Anxiety and Depression in Childhood Rheumatologic Conditions: A Topical Review

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Abstract

This topical review summarizes recent literature on mental health symptoms experienced by children diagnosed with rheumatologic conditions including childhood-onset systemic lupus erythematosus (cSLE), juvenile idiopathic arthritis (JIA), and juvenile dermatomyositis (JDM). Studies, while limited, generally indicate that anxiety and depressive symptoms may be more common among children diagnosed with rheumatologic conditions than non-chronically ill children. Although the rates of clinically significant symptoms are not consistently reported across studies, overall anxiety and depressive symptom rates in cSLE vary between 34%–37% and 6.7%–59%, respectively. A recent systematic review of JIA suggests between 7% and 64% of participants experienced elevated anxiety, and between 7% and 36% of participants reported clinically significant depressive symptoms. Approximately 40% of youth with JDM may experience general psychological distress, but more research is needed. In the available literature, there is mixed support for higher rates of anxiety in JIA as compared to cSLE, and higher rates of depressive symptoms in cSLE as compared to JIA, whereas mental health functioning in JDM is less well understood. Mental health functioning in youth with rheumatologic conditions may be related to increased disease-related impairment. Using consistent mental health screening measures with clinically validated cutoffs would enhance insight into the frequency and impact of anxiety and depressive symptoms experienced. Knowledge would also be enhanced by conducting studies with ethnically representative samples to identify potential disparities in care. An improved understanding of mental health functioning in pediatric patients presenting for rheumatologic care may inform the development and testing of tailored and effective treatments.

Key Words: *Anxiety, childhood-onset systemic lupus erythematosus, depression, juvenile dermatomyositis, juvenile idiopathic arthritis, mental health*

Introduction

Pediatric rheumatologic conditions are chronic, autoimmune diseases requiring systemic immunosuppression and nonpharmacologic treatments to manage both physical and psychosocial symptoms. Among the most common pediatric rheumatologic conditions are childhood-onset systemic lupus erythematosus (cSLE), juvenile idiopathic arthritis (JIA), and juvenile dermatomyositis (JDM), which are the focus of this current review. In the limited research thus far, mental health problems may be more common across these conditions than among healthy individuals and have been shown to have adverse impacts on functioning. The goal of this topical review was to conduct a literature review on mental health impacts of cSLE, JIA, and JDM, compare across conditions when possible, and identify knowledge gaps.

Methodology

For cSLE and JIA, we searched English language original research

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manuscripts and systematic reviews published within the last 5 years, between January 2015 and April 2020 [Table 1]. Since there were comparatively fewer studies examining mental health in JDM, studies from 2009 onward were included.

We looked for mental health terms combined with terms for cSLE, JIA or JDM. Mental health terms included: "Mental health" OR "Anxi OR Depress." Rheumatologic disease terms included "childhood-onset

Table 1. Anxiety and Depressive Symptoms Rates in Childhood Rheumatologic Conditions*

