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Identifying Differences in Risk Factors for Depression and Anxiety in Pediatric Chronic Disease: A Matched Cross-Sectional Study of Youth with Lupus/Mixed Connective Tissue Disease and Their Diabetic Peers

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Abstract

Objective—Depression and anxiety are associated with poor clinical and psychosocial outcomes in youth with chronic disease. To investigate differences in risk factors for depression and anxiety, like central nervous system (CNS) involvement in systemic lupus erythematosus (SLE)/mixed connective tissue disease (MCTD), we compared SLE/MCTD youth to type 1 diabetes mellitus (T1D) peers.

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Study Design—We conducted a cross-sectional study of 50 outpatient pairs, ages 8 years and above, matching SLE/MCTD and T1D subjects by sex and age group. We screened for depression, suicidal ideation and anxiety using the Patient Health Questionnaire 9 and the Screen for Childhood Anxiety Related Disorders, respectively. We collected parent-reported mental health treatment data. We compared prevalence and treatment rates between SLE/MCTD and T1D subjects, and identified disease-specific risk factors using logistic regression.

Results—Depression symptoms were present in 23%, suicidal ideation in 15% and anxiety in 27% of participants. Compared to T1D, SLE/MCTD subjects had lower adjusted rates of depression and suicidal ideation, yet poorer rates of mental health treatment (24% vs 53%). Non-white race/ethnicity and longer disease duration were independent risk factors for depression and suicidal ideation. Depression was associated with poor disease control in both groups, and anxiety with insulin pump use in T1D subjects.

Conclusion—Depression and anxiety are high and undertreated in SLE/MCTD and T1D youth. Focusing on risk factors such as race/ethnicity and disease duration may improve their mental health care. Further study of CNS and other disease-related factors may identify targets for intervention.

Keywords

pediatric; adolescent; mental health; suicidal ideation; chronic disease; disparities

Introduction

Chronic disease presents both physical and emotional challenges for affected children and adolescents. Pediatric-onset systemic lupus erythematosus (SLE) and the SLE-like syndrome of mixed connective tissue disease (MCTD) are chronic autoimmune diseases associated with high morbidity and mortality due to the multi-organ damage, particularly due to central nervous system (CNS) and renal involvement, as well as high-risk immunosuppressive treatment.[1] In contrast to the prevalence of depression in 11%, suicidal ideation in 6% and anxiety in 8% of the United States general adolescent population,[2, 3] these disorders occur in up to 60%, 20% and 35%, respectively, of youth with SLE/MCTD.[4-6] While the cause of this remains unclear, potential reasons include social, cultural and genetic factors in the predominantly non-white SLE/MCTD population, the psychological burden of chronic disease, effects of steroid treatment and CNS inflammation, which is recognized as a cause of mood and anxiety disorders in SLE.[7] Among youth with SLE/MCTD and other chronic disease, there is little known about differences in depression and anxiety etiology between disease groups, and elucidating the contributing factors may guide more effective recognition and treatment of these conditions in these patients. This is of critical importance, as depression and anxiety in chronic disease have been shown to negatively impact clinical and psychosocial outcomes, resulting in poorer disease control, quality of life, school performance, transition to adult care, work productivity and greater healthcare utilization and costs.[8-12]

To explore the role of disease-specific factors in depression and anxiety in youth with SLE/MCTD, we compared these patients to youth with type 1 diabetes mellitus (T1D), who are

similar in their burden of life-threatening disease, potential multi-organ involvement, and requirement for lifelong systemic medication, but different in their lower risk for direct CNS inflammation. In the setting of emerging knowledge of the role of inflammation in psychiatric disorders,[13, 14] we sought to investigate differences in depression and anxiety between these chronic disease groups with known differential risk for CNS inflammation. Using a matched analysis to eliminate confounding by sex and age, which have known associations with both SLE/MCTD[1] and depression/anxiety,[2] we specifically aimed to compare youth with SLE/MCTD and T1D with respect to: 1) prevalence of depression, suicidal ideation and anxiety symptoms; 2) rate of mental health treatment in those with symptoms; and, 3) association of depression and anxiety symptoms with disease-specific factors. We hypothesized that: 1) SLE/MCTD subjects would have a higher prevalence of depression and anxiety than T1D subjects; 2) rates of mental health treatment would not differ, and 3) depression and anxiety would be associated with higher disease burden in both cohorts.

