Correlation between anxiety and depression risk and atopic dermatitis severity in Taiwan: A cross-sectional study

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Background: Limited studies on atopic dermatitis (AD) have investigated the possible covariance of sociodemographic factors with the Hospital Anxiety and Depression Scale (HADS).

Objective: This study aimed to examine the possible covariance between AD severity and HADS scores of patients in Taiwan.

Methods: Patients with AD from a medical center and 2 regional hospitals in Taiwan were enrolled in this cross-sectional study from April 2018 to April 2019. AD severity was measured using the "scoring atopic dermatitis" index, and anxiety and depression were screened based on HADS.

Results: A total of 200 patients were included. After correcting for sociodemographic variables, significantly more borderline (≥8) and abnormal (≥11) cases of anxiety/depression ($P < .05$) were noted in patients with moderate-to-severe AD.

Limitations: First, the cross-sectional study design cannot show causality. Second, baseline data, including a history of underlying cancer or previous psychiatric disorder, were not obtained in the questionnaire and may confound the HADS scores. Finally, a standardized psychiatric clinical interviews study design should be used for higher accuracy in the assessment of psycho-comorbidities.

Conclusion: Higher anxiety and depression risks were noted in patients with moderate-to-severe AD. Except for psychosomatic symptoms, all kinds of anxiety and depression symptoms occurred more frequently in patients with moderate-to-severe AD. (JAAD Int 2022;7:22-30.)

Key words: anxiety; atopic dermatitis; depression; HADS; Hospital Anxiety and Depression Scale; psycho-comorbidities; SCORAD.

INTRODUCTION

Atopic dermatitis (AD) is the most common chronic inflammatory skin disease of childhood[1] and is characterized by chronic distressing pruritus, resulting in sleep disturbance and body image disfiguration.[2] AD mostly occurs during childhood and may persist throughout the lifetime with a waxing and waning clinical course.[3] The worldwide prevalence of AD among the total population is approximately 1% to 20%, whereas the corresponding prevalence in Taiwan ranges from 1.28% to 6.7% based on 2 previous cohort studies conducted in 2010.[1,4,5]

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Several epidemiologic studies have demonstrated multiple dimensions of psychosocial stress, including caregiver stress, personality type, poor family relationships, and even natural disasters (eg, the Hanshin earthquake), to be major aggravating factors for the symptoms of AD.[6,7] Patients with AD are characterized as having irritability and ineffective coping skills for anger and anxiety.[8] Rønnstad et al[9] performed a meta-analysis of 24 studies on AD and found an increased risk of depression, anxiety, and suicide ideation in both adults and children with AD. The prevalence rates of anxiety and depression in pediatric patients with AD were 7.25% and 6.52%, respectively, in a previous study,[10] whereas the prevalence rates of anxiety and depression in patients with AD varied from 17.2% and 10.1%, respectively, in Europe,[11] to 18% and 5%, respectively, in Singapore,[12] to 9.8% and 10.4%, respectively, in Korea.[13]

CAPSULE SUMMARY

- This study aimed to examine the covariance between atopic dermatitis severity and Hospital Anxiety and Depression Scale scores.
- Except for psychosomatic symptoms, all kinds of anxiety and depression symptoms occurred more frequently in patients with moderate-to-severe atopic dermatitis.

A few studies have assessed anxiety and depression in patients with AD using the Hospital Anxiety and Depression Scale (HADS).[14-16] Moreover, in previous studies in patients with non-AD diseases using HADS, patients with characteristics including female gender and an education level of high school or lower tended to have higher Hospital Anxiety and Depression Scale—anxiety (HADS-A) subscores,[17,18] whereas these 2 possible confounders were not controlled in previous studies in patients with AD using HADS. In addition, there is no discussion on the most affected dimensions of HADS in patients with AD.

Thus, the aims of this study were as follows: (1) to examine the impact of AD severity on the prevalence rate of anxiety and depression in adult patients with AD using HADS, (2) to assess the association between HADS scores and demographic characteristics, and (3) to assess the most affected dimensions of HADS in patients with AD in Taiwan.