Condition	Authors	*n* (% female)	Age range (mean)	Race/ethnicity %	Primary study goal and screening measure	Mean (SD)% met cc-offs	
						Anxiety symptoms	Depressive symptoms
cSLE	Petrongolo *et al*., 2020	31 (61)	9-18 (14.5)	African American 38.7 Caucasian 35.5 Latino/Hispanic 12.9 Multiracial 12.9 Caribbean 3.2 African 3.2 Asian American 3.2 Native American 3.2 Other 3.2	Parent illness uncertainty in relation to child mood (PROMIS), anxiety (PROMIS), and HRQOL	39.2 (7.1) Not reported	43.2 (8.4) Not reported
	Cunningham *et al*., 2019	18 (94)	13-19 (16.2)	Caucasian 61 African American 16 Asian American 11 Hispanic/Latino 5 More Than One Race 5	Development of psychological treatment for cSLE (CDI and SCARED)	26.8 (14.5) Not reported	17.4 (7.8) Not reported
	Davis *et al*., 2018	51 (92)	7-22 (16.2)	Caucasian 38.1 Black 38.1 Hispanic 14.3 Asian 9.5	Depressive symptom (PHQ-9) and medication adherence	N/A	Not reported 14 (SI) 59 (mild symptoms)
	Donnelly *et al*., 2018	50 (84)	11-20 (16.2)	African American 46 Caucasian 8 Hispanic 8 Other 8	QOL, anxiety (SCARED) and depressive symptoms (CDI)	17.4 (12.1) 34	9.1 (8.1) 26
	Jones *et al*., 2017	100 (80)	9-20 (15.8)	White 33 African American 48 Hispanic 8Other 11	Feasibility of PROMIS to measure anxiety and mood	51.1 (12.1) Not reported	47.8 (11.9) Not reported
	Uzuner *et al*., 2017	41 (78)	9-18 (14.7)	Not Stated	QOL, anxiety (STAI) and depressive symptoms (CDI)	29.3 (5.3) Not reported	9.3 (6.2) Not reported
	Al-Obaidi *et al*., 2016	27 (81)	4-15 (11.0)	Afro-Caribbean 40.7 Pakistani 14.8Caucasian 25.9Mixed Ethnicity 4.8	MRI findings in youth with neuropsychiatric cSLE and prior mental health dx	Not reported 25.9 prior dx	Not reported 62.9 prior dx
	Knight *et al*., 2016	970 (85)	10-18 (14.7)	African American 42 White 15 Latino 27 Other 16	Psychiatric diagnostic and treatment disparities	Not reported 7	Not reported 19
	Knight *et al*., 2015	50 (86)	>8 (15.6)	Black 36 White 46 Other 18	Depressive (PHQ-9) and anxiety symptoms (SCARED) in cSLE compared to diabetes cohort	Not reported 22	Not reported 20
	Knight *et al*., 2015	16 (81)	15.0 (3.4^)	White 63 Black 25 Asian 6 Latino 6	Qualitative experience of depressive (PHQ-9) and anxiety (SCARED) symptom screening	Not reported 31	Not reported 25 (depressive symptoms) 25 (SI)

Contd...

JIA	Bano *et al*., 2020	100 (46)	<6 (17.4)	Pakistani youth	Depression (CES-D) in youth with JIA in tertiary care	N/A	23.6 (12.7) 72
	Kyvsgaard *et al*., 2020	121 (67)	9-19 (13.3)	Not reported	Is methotrexate-induced nausea is associated with anxiety (BAI)?	26 (22-30) 57 (extreme) 37 (moderate)	N/A
	Rebane *et al*., 2019	195 (78)	18-30 (22)	Not reported	Factors, such as mood (BDI) in relation to pain interference	N/A	9.4 (10.7)
		145 (77)		White 87		48.6 (11.8)	Not reported
	Connelly *et al*., 2019		12-18 (14.5)	American Indian/ AlaskanNative 1	Self-management program and measures of anxiety and depressive symptoms (PROMIS)	N/A	47.2 N/A (11.2)
				Asian 3			N/A
				Black/African American 2			
				Nat. Hawaiian/Pac.Islander 0			
				Other 7			
	Trawicka *et al*., 2019	29 (62)	11-17 (14.3)	Not reported	Internalizing and externalizing problems of chronically ill youth (YSA)	7.7 (6.4) 40.7	7.7 (6.4) 40.7
	Hanns *et al*., 2018	102 (56)	11-16 (3.2)	Not reported	Depressive symptoms (MFQ) in relation to pain, disability, and disease	N/A	13.0 (6.0) 14.7
	Kayan Ocakoglu *et al*., 2018	24 (28)	4-18 (14)	Not reported	Anxiety (SCARED) and depressive (CDI) symptoms	18 (median)	9.0 (8.1)
		51 (55)		Not reported		2-44 (range)	Not reported
	Memari *et al*., 2016		6-18 (11)		Behavior problems (CBCL) in JIA	25 Not reported	Not reported 27

^Baseline data. *There are currently no published peer-reviewed studies of mental health functioning in JDM for inclusion in this table. There were also two systematic reviews of mental health functioning in cSLE (Quilter *et al*., 2019), and JIA (Fair *et al*., 2019). n: Sample, N/A: Not applicable, SD: Standard deviation, cc: Clinical cutoff, cSLE: Childhood-onset systemic lupus erythematosus, JIA: Juvenile idiopathic arthritis, dx: diagnoses, PROMIS: Patient-Reported Outcomes Measurement Information System, QOL Quality of life, HRQOL: Health-related QOL, CDI: Children's Depression Inventory, SCARED: Screen for Childhood Anxiety and Related Emotional Disorders, PHQ-9: Patient Health Questionnaire, SI: Suicidal ideation, STAI: State-Trait Anxiety Inventory, BDI: Beck Depression Inventory, BAI: Beck Anxiety Inventory, YSA: Youth Self Report, MFQ: Mood and Feelings Questionnaire, CES-D: Center for Epidemiologic Studies Depression Scale, CBCL: Child Behavioral Checklist, JDM: Juvenile dermatomyositis