Methods

We conducted a cross-sectional analysis of outpatient youth with SLE/MCTD and T1D at The Children's Hospital of Philadelphia (CHOP). The two cohorts were matched by sex and age group to eliminate confounding by these factors, because pediatric-onset SLE is known to be more prevalent in adolescent females[1] and the incidence of childhood depression and anxiety peaks in adolescent females.[2] Age was grouped according to the American Academy of Pediatrics developmental stages[15] as follows: pre-adolescent (8-11 years inclusive), adolescent (12-17 years inclusive), young adult (18 years and above). SLE/MCTD subjects were consecutively recruited during routine rheumatology and nephrology outpatient visits between June 2012 and May 2013. Subjects had a diagnosis of pediatric-onset SLE if >=4 of 11 SLE classification criteria[16] were fulfilled prior to the 18th birthday. Subjects had a diagnosis of pediatric-onset MCTD if they met either Kahn's or Alarcon-Segovia's criteria[17] prior to the 18th birthday. Exclusion criteria were: age <8 years; limited English proficiency, cognitive or communication deficit precluding questionnaire completion; isolated cutaneous lupus. Of 67 eligible subjects approached, 50 (75%) consented to the study. T1D subjects had a diagnosis of type 1 diabetes mellitus documented in the medical chart and were consecutively recruited from March 2014 to September 2014 during routine outpatient visits to the CHOP Diabetes Center for Children. Exclusion criteria were: age <8 years; limited English proficiency; cognitive or communication deficit precluding questionnaire completion; current steroid use; SLE or MCTD diagnosis. Of 66 eligible subjects approached, 50 (76%) consented to the study. Informed consent from all participants and approval from the CHOP Institutional Review Board was obtained before initiating the study.

Measures

We used cohort group (SLE/MCTD vs T1D) as the measure of exposure for comparisons of mental health symptom prevalence and treatment rates. For both cohorts, we calculated depression, suicidal ideation and anxiety prevalence as the primary outcome. We screened for depression symptoms using the Patient Health Questionnaire -9 (PHQ-9), a 9-item self-

administered depression screening module based on the Diagnostic and Statistical Manual IV (DSM IV) criteria for major depression previously validated in the general adolescent population.[18] Each item assesses feelings over the previous 2 weeks, and is scored from 0 (not at all) up to 3 (nearly every day). Scores range from 0 to 27. A positive depression screen was defined as a score >=5 on the PHQ-9 and included scores in the mild (5-9), moderate (10-14), moderately severe (15-19) and severe (20-27) ranges.[19] A score of >=1 on item 9 of the PHQ-9 questionnaire was considered indicative of suicidal ideation and also considered a positive depression screen regardless of total PHQ-9 score; however, these positive screens were not categorized for depression severity if the total PHQ-9 was <5. We screened for anxiety symptoms using the Screen for Childhood Anxiety Related Disorders (SCARED), a self-administered 41-item anxiety screening tool, previously validated in outpatient children and adolescents.[20] Each item assesses feelings over the previous 3 months with 3 possible responses: “not true or hardly ever true” (score of 0), “somewhat true or sometimes true” (score of 1), and “very true or often true” (score of 2). Scores totaling >=25 indicate a positive screen for anxiety symptoms. Summed scores for item subgroups also indicate the following specific features: generalized anxiety, panic/somatic symptoms, separation anxiety, social anxiety and school avoidance. Depression and anxiety screening was performed using REDCap (Research Electronic Data Capture) electronic survey and data capture tools hosted at CHOP.[21] Upon identification of depression or anxiety symptoms, an educational handout was provided to the family with mental health care referral information. Identified suicide risk was addressed with a suicide prevention protocol consisting of immediate direct questioning of suicidal intent, plan or attempt within the prior week; endorsement of any of these prompted development of a safety plan and urgent referral for immediate psychology/psychiatry evaluation. We included self-reported mental health treatment (Y/N) in those with any symptom (depression, suicidal ideation or anxiety) as a secondary outcome. Assessed by parent/legal guardian survey, treatment included a history of: a previous psychiatric diagnosis, use of psychiatric medications or previous care by a psychiatrist or psychologist in the preceding 12 months.

