participants scoring above clinical threshold, respectively. When clinical threshold and borderline were combined (*t*-scores ≥ 65), 30 (37.5%) participants scored above threshold on the panic disorder subscale, 23 (28.8%) on the major depressive disorder subscale, 17 (21.3%) on the total anxiety scale, and 19 (23.8%) on the total internalizing scale. Scoring results for each subscale are demonstrated in the Figure. Twenty percent of subjects scored above clinical threshold for 1 subscale, 7.5% for 2, 6.2% for 3, and 7.5% for ≥ 4 subscales. Of note, the study did not precipitate any identified distress that required specific intervention by the attending rheumatologist.

Table 1. Demographics and disease characteristics of study participants.

	Median (range)	n (%)
Age, yrs	15 (12-18)	–
School grade	9 (7-12)	–
Sex		
Male	–	22 (28)
Female	–	58 (73)
JIA subtype		
Enthesitis-related arthritis	–	15 (19)
Oligoarticular	–	16 (20)
Polyarticular RF–	–	15 (19)
Polyarticular RF+	–	4 (5.0)
Psoriatic	–	22 (28)
Systemic onset JIA	–	6 (8.0)
Undifferentiated	–	2 (2.5)
Current medications		
NSAID	–	36 (45)
Intraarticular corticosteroid injection	–	1 (1.3)
Oral corticosteroid	–	3 (3.8)
Intravenous corticosteroid	–	0 (0)
DMARD[a]	–	35 (44)
Biologic	–	36 (45)
Disease-related variables		
PtGA VAS (0-10 cm)	3 (0-9)	–
Active joint count	1 (0-39)	
Enthesitis count	0 (0-17)	
Presence of widespread pain		
Yes	–	12 (15)
No	–	65 (81)
Did not specify		3 (4)
PGA VAS (0-10 cm)	1 (0-7)	–

[a] DMARDs include methotrexate, leflunomide, sulfasalazine. DMARD: disease-modifying antirheumatic drug; JIA: juvenile idiopathic arthritis; NSAID: nonsteroidal antiinflammatory drug; PGA: physician global assessment; PtGA: patient global assessment; RF: rheumatoid factor; VAS: visual analog scale.

In the exploratory analysis, females were more likely than males to score above clinical threshold on the panic disorder subscale (P = 0.02). Participants with higher self-reported disease activity were more likely to score above clinical threshold on all anxiety subscales except separation anxiety ($P < 0.05$). Physician report of widespread pain was associated with t-scores ≥ 70 on the obsessive-compulsive disorder subscale (P = 0.01). A higher enthesitis count was also significantly associated with being above clinical threshold for the social phobia subscale (P = 0.03). There were no other statistically significant relationships between t-scores ≥ 70 (above threshold) on each of the subscales and the demographic and clinical characteristics (Table 2).

DISCUSSION

In this study comprising data from almost all consecutively approached adolescents with JIA in a pediatric rheumatology clinic, we demonstrated a significant, and concerning, burden of mental health issues, in keeping with other reports.[3,4] Forty percent of patients scored above clinical threshold in at least one of the individual subscales. One-fifth of patients scored above the clinical threshold for at least 2 subscales. Major depressive disorder and panic disorder were the subscales in which patients exceeded clinical threshold the most frequently (23.8% and 22.5%, respectively).

The high rate of mental health symptoms in this adolescent JIA population has several implications for clinical care, including emphasizing the importance of screening for concomitant mental health disorders, ensuring appropriate access to mental health care, and the need for a shared-care approach between rheumatology and mental healthcare providers. The importance of mental health screening while adolescents are receiving rheumatologic care is further emphasized by a recent study in which adolescents indicated they were most comfortable disclosing mental health concerns to their rheumatologist over other healthcare providers.[4] Second, it is also possible that the rheumatology clinic is the only point of contact with the healthcare system, as primary healthcare utilization is known to decrease as youth progress through adolescence into young adulthood.[15,16] Although mental health screening is imperative in identifying youth for early and effective treatment, access to appropriate mental health care is crucial. Unfortunately, many unmet needs have been described in youth facing mental health challenges, including long delays in receiving appropriate care, high rates of disengagement after receiving care, and difficulties encountered by youth when transitioning from pediatric to adult health care.[17] Given the long-term implications of inadequately treated mental health disease in youth, there has been recent focus on improving youth mental health services nationally and regionally in Canada.[17] At a local and institutional level, it is important for pediatric rheumatologists to advocate for their patients in accessing mental health care given the system-level barriers. Interestingly, one study found that the most cited barrier to accessing mental health services by youth with rheumatic disease is the fear that mental healthcare providers will not be knowledgeable about their rheumatic condition.[15] This underscores the importance of continued dialogue, including disease-specific education, between rheumatology and mental health when caring for these youth.

