

Letter to the Editor

Depression, anxiety, and dermatologic quality of life in adolescents with atopic dermatitis*To the Editor:*

The negative psychosocial effect of atopic dermatitis (AD) on quality of life (QOL) is well established,¹⁻³ with itching, scratching, sleep loss, and social embarrassment among the most commonly reported difficulties contributing to school, work, financial, and social struggles. Increasing evidence suggests that depression and anxiety are also more common in adults with AD and that the association of AD with these psychiatric symptoms might be influenced by factors such as AD disease severity, subjective versus objective assessment of AD severity, and QOL. No studies have objectively assessed the prevalence of depression and anxiety in youth with AD or the association of these symptoms with AD severity or QOL. With the worldwide growing prevalence of AD and mounting evidence of the psychosocial and economic burden of this disease, identifying specific patterns and potential mechanisms of psychiatric symptom comorbidity in age-defined populations is increasingly important for the development of targeted assessments and treatment interventions.

In this pilot study we assessed rates of depressive and anxiety disorders in a clinical sample of adolescents with AD. The larger focus of the study was to examine the relationship of AD severity with depressive and anxiety symptoms (vs disorders) and dermatologic QOL. We proposed a theoretic model that increased AD severity would be associated with increased symptoms of depression and anxiety and that decreased QOL would mediate this relationship. Thirty-six adolescents (age, 13-17 years; mean age, 14.7 years) with a clinical diagnosis of AD were recruited from dermatology and pediatric clinics. Parents completed a questionnaire assessing demographic and medical history variables (see the [Methods](#) section and [Table E1](#) in this article's Online Repository at www.jacionline.org). A board-certified dermatologist confirmed the AD diagnosis and clinically assessed AD severity using the SCORAD index.⁴ The SCORAD index includes 3 AD severity scores: (1) objective, including extent and intensity of lesions; (2) subjective, including pruritus and sleep loss; and (3) total AD score (objective + subjective). Current and lifetime Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) diagnoses of depression and anxiety were assessed by experienced doctoral-level child and adolescent psychiatric clinicians using the Kiddie-Schedule for Affective Disorders and Schizophrenia–Present and Lifetime Version (K-SADS-PL), including separate adolescent and parent interviews; final diagnoses were determined by the expert clinician who integrated the children's and parent's information.⁵ Interviewers were blinded to study objectives and AD severity scores. Standardized self-report measures assessing dermatologic QOL, depressive symptoms, and anxiety symptoms included the Children's Dermatology Life Quality Index (CDLQI; 10 items), the Children's Depression Inventory (CDI; 27 items, 5 subscales), and the Multidimensional Anxiety Scale for Children (MASC; 39 items, 4 primary subscales), respectively (see the [Methods](#) section and [Table E1](#) in this article's Online Repository for further details). Pearson correlations were used to explore bivariate associations among variables. Hierarchic linear regressions were used to test theoretic pathways. All procedures were approved by the institutional

TABLE I. Percentages (and no. of participants) for K-SADS-PL diagnoses of anxiety and depression

Disorder	Current diagnosis*	Lifetime diagnosis*†
Any anxiety disorder	26 (9)	31 (11)
Separation anxiety disorder	0	9 (3)
Specific phobia	11 (4)	11 (4)
Social phobia	14 (5)	14 (5)
Agoraphobia	0	0
Generalized anxiety disorder	3 (1)	3 (1)
Any depressive disorder	9 (3)	17 (6)
Major depressive disorder	6 (2)	14 (5)
Dysthymic disorder	3 (1)	3 (1)
Depressive disorder NOS	0	0

NOS, Not otherwise specified.

*K-SADS-PL data are complete for 35 subjects, and diagnoses are not mutually exclusive.

†Having a past diagnosis, current diagnosis, or both.

review board, and informed consent was obtained from participants and their parents.

We compared rates of anxiety and depressive disorders in our sample with those of published community studies of adolescents. Adolescents with AD had increased rates of any current anxiety disorder (26%; 95% CI, 11.23% to 40.19%) compared with community estimates (3% to 6%); social anxiety disorder was most common (14%; 95% CI, 7.35% to 25.88%). Rates of current depressive disorders (9%; 95% CI, 0% to 17.84%) and lifetime rates of anxiety (31%; 95% CI, 16.05% to 46.81%) and depressive (17%; 95% CI, 4.66% to 29.63%) disorders were increased but did not substantially differ from published ranges (6%, 9% to 32%, and 12% to 24%, respectively; [Table I](#) and see the [Methods](#) section in this article's Online Repository for details regarding these comparisons).