lupus" OR "juvenile idiopathic arthritis" OR "juvenile dermatomyositis." We searched PubMed/Medline (results revealed 1253 abstracts) and cross-checked the search via Google Scholar, which yielded a similar number studies. Studies that focused on pediatric literature were included, and, in the case of mixed pediatric/adult samples, information pertaining to youth were obtained. Research articles that focused solely on adults were generally excluded, except in cases where there were too few pediatric studies available (e.g., JDM). Our abstract-level database search yielded 15 appropriate articles. We also queried co-authors who are experts in the areas of mental health in pediatric rheumatologic conditions broadly (AK, AD, NRC) and in JDM specifically (KA) to identify three additional original research articles. We included a total of 18 articles.

The racial/ethnic group categories in the original research articles were used to describe the extent of diversity in these samples and therefore vary in the manuscript. We have taken this approach since race/ethnicity is often self-reported using categories provided in each study, which may differ across studies.

Results

Childhood-onset systemic lupus erythematosus

A systematic review revealed anxiety (34%–37%) and depressive symptoms (6.7%–59%) were common.[1] A recent study suggested the most common psychosocial problems in youth with cSLE include fatigue (65%), pain (40%), anxiety (37%), and depressive symptoms (30%).[2] Higher levels of fatigue, pain, and anxiety were also related to poorer health-related quality of life (HR-QoL), which is similar to findings that anxiety and peer victimization are predictive of poor QoL in cSLE.[3] Patients categorized by high levels of fatigue and depressive symptoms were more likely to have a poorer HR-QoL after 6 months.[4] There is some evidence of a positive association between depressive symptoms and medication-non-adherence in cSLE.[5] Further, the presence of an anxiety disorder is associated with abnormal MRI findings, the most common of which was white matter hyperintensities.[6]

In terms of factors that impact mental health care for youth with cSLE, belonging to a minoritized racial group was found to be a risk factor for depression in cSLE, and minoritized youth are less likely to be diagnosed and/or treated for mental health problems as compared to racially minoritized youth who are less likely to be treated for mental health.[7,8] Individuals diagnosed with cSLE versus adult-onset SLE are at greater risk for developing depression over the long term. Caregiver uncertainty about their child's illness also affects child mental health.[9]

Even though pediatric rheumatologists recognize that mental health problems are common in youth with cSLE and most believe mental health screening should be standard of care, the vast majority (~98%) do not routinely conduct such screenings.[10] Importantly, youth with cSLE and their parents identified rheumatologists as their primary care physicians and reported mental health care in rheumatology to be preferred.[11] A tailored psychological intervention to address mental health concerns for youth with cSLE has been developed[12] and a randomized clinical trial is currently underway.

Juvenile idiopathic arthritis

Results from a recent systematic review[13] found that children with JIA experience anxiety (7%–64%) and depressive symptoms (7%–36%) at similar rates to children with other chronic health conditions,[14] but at greater rates than healthy youth,[13,14] and these symptoms are related to poorer HR-QoL. Both internalizing and externalizing symptoms may be more common in youth with JIA compared to healthy youth.[15,16] More recent research has found higher rates of depression (>70%) in a sample of youth with JIA presenting to a tertiary care hospital.[17] In addition, increased anxiety related to pain[18] and depressive symptoms[19] may be positively associated with pain interference. Another study found that methotrexate-induced nausea was associated with greater anxiety in JIA, particularly for females.[20] However, it is unknown how mental health symptoms directly impact disease activity,[13] though there is emerging evidence that depression may be related to disease severity[17] and is generally correlated with clinical disease measures.[19] In 2020, a "CAREGIVERS" questionnaire was developed to measure caregiver and clinician perspectives on the impact of JIA, including the psychosocial impact, potentially enabling improvement in the assessment and subsequent quality of care for youth and families.[21] An online self-management program using cognitive behavioral strategies may be beneficial[22] in improving emotional and pain-related outcomes.