In the exploratory analysis, self-reported disease activity correlated with scoring above clinical threshold on all anxiety subscales, except separation anxiety. Scoring above clinical threshold on the panic disorder subscale was associated with female sex, obsessive-compulsive disorder subscale with physician report of widespread pain, and social phobia subscale with higher enthesitis count. Physician-reported disease measures, which included disease activity and active joint count, did not correlate with scoring above clinical threshold on any subscale. Hanns et al found that anxiety and depressive symptoms in youth with JIA did not correlate with active joint count or inflammatory markers; however, they did find that these symptoms were associated with pain, disability, and PGA (patient global assessment was not assessed).[18] The same group examined levels of depression in a prospective JIA cohort and found that depressive symptoms were associated with pain, disability, and active joint count at diagnosis. After 4 years of follow-up, it was higher depressive symptoms at baseline, and not active

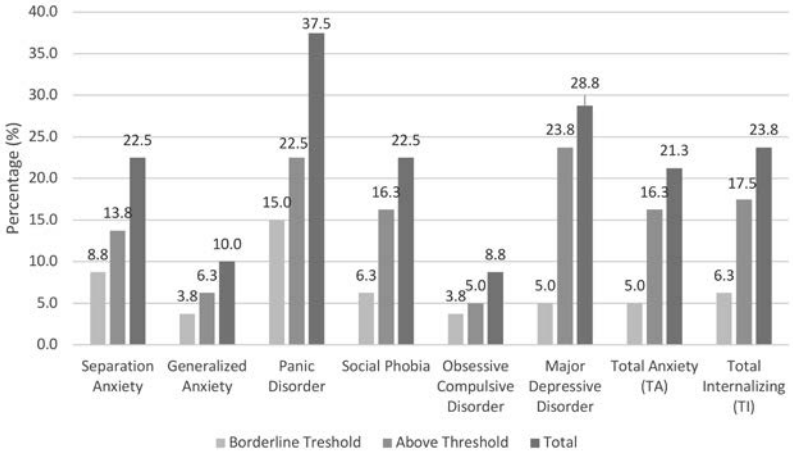

Figure. Percentage of participants scoring above borderline and clinical thresholds by RCADS subscale. RCADS: Revised Child Anxiety and Depression Scale.

Table 2. Comparison of demographic and disease-related variables between participants scoring below and above clinical threshold (*t*-score ≥ 70) on the RCADS subscales.

Subscale	Separation Anxiety *t*-score ≥ 70			Generalized Anxiety *t*-score ≥ 70			Panic Disorder *t*-score ≥ 70		
	No	Yes	*P*	No	Yes	*P*	No	Yes	*P*
Sex (F/M)	48/21 (69.6/30.4)	10/1 (90.9/9.1)	0.27[a]	54/21 (72.0/28)	4/1 (80/20)	> 0.99[a]	41/21 (66.1/33.9)	17/1 (94.4/5.6)	**0.02**[a]
Age, yrs	15.0 (13.0-16.0)	15.0 (13.5-16.0)	0.97	15.0 (13.0-16.0)	15.0 (13.0-15.0)	0.61	15.0 (13.0-15.0)	15 (14.0-16.0)	0.80
AJC	1.0 (0-3.0)	0 (0-4.0)	0.36	1.0 (0-3.0)	1.0 (1.0-7.0)	0.40	1.0 (1.0-3.0)	0.5 (0-6.0)	0.89
PtGA VAS	3.0 (0.5-5.0)	5.0 (1.8-7.0)	0.21	2.8 (0.5-5.0)	6.0 (5.0-8.0)	**0.02**	2.5 (0.5-4.5)	5.0 (2.5-6.0)	**0.03**
PGA VAS	1.5 (0-2.5)	0.50 (0-2.5)	0.51	1.0 (0-2.5)	2.0 (2.0-3.0)	0.11	1.0 (0-2.4)	1.8 (0.5-2.9)	0.38
Enthesitis count	0 (0-0)	0 (0-0)	0.91	0 (0-0)	0 (0-0)	0.98	0 (0-0)	0 (0-1.8)	0.64
WSP, presence/absence	60/9 (87.0/13)	8/3 (72.7/27.3)	0.36[a]	65/10 (86.7/13.3)	3/2 (60/40)	0.16[a]	53/9 (85.5/14.5)	15/3 (83.3/16.7)	> 0.99[a]

