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Disease Severity Is Associated with Alexithymia in Patients with Atopic Dermatitis

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Keywords
Atopic dermatitis · Alexithymia · Comorbidity · Eczema Area and Severity Index

Abstract
Background: Atopic dermatitis (AD) is a chronic inflammatory skin disorder that is associated with higher rates of psychological disorders, but limited evidence supported the association with alexithymia, a psychoaffective dysfunction. ***Objectives:*** This study was aimed to investigate the occurrence of alexithymia in AD patients, compared to healthy subjects. ***Methods:*** This cross-sectional study assessed AD severity by the Eczema Area and Severity Index (EASI) score, sleeplessness and itch by a numeric rating scale (NRS), and alexithymia by the 20-item Toronto Alexithymia Scale (TAS-20) score. The association between disease characteristics and alexithymia was evaluated through several logistic regression models. ***Results:*** 202 AD patients and 240 healthy subjects were included in this study. The alexithymic personality trait (TAS-20 ≥51) was more frequently observed among AD patients compared to the control group (62.4% [126/202] vs. 29.2% [70/240], $p < 0.0001$). In particular, alexithymia (TAS-20 score ≥61) was detected in a significantly higher number of AD patients than in the controls (27.7% [56/202] vs. 7.5% [18/240]; $p < 0.0001$), whereas borderline alexithymia was detected in 34.6% (70/202) of AD patients compared to 21.7% of healthy controls. Alexithymia was more common among severe AD patients (43.6%) compared to mild AD patients (15.6%) and correlated with itch intensity and sleep disturbances. Among clinical variables, ordered logistic regression analyses revealed disease severity as predictor of alexithymia. Indeed, univariate analysis showed EASI score, sleep NRS, and itch NRS being significantly associated with alexithymia, while a multivariate model identified increased EASI score values as predicting factor. ***Conclusion:*** This study described alexithymia in AD patients correlating its occurrence with clinical AD severity markers (EASI score, itch, and sleeplessness) and identifying the increase in EASI score as predicting factor.

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Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disorder clinically characterized by eczematous patches, itching, and dry skin, and a lifetime prevalence of 15–20% in developed countries [1, 2]. AD is associated with higher rates of psychological diseases such as depression, anxiety, suicidal ideation, attention deficit/hyperactivity disorder, obsessive-compulsive disorder, and autism spectrum disorder [3–10]. Although the contribution of AD to the development of neuropsychiatric disorders is unclear, intolerable chronic itch and sleeplessness associated with AD skin manifestations are supposed to have a detrimental effect on patient mental health. In this regard, AD-related immune mediators may have a role in the pathogenesis of childhood neuropsychiatric disorders. Moreover, AD is associated with an increased risk of emotional and behavioral impairment, including attention deficit/hyperactivity disorder [3, 11]. Potential associations between AD and other emotional disturbances, such as alexithymia, have not been deeply investigated. Alexithymia represents a personality trait characterized by the lack of understanding, processing, and describing emotions, reflecting the tendency to have reduced symbolic thinking, limited fantasy life, externally oriented cognitive thinking, difficulty in distinguishing feelings from bodily sensations, and inadequacy in empathy and intuition [12]. This personality trait has been observed in some chronic inflammatory skin disorders, including psoriasis and hidradenitis suppurativa (HS) [13–15], but no association has been found with other skin diseases, such as acne and seborrheic dermatitis [16, 17]. Because alexithymia has been poorly investigated in AD, this multicentric study aimed to investigate its prevalence in AD patients, and its correlation with demographic and clinical variables.

Methods

For further details, see the online supplementary material (see www.karger.com/doi/10.1159/000507246 for all online suppl. material) (Fig. 1) [18–21].