Demographic & Disease Variables

The following variables were collected by survey of the parents/legal guardians for all subjects: race/ethnicity, highest household education level, annual household income, quality of life (QOL) and physical functioning. Race/ethnicity was categorized into 3 mutually exclusive groups: white, black and other (includes Hispanic, Asian/Pacific Islander, Native American and other). Highest household education level was categorized as either 1) less than college (includes incomplete college or less) or 2) college (includes completed associate, bachelors or advanced degree) and above. Annual household income was categorized into 3 groups according to the US national poverty guidelines for the years of study [22]: less than $40000, $40000 and above, and prefer not to answer. QOL was measured using the validated Pediatric Rheumatology Quality of Life Scale (PRQL), a 10-item instrument measuring the core dimensions of physical and psychological health, with scores ranging 0-30 (higher score indicates poor QOL).[23] Physical functioning was assessed by the Child Health Assessment Questionnaire (CHAQ), a validated 30-item instrument that measures 8 functional ability domains and calculates a disability index ranging from 0 to 3 (higher index indicates more disability).[24]

Additional variables abstracted from the electronic medical records for all subjects included: sex, age, primary insurance type, body mass index (BMI), pain score and disease duration. Primary insurance was categorized as Medicaid/Medicare, private or other (includes self-pay and no charge). Pain score was assessed at the time of study visit by participant self-report on a Likert scale of 0 to 10, with higher scores indicating higher pain levels. For SLE/MCTD subjects, disease type, activity, damage, manifestations and treatments were abstracted. Disease type was categorized as SLE or MCTD based on disease criteria as detailed above. Disease activity and organ damage at the study visit were measured for SLE/MCTD patients using the Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA) modification of the SLE disease activity index (SLEDAI)[25, 26] and the SLE International Collaborating Clinics/American College of Rheumatology Damage Index (SDI)[27], respectively. We categorized those with SDI score=0 as “no damage”, and those with score>0 as “damage”. Disease manifestations included the following, as defined by the American College of Rheumatology SLE classification criteria[16] and documented by a rheumatology or nephrology provider at any point in the disease course: cytopenia, arthritis, rash, nephritis, serositis, CNS disease. Antiphospholipid syndrome status was determined according to the 2006 International Consensus Classification Criteria.[28] Immunosuppressive medications included: current use of hydroxychloroquine, methotrexate, mycophenolate mofetil, azathioprine and glucocorticoids; and history of rituximab, cyclophosphamide or dialysis treatment. Current glucocorticoid use was both calculated as a continuous prednisone equivalent daily dose and categorized into 3 groups: 1) no use 2) low-dose (<10 mg daily Prednisone equivalent) and 3) high-dose (>=10 mg daily Prednisone equivalent). For T1D subjects, disease control at the time of visit was measured by glycosylated hemoglobin level (HbA1c) and number of blood glucose checks per day, categorized as suboptimal (<4) and optimal (4 or more).[29] Insulin delivery type (injection vs pump) was abstracted.

Statistical analyses

Means, standard deviations (SD), medians, interquartile ranges (IQR), and frequencies were calculated for demographic and disease-related variables. The presence of depression, suicidal ideation and anxiety symptoms were analyzed as binary outcome variables according to the above criteria for positive screens on the PHQ-9 and SCARED, respectively. Separate logistic regression analyses were used to compare prevalence rates of depression, suicidal ideation and anxiety symptoms, as well as rates of mental health treatment between the SLE/MCTD and T1D cohorts. Specifically, generalized estimating equations were used to adjust for within-pair correlations. We screened for potential confounders and effect modifiers by examining all covariates for pairwise associations with the exposure and outcome variables. We used binary variables for race/ethnicity (white vs non-white) and annual household income (<$40000 vs>=$40000, otherwise missing) to examine these associations. To avoid over-fitting, we included in the multivariate models only covariates with statistically significant pairwise associations ($p<0.2$) with both the exposure and outcome variables. We then fit separate multivariable models for depression and anxiety to adjust for both within-pair correlations and the included covariates. For the disease-specific analyses, we modeled depression and anxiety as separate outcomes, including the following variables: 1) SLEDAI score, SDI score and prednisone equivalent