METHODS

Patient recruitment criteria

This prospective, cross-sectional study was conducted from April 2018 to April 2019 at 1 medical center and 2 regional hospitals in Taiwan. A total of 200 adults with AD between the ages of 20 years and 78 years who visited the dermatology outpatient clinics within the study period were recruited. The Hanifin and Rajka diagnostic criteria for AD were adopted to ensure diagnostic consistency.[19] AD severity was based on the scoring atopic dermatitis (SCORAD) index, which was assessed by the 3 dermatologists (T.C.C., Y.T.C., and C.Y.C.) in our research team. We recruited a similar sample size of patients with mild (SCORAD $<$ 25), moderate ($25 \leq$ SCORAD ≤ 50), and severe (SCORAD $>$ 50) AD. After signing the informed consent form, each patient was interviewed face to face by well-trained interviewers using a questionnaire that included HADS and the other baseline characteristics. The study protocol was approved by the research ethics committees (201802007RINA) of National Taiwan University Hospital.

Assessment tools

HADS, a 14-item self-reporting screening instrument with good reliability and validity, is widely used in psycho-oncology to screen for anxiety and depression in oncology patients.[20,21] It comprises 2 7-item subscales: HADS-A and Hospital Anxiety and Depression Scale—depression (HADS-D). Each item is measured by a symptom frequency range from 0 (representing never having the symptom) to 3 (representing always having the symptom). Both subscales have total scores ranging from 0 to 21, in which higher scores imply a more severe psychologic disease.

Zigmond and Snaith[22] first advocated classifying a patient with a total Hospital Anxiety and Depression Scale (HADS-T) score of ≥14 or a HADS-A/HADS-D score of 8 to 10 as a borderline case and a HADS-A/HADS-D score of ≥11 as an abnormal case. The Chinese version of HADS has been validated and showed good reliability in several studies conducted in the Mandarin-speaking area.[23-26]

Statistical analysis

All data analyses and statistical procedures were performed using SAS statistical software, version 9.4 (SAS Institute Inc). Fisher's exact test was used to compare the distribution of sociodemographic characteristics, except marital status at different severity levels of AD, between patients with HADS scores above clinical cutoff values and those with scores below such cutoff values.

The sociodemographic variables examined consisted of sex, age, education level, marital status, and

Abbreviations used:

AD:	atopic dermatitis
BMI:	body mass index
HADS:	Hospital Anxiety and Depression Scale
HADS-A:	Hospital Anxiety and Depression Scale—anxiety
HADS-D:	Hospital Anxiety and Depression Scale—depression
HADS-T:	total Hospital Anxiety and Depression Scale
SCORAD:	scoring atopic dermatitis

body mass index (BMI). The association between the various HADS scores and the severity level of AD was tested using ordered logistic regression analysis. The corrected *P* values of the HADS scores were computed with an ordered logistic model that controlled for the aforementioned sociodemographic variables. For HADS-A/HADS-D scores, we analyzed both borderline and abnormal cutoff values. A 2-sided *P* value of ≤.05 was deemed significant.

RESULTS

Demographic data

In this cross-sectional study, a total of 200 patients with AD (female, 97; male, 103; mean age, 34.4 ± 12.4 years) who visited a medical center and 2 regional hospitals completed the questionnaire. Of these patients, 13% had an education level of high school or lower (an average of ≤12 years of formal education), whereas 22.5% had a graduate school level of education. Moreover, 28% of the patients were married and 4.5% were separated, widowed, or divorced. Of all patients, 35.5% had an overweight BMI (BMI ≥ 24 kg/m^2) based on the criteria of the Health Promotion Administration of Taiwan for the best adaptation to local conditions.[27] The mean ± SD SCORAD scores were 35.9 ± 18.5 (range, 4.2-86.2). In addition, 35% (*n* = 70), 36% (*n* = 72), and 29% (*n* = 58) of the patients were scored with mild, moderate, and severe AD, respectively. The mean HADS-T, HADS-A, and HADS-D scores were 14.9 ± 5.9 (range, 3-37), 9.1 ± 3.2 (range, 3-19), and 5.8 ± 3.6 (range, 0-19), respectively.