Next we assessed the relationship of AD severity with depression and anxiety symptoms. Objective and total measures of AD severity were not significantly associated with symptoms of depression (CDI total score) or anxiety (MASC total score; [Table II](#) and see [Fig E1](#) in this article's Online Repository at www.jacionline.org). In contrast, subjective AD severity and subscores of sleep loss and pruritus were significantly correlated with symptoms of depression but not with symptoms of anxiety. Both sleep loss and pruritus were entered simultaneously into a multiple regression model as predictors for depression to assess the unique effects in predicting depressive symptoms. The association of depressive symptoms with sleep loss remained significant ($P < .001$), but the association with pruritus became nonsignificant ($P = .40$).

On the basis of these findings, we developed a theoretic model hypothesizing that decreased QOL mediates the relationship between sleep loss and the development of depression given existing evidence of an association of QOL with both AD and depression.² By using hierarchic linear regression, sleep loss was entered in the first step of the regression model; QOL (CDLQI) was entered in the second step, and depression (CDI) was the outcome measure. Findings confirmed reduced QOL as a plausible link (ie, mediator) between sleep loss and depressive symptoms. Shown statistically, the coefficient for sleep loss changed from significant in the first step ($\beta = .49$, $P = .002$) to nonsignificant when QOL was added in the second step ($\beta = .15$, $P = .33$),

TABLE II. Pearson correlation coefficients (and 95% CIs) among AD severity, dermatologic QOL, and depressive and anxiety symptoms

	CDI total depression	MASC total anxiety	CDLQI QOL*
AD Severity			
SCORAD total	0.21 (−0.13 to 0.50)	0.03 (−0.30 to 0.36)	−0.48§ (−0.70 to −0.18)
Objective	0.10 (−0.24 to 0.41)	−0.11 (−0.42 to 0.23)	−0.41‡ (−0.65 to −0.10)
Extent	−0.03 (−0.36 to 0.30)	−0.03 (−0.36 to 0.30)	−0.30 (−0.57 to 0.03)
Intensity	0.15 (−0.19 to 0.46)	−0.14 (−0.45 to 0.20)	−0.45‡ (−0.68 to −0.14)
Subjective	0.46§ (0.16 to 0.69)	0.19 (−0.15 to 0.49)	−0.59§ (−0.77 to −0.33)
Pruritus	0.36‡ (0.04 to 0.62)	0.10 (−0.24 to 0.41)	−0.48§ (−0.70 to −0.18)
Sleep loss	0.49§ (0.19 to 0.71)	0.29 (−0.04 to 0.56)	−0.58§ (−0.76 to −0.31)
QOL†			
CDLQI	−0.68§ (−0.82 to −0.45)	−0.27 (−0.55 to 0.06)	—

*Correlations in the QOL column are with AD severity measures. The signs for the coefficients in this column were changed from positive to negative to highlight the outcome that increased SCORAD severity scores were associated with decreased QOL.

†Correlations in the QOL row are with depression and anxiety symptom measures. The signs for the coefficients in this row were changed from positive to negative to highlight the outcome that increased depressive and anxiety symptoms were associated with decreased QOL.

‡ $P < .05$.

§ $P < .01$.

and the coefficient for QOL was significant ($P = .001$), with a partial correlation coefficient of .55. There were no additional influences of key demographic and medical history variables, including age, sex, race, ethnicity, socioeconomic status, body mass index, pubertal status, comorbid allergic disorders (asthma, allergic rhinitis, and urticaria), or use of glucocorticoid medications on sleep loss, depressive symptoms, or QOL (all P s $> .05$ and $< .99$).

This is the first study, to our knowledge, to assess the presence of DSM-IV depressive and anxiety disorders in adolescents with AD. Diagnoses of current anxiety disorders, particularly social anxiety disorder, were most prevalent and exceeded community estimates. Findings might reflect the social stigma and embarrassment often described by patients with AD and, for adolescents, additional exacerbation of existing social sensitivity and self-consciousness characteristic of this period of development.⁶