daily dose for SLE/MCTD, and; 2) HbA1c, blood glucose checks per day and insulin delivery type for T1D. We performed all statistical analyses using Stata 13 (Stata Corp., College Station, TX).

Results

Demographics & Disease Characteristics

We enrolled 50 SLE/MCTD and 50 T1D subjects matched for sex and age group. Females comprised 43 pairs (86%). There were 10 pre-adolescent (20%), 31 adolescent (62%) and 9 young adult (18%) pairs. Race/ethnicity in the SLE/MCTD cohort was comprised of 23 (46%) white, 18 (36%) black and 9 (18%) subjects of other race/ethnicity. The T1D cohort was comprised of 46 (92%) white participants. Median disease duration for SLE/MCTD subjects was 23 months (IQR 11, 50) and 62 months (IQR 39, 110) for T1D subjects. For the SLE/MCTD cohort, 43 with SLE and 7 with MCTD, the median SLEDAI was 2 (IQR 0, 4) and 10 (20%) had organ damage on the SDI. Three SLE/MCTD subjects had a clinical diagnosis of CNS disease at time of disease presentation, manifested by strokes, chorea and seizure, which were responsive to immunosuppression. For the T1D cohort, the median HbA1c was 7.7% (IQR 6.9, 9) and 72% had an optimal number of blood glucose checks per day. Additional demographic and disease characteristics are shown in Table 1.

Mental Health Symptom Prevalence & Treatment

We identified depression and/or anxiety symptoms in 17 SLE/MCTD (34%) and 19 (38%) T1D subjects (Table 2). For SLE/MCTD subjects, symptoms of depression were identified in 10 (20%), suicidal ideation in 7 (14%), and anxiety in 11 (22%). For T1D subjects, symptoms of depression were identified in 13 (26%), suicidal ideation in 8 (16%) and anxiety in 16 (32%). None of the SLE/MCTD or T1D subjects required urgent referral for suicidal ideation. There was no statistically significant difference between SLE/MCTD and T1D subjects in unadjusted analyses for depression, suicidal ideation or anxiety (Table 2). However, adjusted analyses showed a statistically significant decrease in odds of suicidal ideation (OR=0.3, 95%CI 0.1-0.8, p=0.02) for SLE/MCTD compared to T1D subjects (Table 2). Non-white race was a statistically significant independent risk factor compared to white race in adjusted models for depression (OR=3.7, 95%CI 1.5-9.3, p=0.005) and suicidal ideation (OR=7.4, 95%CI 2.3-25.0, p=0.001). Longer disease duration was also a statistically significant independent risk factor in adjusted models for depression (OR=1.1, 95%CI 1.01-1.19, p=0.02) and suicidal ideation (OR=1.1, 95%CI 1.03-1.27, p=0.006). Of the subjects who screened positive for any symptom (depression, suicidal ideation and/or anxiety), SLE/MCTD subjects (24%) reported lower rates of previous mental health treatment compared to T1D subjects (53%). However, the difference between groups did not achieve statistical significance (OR=0.4, 95%CI 0.2-1.1, p=0.07) (Table 2). We did not perform adjusted analyses for anxiety prevalence or mental health treatment because none of the covariates met inclusion criteria for the multivariable models. Additional mental health characteristics are presented in Table 2.