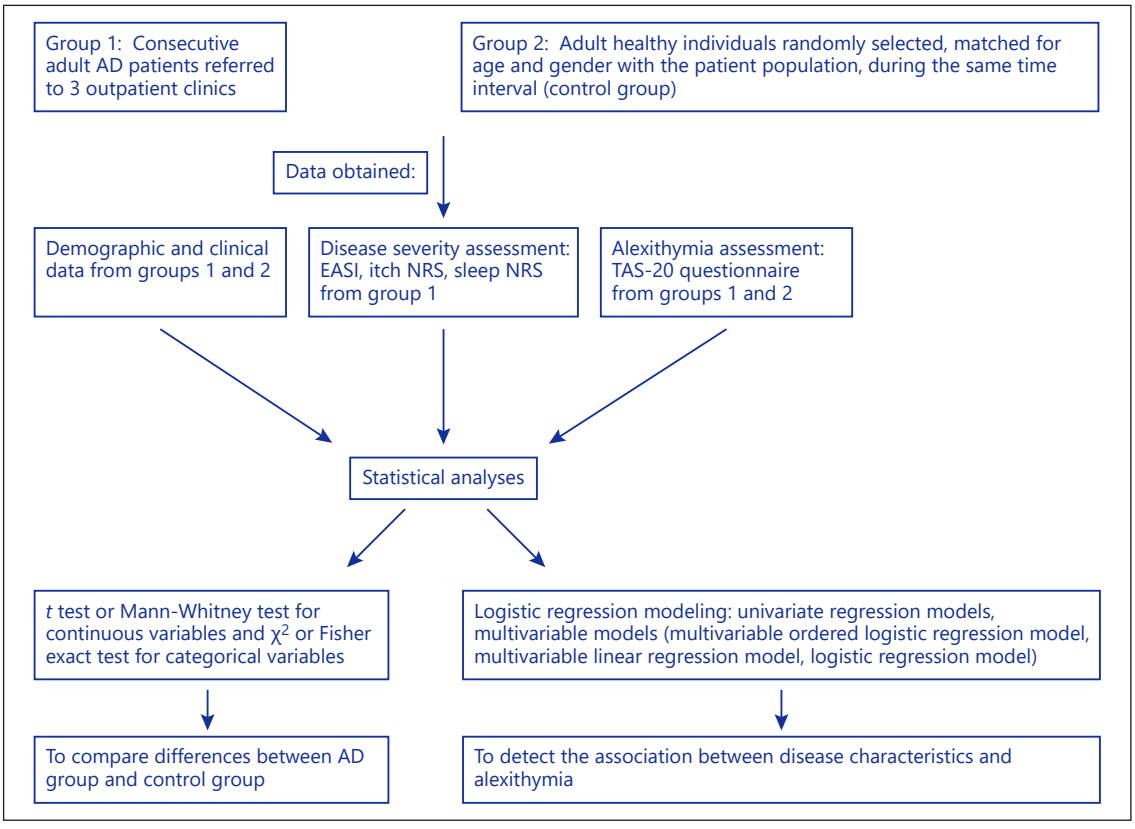

Fig. 1. Flowchart of the Methods. AD, atopic dermatitis; EASI, Eczema Area and Severity Index; NRS, numeric rating scale; TAS-20, 20-item Toronto Alexithymia Scale.

Results

Two-hundred two patients affected by AD were included in this multicentric study with an equal gender distribution (103 males [50.9%], 99 females [49.1%]) and a mean age of 40.9 ± 15.8 years (Table 1). The mean disease duration was 27.6 years (±17; Table 1).

The study population showed a mean Eczema Area and Severity Index (EASI) score of 12.9 (±10.3), a mean sleep numeric rating scale (NRS) score of 5.1 (±2.5), while the mean NRS itch score was 6.7 (±2.2). Based on the EASI scoring system, AD severity was classified as mild in 38.6% (78/202) of patients, moderate in 42.1% (845/202), and severe in 19.3% (39/202). NRS scores related to sleeplessness and pruritus were significantly higher in severe compared to mild AD patients (p < 0.0001; Table 2).

Table 1. Demographic characteristics and disease features of atopic dermatitis (AD) patients and healthy control subjects

	Controls	AD patients	p value
Number	240	202	–
Age (mean ± SD), years	39.7±14.7	40.9±15.6	0.49
Sex male, n (%)	127 (52.9)	103 (50.9)	0.68
EASI	–	12.9±10.3	
NRS sleep	–	5.1±2.5	
NRS pruritus	–	6.7±2.2	

EASI, Eczema Area and Severity Index; NRS, numeric rating scale.