HADS scores according to sociodemographic data

Except for significantly more borderline depression (HADS-D ≥ 8) cases in men, there was no significant difference in age, education level, marital status, and overweight BMI distribution in each group of cases with borderline psychocomorbidities. Among the total 200 patients with AD, 35% (*n* = 70) had mild AD, 36% (*n* = 72) had moderate AD, and 29% (*n* = 58) had severe AD (Table I). In addition, 65.5% (*n* = 121) were borderline cases with psycho-comorbidities (HADS ≥ 14), 67% (*n* = 134) were borderline anxiety cases (HADS-A ≥ 8), and 28.5% (*n* = 57) were borderline depression cases (HADS-D ≥ 8) (Table II).

More anxiety and depression comorbidities occurred in patients with moderate-to-severe AD

In total, 89.7% (*n* = 52), 91.4% (*n* = 53), and 46.6% (*n* = 27) of the patients with severe AD had borderline HADS-T (≥14), HADS-A (≥8), and HADS-D (≥8) scores, respectively; 34.3% (*n* = 24), 47.1% (*n* = 33), and 15.7% (*n* = 11) of the patients with mild AD had borderline HADS-T, HADS-A, and HADS-D, respectively. Additionally, 43.1% (*n* = 25) and 19.0% (*n* = 11) of the patients with severe AD and 18.6% (*n* = 13) and 5.7% (*n* = 4) of patients with mild AD had abnormal HADS-A and HADS-D scores (≥11), respectively.

After correcting for sociodemographic variables, significantly more cases with borderline and abnormal scores in both HADS-A and HADS-D ($P < .05$) were noted in patients with moderate-to-severe AD than in those with mild AD (Table III).

HADS subscale question score distribution

After correcting for sociodemographic variables, patients with moderate-to-severe AD had significantly higher scores ($P < .05$) for almost all anxiety and depression subscale questions, with 2 exceptions as follows: question A5 (“I get a sort of frightened feeling like ’butterflies’ in the stomach”) and question D5 (“I have lost interest in my appearance”). In contrast, patients with mild AD had significantly higher scores than those with moderate-to-severe AD for question A5 ($P < .05$) (Tables IV and V). No significant scoring trend was found for question D5 ($P = .169$).

Relationship between SCORAD and HADS scores

A partial correlation was performed to correct all sociodemographic variances. After correcting all covariance, the Pearson correlation coefficients between HADS-T, HADS-A, and HADS-D scores and SCORAD scores showed positive correlations (r = 0.395, r = 0.348, and r = 0.349, respectively; $P < .001$ for all). After correcting for sociodemographic variables, significantly higher scores of HADS-A, HADS-D, and HADS-T ($P < .05$) were noted in patients with moderate-to-severe AD than in those with mild AD (Table VI).

Table I. Demographic data of patients with different atopic dermatitis severity

Variable	All patients (*N* = 200)	Mild (*N* = 70)		Moderate (*N* = 72)		Severe (*N* = 58)		*P* value
		N	%	*N*	%	*N*	%	
Sex								.363
Female	97	38	54.29%	35	48.61%	24	41.38%	
Male	103	32	45.71%	37	51.39%	34	58.62%	
Age, y (mean ± SD)*	34.35 (12.38)	35.34 (13.66)		35.04 (12.16)		32.28 (10.88)		.960
Education level†	-	-		-		-		.664
Marital status								.116
Unmarried	135	40	57.14%	50	69.44%	45	77.59%	
Married	56	27	38.57%	19	26.39%	10	17.24%	
Separated/divorced/ widowed	9	3	4.29%	3	4.17%	3	5.17%	
BMI (mean ± SD)	23.38 (3.91)	23.19 (3.82)		23.26 (3.87)		23.76 (4.12)		.329
BMI < 24 (21.09 ± 1.69)	129	46	65.71%	50	69.44%	33	56.90%	
BMI ≥ 24 (27.54 ± 3.32)	71	24	34.29%	22	30.56%	25	43.10%	

Fisher's exact test was used to compare the distribution of sociodemographic characteristics at different severity levels of atopic dermatitis.
BMI, Body mass index.
*Age group was divided into 20 to 29 years, 30 to 39 years, 40 to 49 years, 50 to 59 years, and >60 years.
†Education level was divided into high school education or lower level, college education level, and graduate school level.