Juvenile dermatomyositis

In comparison to SLE and JIA, research on mental health conditions in JDM is more limited. In one study, >40% of patients with JDM reported sufficient psychologic distress to warrant referral to a mental health specialist.[23] However, a Norwegian study of adults with juvenile-onset dermatomyositis found no differences in mental health functioning compared to matched healthy controls.[24] Over 40% of adult dermatomyositis patients met the criteria for depression or anxiety, with a third of those patients receiving no mental health care.[25] Patients with JDM had significantly decreased psychosocial functioning scores compared to healthy children, even among those who had responded well to immunosuppressive treatment.[26] Similarly, in another study of 490 patients, 12.8% of patients with JDM had decreased HR-QoL in psychosocial domains, with 5% showing major impairment.[27] JDM is often associated with pain, fatigue, and disrupted sleep, which can adversely impact psychosocial function.[28] In a focus group study with parents of children and young adults with JDM, mental health and access to mental health care were major concerns.[29] The diagnosis of JDM has been shown to increase strain on family relationships and worry amongst parents,[30] and lead to uncertainty, feeling different, and doubt about future for children with JDM.[31]

Discussion

Although research on mental health care in rheumatologic disease is limited, this review nevertheless finds anxiety and depression are prevalent, yet remain infrequently assessed and undertreated. Potential ways to overcome barriers to mental health treatment include training, standardized mental health screening and treatment, as well as multidisciplinary care within the rheumatology setting that includes access to a mental health provider, particularly given that families perceive pediatric rheumatologists as their preferred source for primary care and mental health care.[10,11] Moreover, the rheumatology clinic often serves as the patient's medical home. As such, rheumatologists have the unique opportunity to enhance patient care by screening and referring to the treatment of mental health concerns.

Based on current findings, the variability of screening tools may limit the ability to pinpoint the prevalence and course of anxiety and depression. Therefore, it is important to use consistent, psychometrically sound screening tools with clinical cutoffs so comparisons across and within studies can yield insight into illness prevalence, course, and impact. The American Academy of Pediatrics offers a list of validated tools, including those with clinical cutoffs that are freely available, https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Mental-Health/Documents/MH_ScreeningChart.pdf. Many of these tools have also been used in pediatric rheumatology studies [Table 2].

Table 2. Mental Health Screening Tools Used in Pediatric Rheumatology Settings

Measure name	Screening details	Target age	Admin time (min)	Cutoffs (Yes/No)
Anxiety measures				
BYI-Anxiety Inventory	Total raw score is calculated summing up the 20 items (ranging 0-60). Sum is converted to a T-score. T-scores interpreted: <55=Average. 55.0-59.9=Mildly elevated. 60.0-69.9=Moderately Elevated. 70 and over=Extremely Elevated.	7-18	5	No
SCARED*	A 41-item measure scored on a 3-point Likert scale and summed to create a total score ranging from 0 to 82. A total score ≥25 reflects clinically significant anxiety.	8-18	10	Yes
STAIc	A 4-point Likert scale consisting of 40 questions. Measures state anxiety and trait anxiety. The range of scores for subtests is 20-80. Higher score indicates greater anxiety. A cut point of 39-40 suggested as clinically significant.	9-12	10	Yes
PROMIS*	Anxiety symptoms for past 7 days rated onLikert scale from 1 (never) to 5 (almost always). Sum is converted to a T-score. Higher scores indicate more symptoms. T-scores interpreted: <50=Within normal limits. 50.0-54.9=Mild. 55.0-64.9=Moderate. 65 and over=Severe.	8-17	5	No
CBCL	A 113 question, parent and youth report used to identify the frequency of problem behaviors. Scores below the 93rd percentile are considered normal. Scores between the 93-97th percentile are borderline clinical, and scores above the 97th percentile are in the clinical range	6-18	10	Yes
Depressive symptom measures				
PHQ-9*	Nine-item measure based on DSM-IV criteria for major depression for the prior 2 weeks. Scored on scale0 (not at all) to 3 (nearly every day). Total score range 0-27. Mild depression=5-9, moderate depression=10-14, moderately severe depression=15-19, severe depression=20-27.	12 and older	5	Yes
CDI	Twenty-eight items on depressive symptoms in the past 2 weeks. Each item is presented in three statements of varying symptom severity. Cut point between 17-19 reflects clinically relevant depression.	7-17	5	Yes
MFQc*	The short from has 13 questions; the long form has 33 items. Responses are not true=0, somewhat true=1, true=2. Scores on the short form range from 0-26, and 0-66 on the long form. Scores>12 on short scale and scores>27 on long scale are suggestive of clinical depression but support for these cut-offs is mixed.	6-17	5-10	No
PROMIS*	Depressive symptoms for past 7 days rated from 1 (never) to 5 (almost always). Sum is converted to a T-score. Higher scores indicate more symptoms.T-scores interpreted: <50=Within normal limits. 50.0-54.9=Mild. 55.0-64.9=Moderate. 65 and over=Severe.	8-17	5	No
CES-DC*	A 20-item, self-report inventory with possible scores ranging from 0-60. Cumulative CES-DC scores <15 indicate no depression, whereas scores ≥15 indicate significant depression.	6-17	5	Yes
CBCL	A 113 question, parent and youth report used to identify the frequency of problem behaviors. Scores below the 93rd percentile are considered normal. Scores between the 93-97th percentile are borderline clinical, and scores above the 97th percentile are in the clinical range.	6-18	10	Yes