Disease-specific Factors Associated with Mental Health Symptoms

For the SLE/MCTD subjects, we found an increase in odds of depression symptoms with increased disease activity on the SLEDAI (OR=1.1, 95%CI 1.1-1.2, p<0.001). Patients with organ damage had an increase in odds of depression symptoms compared to those with no organ damage, but this was not statistically significant (OR=2.7, 95% CI 0.9-7.7, p=0.07). None of the 3 SLE/MCTD subjects with CNS involvement had depression, suicidal ideation or anxiety. Prednisone equivalent daily dose was not associated with depression symptoms. None of the SLE/MCTD-specific variables were associated with anxiety symptoms (Table 3). For the T1D subjects, poorer disease control measured by HbA1c showed a statistically significant association with depression symptoms (OR=1.3, 95%CI 1.03-1.55, p=0.02). Blood glucose checks per day and diabetes insulin delivery type were not associated with depression symptoms. However, insulin delivery via pump showed a statistically significant association with anxiety symptoms (OR=3.3, 95%CI 1.1-10.4, p=0.04). HbA1c and blood glucose checks were not associated with anxiety symptoms (Table 3).

Discussion

This cross-sectional comparison of youth with SLE/MCTD and T1D provides new insight into factors contributing to mental health conditions in pediatric patients with chronic disease. Several studies indicate that depression and anxiety rates are high in youth from many chronic disease groups,[6, 10, 12] but little is known about the differences between these groups. As a first step in looking beyond the known associations of depression and anxiety with adolescent age, female sex and the presence of chronic disease, we utilized a matched cross-sectional analysis to compare risk factors for depression and anxiety in two pediatric chronic disease cohorts of similar age group and sex. Although our results do not suggest differences related to CNS inflammation in our sample, our findings shed light on race/ethnic disparities and disease-related risk factors across disease groups, pointing towards a need for improved mental health care for these patients.

Our unadjusted analyses indicated no difference in mental health symptoms between groups, with depression in approximately 25%, suicidal ideation in 15%, anxiety in almost 30%, which are high in comparison to healthy peers.[2] These findings add to the sparse knowledge of depression and anxiety among pediatric patients with SLE/MCTD,[4, 5, 30] and confirm results from prior studies in T1D,[10, 31] stressing the importance of mental health needs in youth with chronic disease. We found a significant association of non-white race with both depression and suicidal ideation, of particular importance for SLE/MCTD patients who are disproportionately non-white.[1] This finding may be related to cultural stigma and socioeconomic barriers to mental health care [32, 33], pointing to potential target areas for improvement in mental health care in this population. We also found increased disease duration to be associated depression and suicidal ideation. Although not unexpected, given the relationship between ongoing chronic illness and psychological stress,[34, 35] this highlights disease duration as a consideration in mental health risk assessment of youth with chronic disease.

After controlling for race/ethnicity and disease duration, our adjusted models suggest that youth with SLE/MCTD are at lower risk for depression and suicidal ideation than their peers

with T1D, contradicting our hypothesis that SLE/MCTD patients are at higher risk for mental health symptoms due to CNS inflammation. There may be several reasons for this. First, a significantly higher proportion of SLE/MCTD subjects were of non-white race, which was an independent risk factor and major driver for depression and suicidal ideation. Controlling for race/ethnicity may have therefore created an artificially lower risk in the SLE/MCTD subjects. Second, our SLE/MCTD cohort may have had a lower risk for CNS inflammation than typical cohorts,[4, 36] due to low disease activity and damage levels, in the setting of milder disease manifestations or aggressive treatment in those with more severe disease. Interestingly, only 6% of the SLE/MCTD subjects had confirmed CNS involvement, none of which had depression or anxiety, and it is possible that aggressive immunosuppression due to their presentation with CNS disease mitigated development of an inflammation-mediated mental health condition. Third, there may be an underestimated component of diabetes-related CNS effects potentiating depression and anxiety in T1D patients: circulating cytokines; direct impact of insulin deficiency on neurotransmitter metabolism; chronic hyperglycemia; iatrogenic hypoglycemia, and; the impact of basal activity of the hypothalamic-pituitary-adrenal axis.[37] Lastly, other factors particular to T1D such as the intensity and degree of parental involvement in diabetes care may result in greater family conflicts and loss of patient autonomy,[38] exacerbating negative psychological consequences in the T1D group. Further investigation of the above hypotheses may shed light on differences in mental health characteristics between these disease groups.