Table II. Demographic data of patients with borderline anxiety and depression in 200 patients with atopic dermatitis

Variable	HADS-T ≥ 14 (*N* = 121)		*P* value	HADS-A ≥ 8 (*N* = 134)		*P* value	HADS-D ≥ 8 (*N* = 57)		*P* value
	N	%		*N*	%		*N*	%	
Sex			.471			.372			.042‡
Female	56	46.28%		68	50.75%		21	36.84%	
Male	65	53.72%		66	49.25%		36	63.16%	
Age, y (mean ± SD)*	33.57 (11.59)		.509	33.52 (11.64)		.494	34.04 (13.78)		.585
Education level†			.502			.952			.490
Marital status			.439			.772			.570
Unmarried	85	70.25%		91	67.91%		42	73.68%	
Married	32	26.45%		38	28.36%		13	22.81%	
Separated/divorced /widowed	4	3.31%		5	3.73%		2	3.51%	
BMI (mean ± SD)	23.53 (4.38)		.295	23.52 (4.18)		.216	23.44 (4.33)		1.000
BMI < 24 (21.09 ± 1.69)	75	61.98%		83	61.94%		37	64.91%	
BMI ≥ 24 (27.54 ± 3.32)	46	38.02%		51	38.06%		20	35.09%	

Fisher's exact test was used to compare the socioeconomic characteristic differences between patients with Hospital Anxiety and Depression Scale scores above clinical cutoff values and those with scores below such cutoff values.
BMI, Body mass index; *HADS-A*, Hospital Anxiety and Depression Scale—anxiety; *HADS-D*, Hospital Anxiety and Depression Scale—depression; *HADS-T*, Hospital Anxiety and Depression Scale—total.
*Age group was divided into 20 to 29 years, 30 to 39 years, 40 to 49 years, 50 to 59 years, and >60 years.
†Education level was divided into high school education or lower level, college education level, and graduate school level.
‡$P < .05$.

DISCUSSION

Our study found that adults with moderate-to-severe AD had a significantly higher proportion of cases with borderline and/or abnormal HADS-A and HADS-D scores, indicating a tremendous psychological burden in patients with AD (Table III). Borderline and/or abnormal HADS-A and HADS-D scores were also associated with high SCORAD scores but not with other sociodemographic factors, including age, sex, marital status, education level, and BMI. AD severity is understood to be one of the leading causes of anxiety and depression development in adult patients with AD (Table VI).

Table III. Borderline (HADS subscore≥8) and abnormal (HADS subscore≥11) anxiety/depression cases distribution in different AD severity groups

	Mild AD (SCORAD score < 25)		Moderate AD (25 ≤ SCORAD score ≤ 50)		Severe AD (SCORAD score > 50)		Crude *P* value	Corrected *P* value*
HADS-T								
<14	46	65.71%	27	37.50%	6	10.34%	<.001†	<.001†
≥14	24	34.29%	45	62.50%	52	89.66%		
HADS-A								
<8	37	52.86%	24	33.33%	5	8.62%	<.001†	<.001†
≥8	33	47.14%	48	66.67%	53	91.38%		
HADS-A								
<11	57	81.43%	48	66.67%	33	56.90%	.01†	.001†
≥11	13	18.57%	24	33.33%	25	43.10%		
HADS-D								
<8	59	84.29%	53	73.61%	31	53.45%	.001†	<.001†
≥8	11	15.71%	19	26.39%	27	46.55%		
HADS-D								
<11	66	94.29%	65	90.28%	47	81.03%	.053	.02†
≥11	4	5.71%	7	9.72%	11	18.97%		

The association between the various Hospital Anxiety and Depression Scale scores and the severity level of atopic dermatitis was tested using ordered logistic regression analysis.