This is also the first study to specifically investigate the relationship between AD severity and symptoms of depression and anxiety in adolescents. Interestingly, subjective report of sleep loss was the only AD severity measure found to be associated with symptoms of depression; no objective or subjective AD severity measures were related to symptoms of anxiety. Decreased dermatologic QOL was associated with both sleep loss and depressive symptoms, thus establishing a potential mediating role of QOL in this relationship. We suggest that chronic sleep loss contributes to emotional and physical fatigue that negatively affects existing social sensitivity and social relationships central to an adolescent's QOL and resultant increased depression. Alternatively, findings might reflect the negative effect of depression on QOL, with resulting exacerbation of sleep disturbance commonly associated with AD.⁷ A longitudinal study examining the temporal nature of these relationships is needed to formally test possible causal pathways, including the potential effect of treatments for AD and sleep loss on depression and anxiety. Future investigations should also examine the unique relationships between AD severity, sleep, and anxiety/depression in a larger sample of adolescents with a wide range of AD severity compared with a control group of adolescents without AD (eg, other chronic skin disease) and include multi-informant-derived subjective and objective measures of all key variables.

Depressive and anxiety symptom assessments were each limited to a single self-report measure in this study, whereas depression and anxiety disorders were determined by integrating information from the children's and parent's standardized

interviews by an expert clinician. Moreover, it is important to note that depression and anxiety symptom measures are designed to assess clinical symptoms that might or might not specifically predict the presence of depressive and anxiety disorders. For example, prior studies suggest that the MASC is limited as a screening instrument for DSM-IV anxiety diagnoses,⁸ which is in contrast to the ability of the CDI to predict DSM-IV depressive disorders.⁹ This might have contributed to the increase in anxiety disorders, but not anxiety symptoms, in this sample in contrast to findings for depression. Future studies should consider comparison of different child- and parent-reported measures of anxiety and depression, with results of diagnostic clinical interviews to further identify which symptoms are most salient in this group of youth.

Limitations of this study include the inability to assess the causal directionality of the associations given the cross-sectional nature of the study, limited sample size, lack of a comparison group, and relatively few subjects with moderate or severe AD and psychiatric symptom severity. Finally, rates of psychiatric disorders were compared with historical community prevalence estimates, and increased rates of current anxiety disorders might, in part, also reflect the increased bias of study participation by subjects with more current anxiety.

In conclusion, anxiety and depressive disorders were prevalent in this pilot study of adolescents with AD. With respect to anxiety and depressive symptoms, the results support a theoretic model suggesting that in adolescents decreased QOL links the association between AD-induced sleep loss and depression. Findings further highlight the importance of an integrated clinical assessment of objective and subjective symptoms of AD and psychiatric symptoms of depression and anxiety.

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METHODS

Recruitment and screening

Subjects were recruited with flyers and physician referrals. Parents of adolescents with AD interested in the study were screened for participation to determine eligibility. Because the present study was part of a larger assessment that included biological correlates of AD, adolescents were screened out if AD treatments included topical corticosteroids of greater than moderate strength (class III or above) or inhaled corticosteroids with a strength of greater than 44 µg of fluticasone^{E1} or if they had major medical disorders to minimize potential systemic alterations of immune and hypothalamic pituitary adrenal axes. Of the 64 adolescents screened, 18 did not meet the study criteria, 10 elected not to participate, and 36 participated in the study.

Demographic and medical history

Parents completed a questionnaire assessing the child's sex, age, race, and ethnicity; family income and parental education were used to measure socioeconomic status. Parents also reported on the child's medical history, including a coexisting lifetime history of asthma, allergic rhinitis, and urticaria. Current medications for allergic conditions, psychiatric conditions, or both were grouped as follows: glucocorticoids (eg, hydrocortisone, mometasone, and fluticasone), nonglucocorticoids (eg, loratadine, cetirizine, and albuterol), calcineurin inhibitors (pimecrolimus and tacrolimus), and psychotropics (eg, fluoxetine, sertraline, and methylphenidate). Approximately 75% of the adolescents were using medications to treat AD, other allergies, or both; 47% had asthma, 58% had allergic rhinitis, and 44% had urticaria (see Table E1, "Demographic"). Height and weight were obtained to assess body mass index, and Tanner Scales^{E2} were completed by adolescents to approximate pubertal status.

Measures

To assess dermatologic QOL, we used the CDLQI.^{E3} Ten items evaluate the effect of AD on symptoms and feelings, leisure, school or holiday, personal relationships, sleep, and treatment. Items are scored according to degree of effect, ranging from 0 (not at all) to 3 (very much), with higher total (summed) scores indicative of poorer QOL. In the present study the Chronbach α coefficient of reliability for the CDLQI was .88.