We found that those with poor disease control had higher rates of depression. There was a significant association between depression and increased SLE disease activity, not previously described in pediatric SLE, but in agreement with prior studies in adults.[9, 39] There was a borderline association of depression with SLE damage, which may related to psychological distress from physical limitations, but also raises the possibility of contributing post-inflammatory changes. We found an association between poor disease control measured by HbA1c and depression symptoms as previously described.[10] We cannot know from our data, however, if the poor disease control results in depression, or if depression results in decreased treatment adherence leading to poor disease control. With regard to disease-specific treatment factors, we did not find an association between steroid dose and depression or anxiety, as has been described in the literature.[40] Intriguingly, we found insulin delivery by pump (compared to injections) in the T1D cohort to be the only association. The reason for this is unclear and larger studies are needed to confirm our finding; however, potential contributing factors include: 1) the demands of insulin pump management for adolescents with type 1 diabetes,[41]; 2) concerns about body image and social acceptance, noted particularly in adult women on insulin pump therapy in one study,[42] of relevance to our predominantly female adolescent T1D cohort; and 3) the possibility that anxious families may be more likely to choose pump therapy.

Recognition and treatment of mental health problems is crucial for youth with chronic disease, as depression and anxiety have been associated with clinical and psychosocial outcomes.[8-12] Moreover, the high rate of suicidal ideation in 15% of our subjects highlights the need for improved mental health intervention in these youth. Yet mental health treatment in symptomatic patients was not high in our cohort with overall rate just below 40%. Furthermore, treatment rates were disparate at 53% in T1D subjects, but only 24% in SLE/

MCTD subjects. Socioeconomic and racial/ethnic differences may play a role,[43] but our small sample size precluded assessment of these factors in an adjusted model. Additionally, cultural factors related to treatment acceptability and access,[44] and provider-level factors may be important contributors to differences in mental health symptom recognition and referral. While neither subspecialty recruitment site had a formal mental health screening or referral practice, insight could be gained from future investigation of subspecialty provider attitudes, resources and referral practices related to mental health.[44] Nevertheless, our results call for efforts to improve mental health screening and intervention in youth with chronic diseases like SLE/MCTD and T1D. Although primary care providers have been identified as mediators for mental health intervention in youth in general,[45] those with chronic disease like SLE/MCTD typically see their subspecialty providers more often [6] and may benefit from intervention at subspecialty care sites.[6] Recent literature indicating successful implementation of depression screening in youth with T1D at outpatient diabetes clinic visits [46] is encouraging for feasibility of subspecialty-based intervention, potentially increasing mental health treatment rates, reducing disparities in care and improving outcomes. Further investigation of effective strategies for mental health symptom recognition and intervention for youth with chronic disease is needed.

There are several limitations to our study and our results must be interpreted cautiously. First, selection bias is possible if those choosing to participate in the study differed from those not participating in both their exposure status and risk for depression and anxiety; for example, SLE/MCTD subjects with CNS inflammation may have been less likely to participate and also more at risk for depression and anxiety. Second, we are unable to establish causation between disease activity/control and mental health symptoms due to our cross-sectional design. Third, due to our small sample size, we were limited in our power to detect associations, and in our ability to include demographic and disease factors in our adjusted models. Fourth, it is possible that our results, based on validated self-report screening tools rather than structured diagnostic interviews, may overestimate clinically relevant symptoms. However, we expect that this potential misclassification of outcome would be non-differential between groups. Furthermore growing evidence supports the recognition of mild or subthreshold depression in childhood because persistent symptoms, regardless of severity, convey increased risk for development of major depression and suicidal behavior in later years.[47] Lastly, the characteristics of our cohorts may reduce generalizability, due to low disease activity and damage in the SLE/MCTD subjects and high levels of adherence in the T1D subjects. This highlights the relevance of our results, however, as more typical patients with worse disease control are likely to have even higher rates of depression and anxiety. Larger, longitudinal studies of more diverse populations of youth with chronic disease are therefore needed to confirm and further explore our findings.

