The anxiety and depression disorder in adults with atopic dermatitis: experience of a dermatology hospital

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Abstract

The objectives of this study are to identify the proportion of atopic dermatitis adult patients having anxiety and depression disorder and to measure the relationship between anxiety and depression disorder and characteristics of atopic dermatitis. A cross-sectional study with convenience sampling was conducted. Diagnostic criteria for atopic dermatitis were based on modified Hanifin and Raijka criteria and the severity of anxiety-depression disorder was evaluated using the hospital anxiety and depression scale. In this study, 208 patients were enrolled. The percentage of patients with anxiety and subthreshold anxiety were 11.1% and 34.1%, respectively. 5.3% of patients had depression and 39.4% of patients suffered from subthreshold depression. The proportion of patients with mixed anxiety-depressive disorder was 1.44%. Patients with severe atopic dermatitis were more likely to endure anxiety but not depression. Allergies or autoimmune diseases and scoring atopic dermatitis C were two independent risk factors of depression whereas edema and excoriation were two independent risk factors related to anxiety in atopic dermatitis patients. These findings suggest that atopic dermatitis is associated with anxiety and depression. Allergies, autoimmune diseases, pruritus, and insomnia had a correlation with anxiety and depression disorder.

Introduction

Atopic dermatitis is a common chronic inflammatory skin disease with a prevalence of 20-30% of the children population and about 3-5% of the adult population. Although most cases of atopic dermatitis do not affect health or endanger life, chronic symptoms along with prolonged treatment affect aesthetic features, psychology, and patients' life quality. A study on atopic dermatitis in children has noted that generalized atopic dermatitis can seriously affect the quality of life, which is similar to cystic fibrosis, severe renal impairment, and cerebral palsy.[1] For localized atopic dermatitis, the severity of the effect is at the same level of rheumatoid arthritis and diabetes. Atopic dermatitis causes guilt, low self-esteem about body image. At the same time, itching results in discomfort, making patients suffer from insomnia, anxiety, and depression.[2] In contrast, insomnia, anxiety and depression disorder could initiate or aggravate atopic dermatitis, forming a pathological circle.[3] Around the world, many studies have been conducted to understand the interplay between physical disorders and psycho-psychiatric disorders, including atopic dermatitis. A descriptive cross-sectional study of a population of 2893 adults conducted in the US in 2019 showed a significant increase in the risk of anxiety-depressive disorders.[4] Another population study in the US found that adults with atopic dermatitis had the risk of moderate to severe depression 2 to 5 times higher than that of the general population.[5] Furthermore, anxiety and depression disorders in atopic dermatitis patients can increase suicidality. Research of Gupta *et al.* on 146 patients suffering from mild to moderate atopic dermatitis recorded 2.1% of patients had suicidal thoughts and 2.7% of patients wished to die.[6] However, many dermatologists are now unaware of the impact of atopic dermatitis on the life quality of patients.[7] Moreover, in Vietnam, there are currently no studies on anxiety and depression disorder in atopic dermatitis patients.

Materials and Methods

A cross-sectional study with convenience sampling was conducted. Atopic dermatitis adult patients (≥18 years old) at the outpatient clinic at Ho Chi Minh City Hospital of Dermatology and Venereology (Vietnam) from September 2019 to September 2020 were included in this study. Inclusion criteria: patients met the diagnostic criteria for atopic dermatitis based on revised Hanifin and Rajka criteria in 2003,[8] and agreed to participate in the study. Exclusion criteria: patients are in the course of treatment for acute and chronic medical diseases such as liver, kidney, cardiovascular, and endocrine diseases, have mental disorders, are pregnant, and lactating. The

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Key words: adult; atopic dermatitis; anxiety; depression.

Contributions: NMV, has given substantial contributions to the concept, design, definition of intellectual content, literature search, clinical studies, data acquisition, data analysis, manuscript preparation, manuscript editing; VTTT, has given substantial contributions to the conception and design of the study; LNDT, has given substantial contributions to data analysis, statistical analysis, manuscript editing and manuscript review; HTXT, has given substantial contributions to data analysis, statistical analysis, manuscript editing and manuscript review; LTTH, has given substantial contributions to the conception and design of the study, data analysis; PVB has given substantial contributions to the statistical analysis, manuscript editing and manuscript review.

Conflict of interest: the authors declare no potential conflict of interest.

Funding: none

Ethical approval: the study was approved by The Board of Ethics of Pham Ngoc Thach University of Medicine (419/ĐHYKPNT – HĐĐĐ).

Informed consent: informed consent was obtained from all subjects involved in the study.

Availability of data and material: data and materials are available by the authors.

Received for publication: 11 May 2022.
Accepted for publication: 16 May 2022.

Licensee PAGEPress, Italy
Dermatology Reports 2023; 15:9524
doi:10.4081/dr.2022.9524

study was approved by the Board of Ethics of Pham Ngoc Thach University of Medicine (419/ĐHYKPNT – HĐĐĐ) and the author obtained informed consent from all participants. We assessed the severity of atopic dermatitis using the Scoring Atopic Dermatitis (SCORAD),[8] as follows: mild <25 points, moderate =25-50 points, and severe >50 points. The level of anxiety-depressive disorder was evaluated using the hospital anxiety and depression scale.[9] The value is determined as follows: 0-7=Normal, 8-10=Borderline abnormal, 11-21=Abnormal.

Data were entered, and processed using SPSS 16.0 software (IBM, New York, USA). The Chi-square test ($\chi 2$) was used to identify the relationship between qualitative variables. If the expected value is less than 5, then Fisher's exact test is used. Mean values were compared using student t-test. Logistics regression was used to investigate the relationships between clinical characteristics. P values less than 0.05 were considered statistically significant.