To investigate alexithymia in an AD population, a control group consisting of 240 healthy subjects was included. Demographic features of the control group did not significantly differ from the AD population (Table 1). The 20-item Toronto Alexithymia Scale (TAS-20) score showed a significantly higher mean score in the AD population compared to control individuals (52.9 ± 11.5 vs. 43.6 ± 11.4, p <0.0001). The alexithymic personality trait (TAS-20 ≥51) was more frequently observed among AD patients compared to the control group (62.4% [126/202] vs. 29.2% [70/240], p < 0.0001; Table 1). In particular, alexithymia (TAS-20 score ≥61) was detected in a significantly higher number of AD patients than in the controls (27.7% [56/202] vs. 7.5% [18/240]; p < 0.0001), whereas borderline alexithymia was detected in 34.6% (70/202) of AD patients compared to 21.7% of healthy controls (p < 0.0001; Fig. 2). Dissecting mild-to-moderate AD versus moderate-to-severe AD based on EASI score <16 or ≥16, the mean TAS-20 score was shown to be significantly higher in moderate-to-severe AD patients (56.1 ± 11.1 vs. 51.4 ± 11.4, p < 0.0007) who showed more frequently the alexithymic trait (78.4% [58/64] vs. 53.9% [68/126], p < 0.001). As shown in Table 3, TAS-20 score ≥61 was detected in 20.6% (26/126) of mild-to-moderate patients (EASI <16), whereas its occurrence was significantly higher in the moderate-to-severe AD (EASI ≥16) subgroup (40.5%, 30/64, p < 0.001).

Analyzing mean scores of the 3 domains constituting the TAS-20 questionnaire in AD patients versus healthy controls, we detected the domain "difficulty in identifying feelings" scoring 15.5 ± 0.14 versus 14.15 ± 0.18, "dif-

Table 2. Clinical features and TAS-20 score details among patients with EASI-classified mild (EASI <7), moderate (EASI 7–21), and severe (EASI >21) atopic dermatitis

	EASI <7	EASI 7–21	EASI >21	p value
Number	77	84	39	–
Age (mean ± SD), years	44.6±17.9	38.7±14.6	38.8±12.0	0.026
Sex male, %	49.3	47.6	61.5	0.33
TAS-20, n (%)				
<50	39 (50.6)	24 (28.6)	11 (28.2)	0.004
51–60	26 (33.8)	33 (39.3)	11 (28.2)	
≥61	12 (15.6)	27 (32.1)	17 (43.6)	
Alexithymic trait	38 (49.3)	60 (11.9)	28 (17.8)	0.007
Mean TAS-20 ± SD	50.3±11.0	54.5±11.4	56±11.6	0.005
Mean NRS sleep ± SD	3.2±2.1	5.6±2.12	7.3±1.7	<0.0001
Mean NRS pruritus ± SD	4.7±2.2	7.6±1.5	8.2±1.2	<0.0001

EASI, Eczema Area and Severity Index; NRS, numeric rating scale; TAS-20, 20-item Toronto Alexithymia Scale.

Table 3. Clinical features and TAS-20 score details between moderate-to-severe (EASI ≥16) and mild-to-moderate (EASI <16) atopic dermatitis

	EASI <16	EASI ≥16	*p* value
Number	126	64	–
Age (mean ± SD), years	41.8±17.1	39.5±13.1	0.69
Sex male, *n* (%)	55 (43.6)	47 (63.5)	0.007
TAS-20, *n* (%)			
<50	58 (46.0)	16 (21.6)	0.001
51–60	42 (33.3)	28 (37.8)	
>61	26 (20.6)	30 (40.5)	
Alexithymic trait, *n* (%)	68 (53.9)	58 (78.4)	0.001
Mean TAS-20 ± SD	51.4±11.4	56.1±11.1	0.0007
Mean NRS sleep ± SD	4.0±2.3	6.8±1.6	<0.0001
Mean NRS pruritus ± SD	6.0±2.4	7.8±1.4	<0.0001

EASI, Eczema Area and Severity Index; NRS, numeric rating scale; TAS-20, 20-item Toronto Alexithymia Scale.

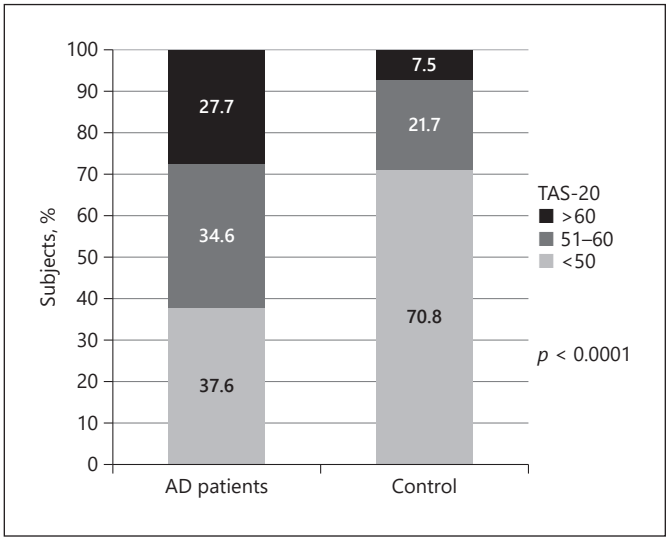

Fig. 2. Twenty-item Toronto Alexithymia Scale (TAS-20) scores in atopic dermatitis (AD) patients compared to the control group. Prevalence of alexithymia (TAS-20 score ≥61), borderline alexithymia (TAS-20 score 51–60), and absence of alexithymia (TAS-20 score ≤50) in AD patients versus healthy subjects (control group). Differences between the 2 subject groups for each TAS-20 score class were statistically significant ($p < 0.0001$).