In conclusion, depression, suicidal ideation and anxiety were high and undertreated in our SLE/MCTD and T1D cohort. Those of non-white race/ethnicity, longer disease duration and with poor disease control were at higher risk for depression; insulin pump use was associated with higher rates of anxiety. Focusing on these risk factors may improve mental health treatment, and further investigation of socio-cultural factors influencing disparities in care of these youth is needed. Although we did not observe CNS involvement as a

contributing factor, further study of this and other disease-related factors may identify targets for intervention.

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Abbreviations

SLE	systemic lupus erythematosus
MCTD	mixed connective tissue disease
T1D	type 1 diabetes mellitus
CNS	central nervous system
CHOP	Children's Hospital of Philadelphia
PHQ-9	Patient Health Questionnaire
SCARED	Screen for Childhood Anxiety Related Disorders
QOL	quality of life
SLEDAI	Systemic lupus erythematosus disease activity index
SDI	Systemic lupus erythematosus International Collaborating Clinics/American College of Rheumatology Damage Index
HbA1c	hemoglobin A1c
IQR	interquartile range
OR	odds ratio

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Table 1

Demographic & Disease Characteristics for the Matched SLE/MCTD and T1D Cohorts

	SLE/MCTD N=50	T1D N=50	p-value
Female, N (%)	43 pairs (86)		-
Age group, N (%)			
Pre-adolescent (8-11 years)	10 pairs (20)		-
Adolescent (12-17 years)	31 pairs (62)		-
Young adult (18 years and above)	9 pairs (18)		-
Age in years, mean (SD)	15.6 (3.0)	15.0 (3.3)	0.04
Race/Ethnicity, N (%)			<0.001
Black	18 (36)	3 (6)	
White	23 (46)	46 (92)	
Other	9 (18)	1 (2)	
Highest household education, N (%)			1.0
Less than college	9 (18)	9 (18)	
College and above	41 (82)	41 (82)	
Annual household income, N (%)			0.34
<$40000	10 (20)	8 (16)	
$40000 and above	30 (60)	40 (80)	
Prefer not answer	10 (20)	2 (4)	
Insurance*, N (%)			<0.01
Medicaid	20 (40)	6 (12)	
Private	30 (60)	36 (72)	
Other	0 (0)	0 (0)	
BMI in kg/m^2*, median (IQR)	22 (20, 25)	23 (20, 25)	0.86
PRQL*, median (IQR)	0 (1,4)	4 (2,6)	0.01
Pain score*, median (IQR)	0 (0,0)	0 (0,0)	0.29
CHAQ score*, median (IQR)	0 (0,0)	0 (0,0)	0.21
Disease duration in months*, median (IQR)	23 (11,50)	62 (39,110)	<0.001
SLEDAI*, median (IQR)	2 (0, 4)	-	
SDI, N (%)			
No damage (score=0)	40 (80)	-	
Damage (score>0)	10 (20)	-	
SLE/MCTD manifestations			
Cytopenia	42 (84)	-	
Arthritis	37 (74)	-	
Rash	6 (12)	-	
Nephritis	6 (12)	-	

	SLE/MCTD N=50	T1D N=50	p-value
Serositis	6 (12)	-	
CNS disease	3 (6)	-	
Anti-phospholipid syndrome	3 (6)	-	
SLE/MCTD treatment, N (%)			
Hydroxychloroquine	49 (98)	-	
Methotrexate	11 (22)	-	
Mycophenolate Mofetil	25 (50)	-	
Azathioprine	2 (4)	-	
Glucocorticoids			
None	16 (32)	-	
Low-dose	28 (56)	-	
High-dose	6 (11)	-	
Prednisone equivalent daily dose in mg, median (IQR)	5 (2.5, 10.0)	-	
History of rituximab	7 (14)	-	
History of cyclophosphamide	8 (16)	-	
History of dialysis	1 (2)	-	
HbA1c*, median (IQR)	-	7.7 (6.9,9)	
Blood glucose checks per day*, N (%)			
> 4	-	6 (12)	
4 or more	-	36 (72)	
Insulin delivery type*, N (%)	-		
Injection	-	21 (42)	
Pump	-	21 (42)	

Demographic and disease characteristics for the SLE/MCTD and T1D cohorts are shown.