Current and lifetime DSM-IV^{E4} diagnoses of anxiety and depression were assessed by using the K-SADS-PL.^{E5} K-SADS-PL data for one of the 36 participants were incomplete and therefore not included in the analysis of these data. Percentages of subjects with a current and lifetime diagnosis of anxiety and depression were determined and compared with prevalence percentages reported in community studies of the general adolescent population.^{E6-E11}

Symptoms of depression were assessed by using the CDI, a widely used 27-item self-report measure.^{E12} The subscales of the CDI assess negative mood, interpersonal problems, ineffectiveness, anhedonia, and negative self-esteem over the past 2 weeks. The Chronbach α coefficient of reliability for the CDI total score (CDI total) was .90 and ranged from .58 to .75 for CDI subscales. Symptoms of anxiety were assessed with the MASC, a well-established 39-item self-report measure of anxiety symptoms.^{E13} Subscales include physical symptoms (secondary subscales of tense/restless; somatic/autonomic), harm avoidance (secondary subscales of perfectionism; anxious coping), social anxiety (secondary subscales of humiliation/rejection; performance), and separation anxiety. The Chronbach α coefficient for the MASC total score (MASC total) was .90 and ranged from .52 to .86 for MASC subscales.

Total scores on the SCORAD index,^{E14} CDI, and MASC ranged from subclinical to clinical, and scores for the CDLQI spanned close to the measure's maximum limit (see Table E1, "Medical and psychiatric"). By using the SCORAD objective score for AD severity, most subjects were classified as

having mild disease (61%) compared with either moderate (33%) or severe (6%) disease.

Statistical analyses

Because distributions of SCORAD, CDLQI, CDI, and MASC scores were skewed (see Table E1, "Medical and psychiatric"), values were log transformed (after adding a constant [1] to eliminate zeroes) before analyses. Pearson correlations assessed the bivariate associations among variables (Table II and see Fig E1). Hierarchic linear regressions tested the theoretic model hypothesizing that AD severity predicts increased depressive and anxiety symptoms because of its association with reduced dermatologic QOL. Such an effect is demonstrated when (1) AD severity and depressive/anxiety symptoms are significantly correlated, (2) the CDLQI score is significantly correlated with both of these variables, and (3) only the CDLQI score remains significant when both AD severity and the CDLQI score are included in the regression model.^{E15} Pearson correlations, independent-samples *t* tests, and ANOVAs were used to assess the potential influence of demographic and medical history variables on the outcomes.

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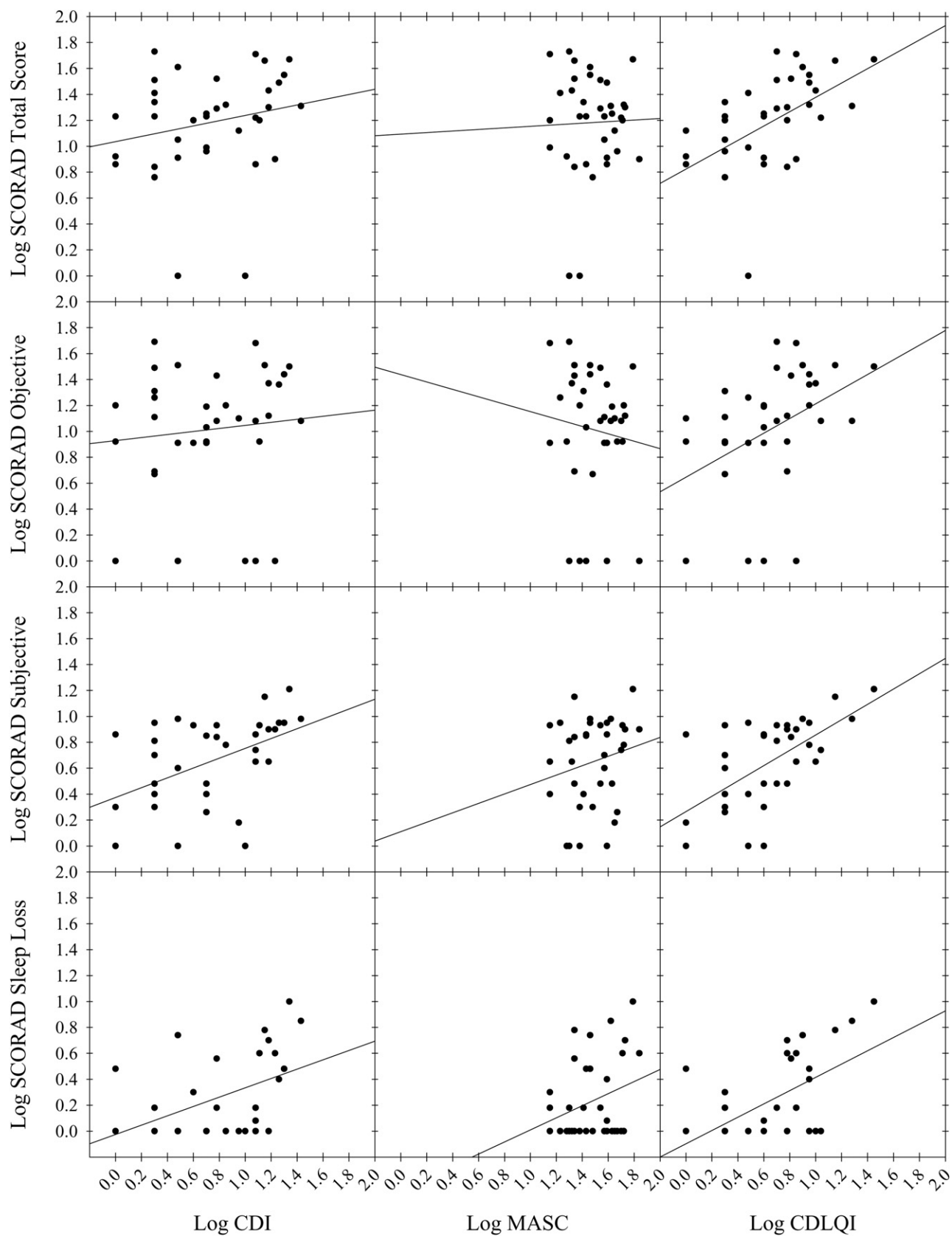