AD, Atopic dermatitis; *HADS-A*, Hospital Anxiety and Depression Scale—anxiety; *HADS-D*, Hospital Anxiety and Depression Scale—depression; *HADS-T*, Hospital Anxiety and Depression Scale—total; *SCORAD*, scoring atopic dermatitis.

*Corrected *P* value: after controlling for covariance, including age, sex, marital status, education level, and body mass index.

†$P < .05$.

Compared with the previous studies on AD-related anxiety/depression, our mean HADS-T and HADS-A scores (14.9 ± 5.9 and 9.1 ± 3.2, respectively) were slightly higher than those in the previous case-control studies in the United States (HADS-T, 13.6; HADS-A, 7.7),[14] Germany (HADS-A, 8.2 ± 4.1),[15] and Singapore (HADS-A, 7.2).[12] In contrast, our mean HADS-D scores (5.8 ± 3.6) were similar to those of the previous studies (HADS-D: the United States, 6.0; Germany, 4.9 ± 3.8; Singapore, 5.0). In comparison to major chronic diseases in the Mandarin-speaking area, according to our study, the HADS-A score of patients with AD was higher than that of patients with painful metastatic cancer (HADS-A, 7.3 ± 3.6),[28] myocardial infarction (HADS-A, 7.7 ± 3.6),[29] and hypertension (HADS-A, 5.5 ± 0.4).[30] Thus, more caution should be taken in screening for psycho-affected disorders, especially anxiety in patients with AD.

The HADS subscores distribution of anxiety and depression corresponding to AD severity were provided in Figs 1 and 2. Interestingly, patients with mild AD received significantly higher scores than those with moderate-to-severe AD for question A5 (“I get a sort of frightened feeling like ’butterflies’ in the stomach”). According to previous studies, there are 2 debated concepts about question A5. First, the phrase “a feeling like butterflies in the stomach,” which is from the British dialect, is translated in various ways in other languages.[31,32] Achieving the most suitable translation for question A5 is a challenging task and may not effectively reflect patients’ anxiety. Second, question A5 is not a pure anxiety item and refers to somatic symptoms, which may be “noise” to anxiety scores.[21,22,33] No significant scoring differences in question D5 (“I have lost interest in my appearance”) were noted for different AD severity groups. We supposed that cosmetic outcomes are of considerable significance for all patients with AD, even those with mild AD.

HADS is a useful screening tool with good reliability and validity for detecting psycho-affective disorders in Taiwanese patients with AD. In our study, the prevalence rates of anxiety and depression (HADS-A/HADS-D ≥11) were 18.57% and 5.71%, respectively, in patients with mild AD and 43.1% and 18.97%, respectively, in patients with severe AD. The demographic parameters (sex, age, education level, marital status, and BMI) did not significantly affect the HADS scores. Therefore, AD severity seemed to be the main driver of anxiety and depression development in patients with AD. Effective psychological interventions for anxiety and depression in patients with AD were suggested based on the following 2 biological rationales. First, interleukin 1β and interleukin 6 produced by mast cells and basophils may induce sickness behavior, sharing similar symptoms with depression, such as

Table IV. Hospital Anxiety and Depression Scale—anxiety questions score distribution