*The percentages do not sum to 100% due to missing data as follows: SLE/MCTD subjects - PRQL for 11, CHAQ for 10, SLEDAI for 7 (missing lab data), pain score for 6; T1D subjects - insurance, BMI, pain score, disease duration, HbA1c, blood glucose checks per day, insulin delivery type for 8; CHAQ for 1.

Table 2

Mental Health Characteristics for the Matched SLE/MCTD and T1D Cohorts

	SLE/MCTD N=50	T1D N=50	OR (95%CI) reference group= T1D	
			Unadjusted	Adjusted
Any symptom (depression and/or anxiety), N (%)	17 (34)	19 (38)	-	-
Depression, N (%)	10 (20)	13 (26)	0.8 (0.4-1.6) p=0.48	0.4 (0.2-1.0) p=0.06
PHQ-9 score in depressed, mean (SD)	11 (5)	8 (5)	-	-
Suicidal ideation, N (%)	7 (14)	8 (16)	0.9 (0.4-2.1) p=0.76	0.3 (0.1-0.8) p=0.02
Anxiety, N (%)	11 (22)	16 (32)	0.7 (0.3-1.4) p=0.31	-
SCARED score in anxious, median (IQR)	31 (28, 41)	33 (30, 39)	-	-
Anxiety category in anxious, N (%)				
Generalized anxiety	8 (72)	4 (25)	-	-
Panic/Somatic Symptoms	4 (36)	7 (44)	-	-
Separation Anxiety	7 (63)	5 (31)	-	-
Social Anxiety	7 (63)	8 (50)	-	-
School Avoidance	4 (36)	2 (13)	-	-
Co-morbid depression & anxiety, N (%)	4 (24)	4 (21)	-	-
Mental health treatment in symptomatic, N (%)	4 (24)	10 (53)	0.4 (0.2-1.1) p=0.07	-

Mental health characteristics for the matched SLE/MCTD and T1D cohorts are shown. One SLE/MCTD and 6 T1D subjects positive for depression (due to suicidal ideation) but not meeting categorization criteria (due to total PHQ-9 score <5) were omitted. SCARED score was missing for 1 SLE/MCTD subject. Estimates from analyses separately comparing depression, suicidal ideation and anxiety prevalence between the SLE/MCTD and T1D (reference group) cohorts are shown. The covariates included in the adjusted models for depression and suicidal ideation are race/ethnicity and disease duration.

Table 3

Regression Analyses of Disease-Specific Risk Factors for Depression and Anxiety in SLE/MCTD and T1D Subjects

Risk Factor	Depression OR (95% CI)	Anxiety OR (95% CI)
SLE/MCTD		
SLEDAI	1.1 (1.1-1.2) p<0.001	1.0 (0.9-1.2) p=0.47
SDI		
No damage (score=0)	--	--
Damage (score>0)	2.7 (0.9-7.7) p=0.07	1.7 (0.5-5.1) p=0.37
Prednisone equivalent daily dose	1.0 (0.9-1.1) p=0.67	1.0 (0.9-1.1) p=0.99
T1D		
HbA1c	1.3 (1.03-1.55) p=0.02	1.2 (0.9-1.5) p=0.14
Blood glucose checks/day		
4 or less	--	--
> 4	0.7 (0.2-1.7) p=0.39	0.8 (0.3-1.9) p=0.59
Insulin delivery type		
Injection	--	--
Pump	2 (0.7-5.6) p=0.19	3.3 (1.1-10.4) p=0.04

Odds ratios (OR) for disease-specific risk factors included in the analyses of depression and anxiety prevalence by disease group are shown. Analysis of the SLEDAI variable was limited to 43 SLE/MCTD subjects with available data. Analysis of T1D-specific variables was limited to 42 T1D subjects with available data. Reference groups are denoted by "—".