	Social Phobia *t*-Score ≥ 70			Obsessive-Compulsive Disorder *t*-Score ≥ 70			Major Depressive Disorder *t*-Score ≥ 70		
	No	Yes	*P*	No	Yes	*P*	No	Yes	*P*
Sex (F/M)	48/19 (71.6/28.4)	10/3 (76.9/23.1)	> 0.99[a]	54/22 (71.1/28.9)	4/0 (100.0/0)	0.57[a]	53/8 (86.9/13.1)	15/4 (78.9/21.1)	0.47[a]
Age, yrs	15.0 (13.0-16.0)	16.0 (14.0-16.0)	0.46	15.00 (13.0-16.0)	15.00 (14.8-15.5)	0.68	15.0 (13.0-16.0)	15.0 (13.0-16.0)	0.68
AJC	1.0 (1.0-3.0)	1.0 (0-11.0)	0.38	1.00 (0-3.0)	6.00 (0-12.3)	0.60	1.0 (0-3.0)	1.0 (0-8.0)	0.62
PtGA VAS	2.5 (0.5-4.9)	5.0 (3.0-7.5)	**0.03**	3.00 (0.5-5.0)	6.75 (5.6-7.9)	**0.01**	2.5 (0.50 4.5)	4.7 (1.5-7.23)	0.06
PGA VAS	1.0 (0-2.5)	2.0 (0.5-3.0)	0.22	1.3 (0-2.5)	2.0 (0.8-3.1)	0.62	1.0 (0-2.0)	2.0 (0.5-3.0)	0.25
Enthesitis count	0 (0,0)	0 (0-5.0)	**0.03**	0 (0-0)	0 (0-2.3)	0.61	0 (0-0)	0 (0-0)	0.70
WSP, presence/absence	56/11 (83.6/16.4)	12/1 (92.3/7.7)	0.68[a]	67/9 (88.2/11.8)	1/3 (25.0/75)	**0.01**[a]	53/8 (86.9/13.1)	15/4 (78.9/21.1)	0.47[a]

Values are expressed as median (IQR) or n (%). Values in bold are statistically significant. [a]Fisher exact test was used to compare proportions (Mann-Whitney *U* test was used for all other comparisons). AJC: active joint count; PGA: physician global assessment; PtGA: patient global assessment; VAS: visual analog scale; WSP: widespread pain.

joint count, that predicted disability and pain.[19] Fair et al, who recently studied mental health using the Patient Reported Outcomes Measurement Information System (PROMIS) found no correlation with disease activity as measured by the clinical Juvenile Arthritis Disease Activity Scale.[5] Taken together, it appears that disease activity (eg, active joint count) may not be the dominant factor driving key PROs over time; rather, mental health and cognitive variables may be more important.

After major depressive disorder, panic disorder was the scale that had the most participants scoring above clinical threshold. If borderline threshold is included, the panic disorder subscale was the most frequently endorsed with over one-third of participants (37.5%) borderline or above. Female participants were also more likely to score above clinical threshold on this scale. To our knowledge, panic disorder symptom prevalence, which may be unique to the questionnaire we used, has not been reported previously. Other studies in JIA have focused primarily on a global assessment of anxiety and depression alone.[3,8,18,19] An exception was the study by Bomba et al, where anxiety was broken down into subscales (generalized anxiety, social anxiety, separation anxiety, school anxiety) and higher scores were seen in patients compared with controls in all subscales; however,

panic disorder was not assessed.[20] Interestingly, panic disorder, among other psychiatric disorders, may involve dysfunctional interoception—the perception of the physiological state of the body—which can also be dysfunctional in many chronic inflammatory conditions such as arthritis.[21] Why panic disorder was proportionately more common in our sample of youth with JIA deserves further study.

It is important to note limitations in our study, including measurement of a narrow range of PROs. We did not measure patient-reported pain, disability, or health-related quality of life, all of which are also important when considering mental health in this population. As the study was cross-sectional, we did not capture how mental health and other variables change over time. Psoriatic JIA appeared to be overrepresented in our study population, whereas oligoarticular JIA was underrepresented, compared with typical estimates of JIA subtype distribution.[22] Children with oligoarticular JIA generally have more favorable outcomes and are seen less often in follow-up, which likely explains less recruitment over our 3-month study. Finally, the study was completed prior to the coronavirus disease 2019 (COVID-19) pandemic, a time during which adolescents were experiencing higher levels of mental health symptoms compared to pre-pandemic levels.[23]

In conclusion, this study of Canadian adolescents with JIA adds to the emerging literature highlighting the crucial need to understand the multifaceted relationship between mental health and rheumatic disease. It is very encouraging that researchers from around the world, in consultation with youth, and parents, have recently defined actionable priorities for a mental health research agenda in this vulnerable population.[2]

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