ficulty in describing feelings" of 14.3 ± 0.21 versus 12.3 ± 0.18, and "externally thinking oriented" of 21 ± 0.35 versus 20.2 ± 0.24.

Among clinical variables, ordered logistic regression analysis revealed disease severity as predictor of alexithymia. Indeed, univariate analysis showed EASI score, sleep NRS, and itch NRS being significantly associated with alexithymia, while a multivariate model identified increased EASI score values as predicting factor: for each unit increase in EASI score, patients had a 9% enhanced likelihood to be in a higher alexithymia grade ($p < 0.001$; Table 4). Furthermore, for each unit increase in EASI score, a 11% higher likelihood to have an alexithymic personality trait was detected ($p < 0.001$; Table 4). Along these lines, each unit increase in EASI score was significantly associated with a 0.35-fold higher TAS-20 score value, as detected by linear regression analysis ($p < 0.005$). This evidence found confirmation in a significantly higher number of alexithymic patients in severe AD (EASI > 21) compared to the mild AD (EASI <7) subcohort (43.6 vs. 15.6%, $p < 0.004$), while the no-alexithymia number (TAS-20 <50) was significantly lower in severe AD compared to the mild AD subcohort (28.2 vs. 50.6%, $p < 0.004$; Table 2). Other clinical variables – including (i) body mass index (mean score: 23.5 ± 3.3, with only 3 patients classified as obese); (ii) the presence of atopic diseases such as rhinitis (29.7%), asthma (21.3%), conjunctivitis (9%), and food allergies (1%); other comorbidities (i.e., hypertension) – were identified in the AD patient population and were tested in both univariate and multivariate regression models; they were shown not to be significantly associated with alexithymia (data not shown).

Discussion

Alexithymia is a psychoaffective dysfunction characterized by the inability to identify, describe, and express feelings, restricted imagination, paucity of fantasy, dream construction, and concrete, logical, and realistic thinking [22]. It has been associated with psychiatric conditions (i.e., depression and anxiety), eating disorders, unhealthy behaviors (i.e., alcohol abuse, poor nutrition and sedentary lifestyle), reduced work productivity and impairment of intimate relationships, both personal and sexual [12, 22–24]. Notably, the presence of alexithymia increases the risk of other psychiatric disorders, and it reduces the likelihood of response to conventional therapies for these disorders [22–24]. The association with other chronic inflammatory skin diseases such as psoriasis and HS is consolidated whereas only paucity of evidence supported the association with AD [25–27]. In this study we included a large AD population (202 patients vs. 240 controls), and we found the alexithymic personality trait in 64.8% of patients compared to 29.2% of the control group ($p < 0.0001$). In particular, alexithymia (TAS-20 score

Table 4. Linear regression analysis for predictors of TAS-20 scoring and predictors of alexithymic personality trait

	Predictors of TAS-20				Predictors of alexithymic personality trait			
	univariate analysis		multivariate analysis		univariate analysis		multivariate analysis	
Sex male	0.56 (–1.75 to 2.89)	0.63			1.11 (0.99 to 1.01)	0.56		
Age	0.05 (–0.03 to 0.13)	0.20			1.00 (0.99 to 1.01)	0.49		
EASI	0.24 (0.09 to 0.39)	0.002	0.35 (0.11 to 0.61)	0.005	1.04 (1.01 to 1.079)	0.006	1.11 (1.04 to 1.19)	0.001
NRS sleep	0.86 (0.14 to 1.57)	0.020	–0.08 (–1.05 to 0.87)	0.86	1.17 (1.02 to 1.35)	0.023	0.93 (0.77 to 1.14)	0.53
NRS pruritus	0.96 (0.16 to 1.76)	0.019	0.15 (–0.85 to 1.16)	0.76	1.20 (1.03 to 1.40)	0.018	0.98 (0.80 to 1.21)	0.89

EASI, Eczema Area and Severity Index; NRS, numeric rating scale; TAS-20, 20-item Toronto Alexithymia Scale.