FIG E1. Log-transformed SCORAD scores (total, objective, subjective, and sleep loss) plotted against log-transformed measures of depressive symptoms (*CDI*), anxiety symptoms (*MASC*), and dermatologic QOL (*CDLQI*). Of note, 2 subjects had SCORAD total scores of zero because of the absence of active AD symptoms during assessment; excluding these subjects from analyses did not change the study results (Table II).

TABLE E1. Demographic, medical, and psychiatric variables

Variables	No. (% of n)	Mean ± SD	Range (Max)
Demographic			
Sex			
Male	15 (42)		
Female	21 (58)		
Race			
American Indian or Alaska native	1 (3)		
Black or African American	4 (11)		
White	29 (81)		
Biracial or multiracial	2 (6)		
Ethnicity			
Hispanic or Latino	4 (11)		
Not Hispanic or Latino	32 (89)		
Mother's education*			
<4-y College graduate	20 (56)		
≥4-y College graduate or beyond	16 (44)		
Father's education*†			
<4-y College graduate	14 (40)		
≥4-y College graduate or beyond	17 (49)		
Age (y)		14.7 (1.3)	13.1-17.8 (18.0)
Medical and psychiatric			
Pubertal status		3.8 (0.9)	1.5-5.0 (5.0)
Body mass index percentile		75.1 (24.6)	13.5-99.5 (100)
Other allergic disease			
Asthma	17 (47)		
Allergic rhinitis	21 (58)		
Urticaria	16 (44)		
Use of medication‡			
Glucocorticoid	21 (58)		
Nonglucocorticoid allergy medication	20 (56)		
Calcineurin inhibitors	6 (17)		
Psychotropics	5 (14)		
SCORAD total		19.5 (14.1)	0-53.1 (103)
Objective		14.8 (12.3)	0-47.6 (83)
Extent percentage		8.7 (13.9)	0-63.0 (100)
Intensity		3.7 (3.0)	0-13.0 (18)
Subjective		4.8 (3.7)	0-15.3 (20)
Pruritus		3.5 (2.4)	0-8.0 (10)
Sleep loss		1.3 (2.1)	0-9.1 (10)
CDLQI		5.0 (5.4)	0-27 (30)
CDI total		7.0 (6.9)	0-26 (54)
MASC total		32.2 (14.0)	13-68 (117)

Max, Maximum value possible.

*Included along with family income (median, \$75,000) in the calculation of socioeconomic status.

†Not all participants had a father in the home.

‡Medication types not mutually exclusive; glucocorticoid inhaled medication, 44 µg of fluticasone or less; less than class III topical agents.