	HADS-A1			HADS-A2			HADS-A3			HADS-A4			HADS-A5			HADS-A6			HADS-A7		
	Mean ± SD	Median	*P* value*	Mean ± SD	Median	*P* value*	Mean ± SD	Median	*P* value*	Mean ± SD	Median	*P* value*	Mean ± SD	Median	*P* value*	Mean ± SD	Median	*P* value*	Mean ± SD	Median	*P* value*
All patients	1.29 ± 0.762	1	<.001†	1.23 ± 0.946	1	.014†	1.43 ± 0.823	1	.039†	1.1 ± 0.723	1	<.001†	2.55 ± 0.707	3	.016†	0.75 ± 0.75	1	<.001†	0.76 ± 0.691	1	<.001†
Mild AD	1 ± 0.702	1		1 ± 0.963	1		1.24 ± 0.842	1		0.87 ± 0.741	1		2.69 ± 0.578	3		0.41 ± 0.551	0		0.51 ± 0.631	0	
Moderate AD	1.29 ± 0.759	1		1.22 ± 0.907	1		1.43 ± 0.802	1		1.06 ± 0.69	1		2.6 ± 0.705	3		0.71 ± 0.638	1		0.81 ± 0.705	1	
Severe AD	1.66 ± 0.690	2		1.53 ± 0.903	1		1.64 ± 0.788	1		1.43 ± 0.624	1		2.31 ± 0.799	2		1.19 ± 0.868	1		0.98 ± 0.662	1	

AD, Atopic dermatitis; *HADS-A*, Hospital Anxiety and Depression Scale—anxiety.
*Corrected *P* value: after controlling for covariance, including age, sex, marital status, education level, and body mass index.
†$P < .05$.

Table V. Hospital Anxiety and Depression Scale—depression questions score distribution

	HADS-D1			HADS-D2			HADS-D3			HADS-D4			HADS-D5			HADS-D6			HADS-D7		
	Mean ± SD	Median	*P* value*	Mean ± SD	Median	*P* value*	Mean ± SD	Median	*P* value*	Mean ± SD	Median	*P* value*	Mean ± SD	Median	*P* value*	Mean ± SD	Median	*P* value*	Mean ± SD	Median	*P* value*
All patients	0.52 ± 0.679	0	.013†	0.55 ± 0.813	0	.025†	0.94 ± 0.688	1	<.001†	1.01 ± 0.916	1	<.001†	1.06 ± 1.045	1	.169	0.77 ± 0.837	1	<.001†	0.95 ± 0.867	1	.003†
Mild AD	0.36 ± 0.660	0		0.34 ± 0.74	0		0.7 ± 0.645	1		0.76 ± 0.842	1		0.83 ± 1.035	0		0.43 ± 0.714	0		0.79 ± 0.849	1	
Moderate AD	0.56 ± 0.710	0		0.61 ± 0.848	0		0.9 ± 0.675	1		0.89 ± 0.865	1		1.22 ± 1.078	1		0.85 ± 0.85	1		0.89 ± 0.881	1	
Severe AD	0.69 ± 0.627	1		0.74 ± 0.807	1		1.26 ± 0.637	1		1.45 ± 0.921	1		1.14 ± 0.981	1		1.09 ± 0.823	1		1.22 ± 0.817	1	

AD, Atopic dermatitis; *HADS-D*, Hospital Anxiety and Depression Scale—depression.
*Corrected *P* value: after controlling for covariance, including age, sex, marital status, education level, and body mass index.
†$P < .05$.

Table VI. Impact of atopic dermatitis severity on Hospital Anxiety and Depression Scale scores (mean ± SD)

	HADS-T			HADS-A			HADS-D		
	Mean ± SD	Median	Corrected *P* value*	Mean ± SD	Median	Corrected *P* value*	Mean ± SD	Median	Corrected *P* value*
All patients	14.9 ± 5.92	15		9.10 ± 3.177	9		5.80 ± 3.606	6	
Mild AD	11.93 ± 5.701	11	<.001†	7.73 ± 3.225	7	<.001†	4.20 ± 3.399	3	<.001†
Moderate AD	15.03 ± 5.121	15		9.11 ± 2.905	9		5.92 ± 3.236	6	
Severe AD	18.33 ± 5.26	17		10.74 ± 2.659	10		7.59 ± 3.459	7	

AD, Atopic dermatitis; *HADS-A*, Hospital Anxiety and Depression Scale—anxiety; *HADS-D*, Hospital Anxiety and Depression Scale—depression; *HADS-T*, Hospital Anxiety and Depression Scale—total.
*Corrected *P* value: after controlling for covariance, including age, sex, marital status, education level, and body mass index.
†$P < .05$.