≥61) was observed in about a 4-fold higher number of AD patients than in the control group, and it was significantly associated with disease severity. Indeed, it was significantly more common among severe AD patients (43.6%) compared to mild AD patients (15.6%) and correlated with itch intensity and sleep disturbances.

Notably, a 1-point increase in the EASI was associated with an 11% higher likelihood to have an alexithymic personality trait (TAS-20 score ≥51), highlighting how severe AD patients may represent a more complex AD subpopulation having psychological disturbances to be considered in the holistic care approach. Overall, a few studies described the prevalence of alexithymia in small cohorts of patients, and none of them investigated the potential correlation with AD clinical variables. A previous study on 62 AD patients [26] showed a prevalence similar to our findings (AD patients vs. controls: 22.6 vs. 4.9%). Another study including 25 AD patients found a higher prevalence of alexithymia in AD patients (44%) as well as within the control group (20.7%) [27]. Moreover, no studies analyzed so far the association of alexithymia with AD severity that, in contrast, was found in our study, showing alexithymia to be more prevalent in severe AD patients. Nevertheless, it is not exclusively associated with AD as it has also been detected in other common inflammatory skin disorders, such as psoriasis and HS. In HS, alexithymia was observed in 37.2% of patients [15], with a prevalence of the alexithymic personality trait in HS patients of 61.6%, compared to the healthy (21.95%) and obese (32%) control groups ($p < 0.001$) [15]. In psoriasis, prevalence rates ranged from 24.8 to 32.4%, and, conversely to AD, no significant difference between mild and severe psoriasis was observed in terms of alexithymia occurrence, while a significant relationship was determined with female gender and sensitive area involvement, such as the face, hands, and genital area [13]. Moreover, alexithymia was recognized as contributor to the development of somatization, interpersonal sensitivity, anxiety, and phobic anxiety in psoriasis patients [13]. However, it is considered a stable personality trait that, unlike anxiety and depression, should not change over time, but a reversion with therapeutic interventions has been reported, suggesting that alexithymia might be partly modifiable [28, 29]. The current hypothesis is that a dimension of alexithymia, "trait alexithymia," constitutes a psychological trait that does not change over time, while another dimension, "state alexithymia," may vary based on psychological status or by therapeutic intervention impacting on patients' quality of life and, more in general, on well-being [22, 28, 29].

Because this study is a cross-sectional study enrolling all consecutive AD patients accessing to each dermatology clinic, it did not discriminate between untreated patients and patients undergoing therapy, and it did not follow up patients longitudinally. Another limitation of this study is the lack of patients' quality of life evaluation that would be informative in correlating alexithymia with the disease burden. Further studies will be useful to test potential modifications in TAS-20 score during therapies for AD and including the assessment of quality of life and other patients' life aspects such as work productivity and sexual activity. Moreover, longitudinal studies analyzing causality between alexithymia and AD, and mutual impairment (alexithymia could negatively impact on patient perception of disease severity, and it could lower compliance or induce undertreatment) would be insightful, as well as studies investigating whether alexithymia improvement might lead to AD amelioration and better patient self-care. Nevertheless, important findings emerged from our study investigating alexithymia on a large population of AD patients and describing the correlation between alexithymia and with clinical AD severity markers

(EASI score, itch, and sleeplessness). In particular, the increase in EASI score was identified as predicting factor; a 1-unit increase in EASI score determined a 11% higher likelihood to have the alexithymic personality trait. Considering the psychiatric burden (somatization, interpersonal sensitivity, anxiety, and depression) that could be associated with alexithymia, the introduction of the TAS-20 questionnaire into daily practice might be useful at the first visit and when disease severity increases (from a mild to a severe form, for instance) in order to obtain a holistic evaluation of AD patient well-being and to eventually set a therapeutic plan that includes psychological counseling and support.

Key Message

Atopic dermatitis is associated with alexithymia, and this association is significantly more frequent among patients with moderate-severe atopic dermatitis.

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Statement of Ethics

The study was approved by the local ethical committee of each university department (study protocol No.: 0028897/19; ID: 2615) and was carried out in accordance with the 1964 Helsinki Declaration. All subjects gave their written informed consent prior to participation in the study.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

A.C., N.G., G.G., and K.P.: conceived of the study. N.G., G.G., M.E., M.V., and F.B.: acquired clinical data. A.C., M.E., P.G., C.D.S., M.C.F., A.C., and K.P.: analyzed, interpreted, and synthesized the data. A.C. and K.P.: wrote the manuscript. All authors gave final approval of the version to be published, agreeing to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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