*Measure is freely available. BYI: Beck Youth Inventories, STAIc: State-Trait Anxiety Inventory for children, SCARED: Screen for Childhood Anxiety and Related Emotional Disorders, PHQ-9: Patient Health-Questionnaire, CDI: Children's Depression Inventory, CBCL: Child Behavioral Checklist, MFQc: Mood and Feeling Questionnaire for children, PROMIS: Patient-Reported Outcomes Measurement Information System, CES-DC: The Center for Epidemiological Studies Depression Scale for children, DSM: The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition

Mental health burden and its relationship to rheumatologic conditions, and the impact of mental health on patient outcomes, were among the most important research priorities identified by the multidisciplinary team and patient/caregiver members of the Childhood Arthritis and Rheumatology Research Alliance Mental Health Workgroup.[32] In addition, a recent survey among interdisciplinary cSLE clinicians reported mental health

as a middle-priority research topic compared to other illness domains.[33] Despite limited evidence of the direct association between mental health and disease severity, there is clearer evidence of a relationship between anxiety and depressive symptoms and factors pertinent to treatment, such as medication adherence,[5] and pain experience.[18]

At present, most research on mental health functioning in youth with rheumatologic conditions is cross-sectional; therefore, additional longitudinal studies are needed. Moreover, rigorous controlled trials that assess feasibility, acceptability, and that employ a mixed methods approach to qualitatively capture patient and caregiver perspectives would enhance future research and insights. Further, additional primary mental health investigations in the field of JDM would enhance clinician's responses to the mental health needs of youth patients.

Our knowledge of mental health within specific disease groups would also be enhanced by conducting studies with racially and ethnically representative samples to identify disparities in care, and opportunities to achieve health equity for children with rheumatologic conditions. At present, some studies did not report racial/ethnic groups at all, limiting the capacity for sub-analysis. Further investigations that report racial/ethnic groups will allow us to identify differences in mental health care and overall health outcomes among these groups, in addition to enhancing understanding of socioeconomic and environmental circumstances. Race/ethnicity are not biological categories, they are only social constructs; however, racism and discrimination are real experiences with a significant influence on health outcomes, leading to health disparities. Therefore, data analysis must be conducted to account for the influence of race/ethnicity (as proxies for racism/discrimination) as well as other factors (e.g., socioeconomic status and geography) that may relate to mental health outcomes.[34] We know that disparities exist, and by working to further identify these disparities, we can work toward eliminating them. For example, capturing such information may bolster new treatment techniques and may increase clinician knowledge regarding how patients and caregivers may be optimally supported. In summary, investigating anxiety and depression in youth with rheumatologic conditions is important because these are common problems posing threats to recovery and treatment adherence. Enhanced understanding of mental health functioning in youth with rheumatologic conditions may offer clinically meaningful insights into disease management.

Summary

Our analysis of recent literature suggests that depression and anxiety symptom prevalence rates across pediatric rheumatologic conditions vary, with mixed support that anxiety may be more pronounced in JIA as compared to cSLE, whereas depressive symptoms may be more prominent in cSLE versus JIA.[1,13] However, this might be attributed to the small number of primary investigations on mental health, and the use of small and potentially unrepresentative samples. Mental health in JDM, in particular, is not well understood and deserves further study. The variation in self-report scales used is an additional challenge that has been previously documented in rheumatologic literature.[35] Consistent use of measures with clinically validated cutoffs would improve understanding of patient mental health. In addition, the presence of mental health conditions may impact disease severity or treatment adherence across conditions. More research is needed to understand the prevalence of mental health problems, their relationship with disease outcomes, disparities in care as related to race/ethnicity, and devising optimal mental health treatments in patients with rheumatologic conditions.

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Conflicts of interest

There are no conflicts of interest.

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