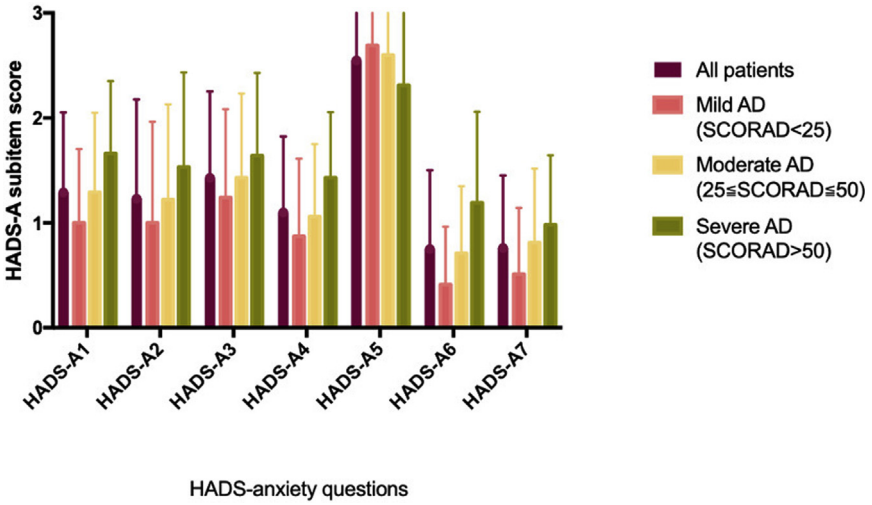

Fig 1. HADS-anxiety questions score distribution corresponding to different atopic dermatitis severity.

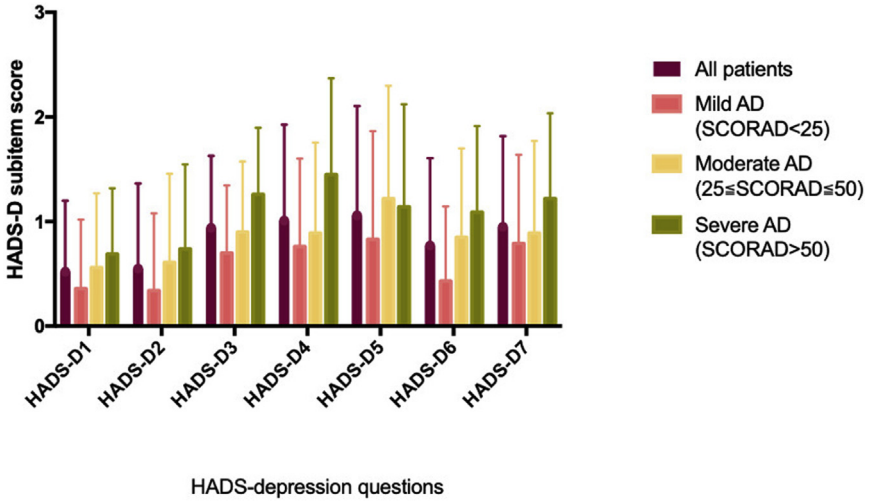

Fig 2. HADS-depression questions score distribution corresponding to different atopic dermatitis severity.

anhedonia, fatigue, and different sleep patterns.[34,35] Another meta-analysis study of 24 original articles supported a higher interleukin 6 concentration in patients with major depression disorder.[36] A Finnish twin cohort study claimed that AD and depression possibly shared the same genetic vulnerable components.[37] A meta-analysis study of 5 randomized controlled trials revealed that customized behavioral interventions, such as habit reversal for scratching,[38] autogenic training[39] to learn how to relax, and thinking pattern reconstruction, have benefits for AD disease control. Considering the strong heterogeneity within anxiety disorders, early detection in patients with moderate-to-severe AD and multidisciplinary care by psychiatrists and dermatologists are important for providing the most suitable treatment plan, such as cognitive behavioral therapy or pharmacotherapy.[40]

Conflicts of interest

None disclosed.

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