Results

A total of 208 patients (85 males and 123 females) participated in this study. The percentage of patients with onset before 12 years was 97.1%. Patients with autoimmune-allergic comorbidities accounted for 46.2%. Itching was always present (100%), dry skin accounted for most cases (99.5%). The mean score of SCORAD was 53.5 (12.8), equivalent to severe atopic dermatitis. Moderate and severe atopic dermatitis accounted for most of the cases with 44.2% and 55.3%, respectively.

The proportion of patients with anxiety and subthreshold anxiety was 11.1% and 34.1%, respectively. The percentage of patients with depression was 5.3% and with subthreshold depression was 39.4%. The proportion of patients with mixed anxiety-depressive disorder accounted for 1.44%, while 35.1% of patients were normal.

42.6% and 14% of patients with severe atopic dermatitis suffered from subthreshold anxiety and anxiety, respectively, which has a significant difference with moderate patients (P=0.002, Chi-square test). There were 44.3% and 7% of severe atopic dermatitis patients who had subthreshold depression and depression, correspondingly, but no significant difference was observed between the moderate and severe subgroups (P=0.1, Chi-square test) (Table 1). The factors associated with subthreshold anxiety were papules, excoriation, SCORAD B score, insomnia score, SCORAD C score, and total SCORAD score. However, when all these factors were included in the multivariate logistic regression analysis, no independent risk factors were observed (Table 2).

The results of multivariable logistic regression noted that edema and excoriation were independently related to anxiety disorders (Table 3).

The multivariate regression analysis showed that there were only two factors related to subthreshold depression, namely comorbidities and SCORAD C score (Table 4). In multivariable logistic regression analysis, only excoriation is an independent risk factor related to depression (OR 3.22; 95% CI 1.12-9.23). Atopic dermatitis patients with excoriation were at risk of depression 3.22 times as high as that in patients without excoriation (Table 5).

Discussion

In our study, the number of patients with anxiety was 11.1%, lower than that with subthreshold anxiety, 34.1%. There were 5.3% and 39.4% of patients experiencing depression and subthreshold depression, correspondingly. Our results are in agreement with the research of Ring *et al.* in

Table 1. The relationship between anxiety and depression disorder and severity of illness according to the SCORAD scale (n=208).

HADS		SCORAD scale, n (%)		
		Mild	Moderate	Severe
HADS-A, n (%)	Normal	1 (100)	63 (68.5)	50 (43.4)
	Borderline abnormal	0 (0)	22 (23.9)	49 (42.6)
	Abnormal	0 (0)	7 (7.6)	16 (14.0)
P			0.002	
HADS-D, n (%)	Normal	1 (100)	58 (63)	56 (48.7)
	Borderline abnormal	0 (0)	31 (33.7)	51 (44.3)
	Abnormal	0 (0)	3 (3.3)	8 (7.0)
P			0.1	

Table 2. Relationship between subthreshold anxiety and clinical features (n=208).

Clinical features	Mean ± standard deviation		P
	Normal	Abnormal	
SCORAD A	38.52±12.2	43.85±13.6	0.063*
Erythema	1.77±0.69	1.87±0.55	0.525*
Edema	0.59±0.65	1.13±0.63	< 0.001*
Ooozing/Crusting	0.85±0.63	1.17±0.98	0.142*
Excoriation	1.64±0.61	2.09±0.79	0.003*
Lichen	2.11±0.69	2±0.9	0.494*
Dry skin	2.39±0.66	2.3±0.82	0.567*
SCORAD B	9.36±2.53	10.57±2.97	0.045*
Itching	6.4±1.7	7.13±1.98	0.071*
Insomnia	3.87±2.26	5.65±1.97	0.001*
SCORAD C	10.3±3.3	12.78±3.7	0.002*
Total SCORAD score	50.76±12.73	58.53±14.14	0.01*

*Student t-test.

Table 3. Multivariate logistic regression analysis between anxiety and clinical features (n=208).

Clinical features	P	95% Confidence interval	Odds ratio
Edema	0.004	1.56-10.6	4.06
Excoriation	0.021	1.22-12.31	3.88
SCORAD B	0.088	0.17-1.13	0.44
Insomnia	0.158	0.85-2.66	1.51
SCORAD C	0.362	0.49-1.3	0.8
Total SCORAD	0.335	0.89-1.4	1.12

which the rate of depression is about 3%.[7] A study by Silverberg *et al.* also witnessed the proportion of anxiety patients similar to our study, but the prevalence of depression (28.6%) was higher.[10] Geographical factors and race may be behind this difference. Moreover, this study had a higher rate of severe atopic dermatitis patients than our study. The mechanism in which atopic dermatitis leads to anxiety and depression is still unknown, but some theories suggest that the chronic, recurrent nature of atopic dermatitis and itching are accountable for insomnia, and social isolation due to manifestations of the cutaneous lesions that may impact the mental health negatively.[11]

The rate of patients having mixed anxiety-depressive disorder accounted for 1.44%. Similar results were obtained in ample studies in which patients with atopic dermatitis suffer from anxiety more than depression.[12-15] 25% of our patients endured borderline abnormal/abnormal anxiety or depression. Similar conclusion was drawn by Tsintsadze *et al.* who reported that the co-morbidity of anxiety and depression in atopic dermatitis patients was 26.7%.[16] Anxiety may precede and lead to depressive disorder in patients with atopic dermatitis. Furthermore, our study noted that patients with severe atopic dermatitis were more prone to anxiety. However, we did not observe this statistical difference in the group of patients with depression (Table 1). According to Whiteley *et al.*, patients with severe atopic dermatitis have a higher risk of bipolar disorder and depression than mild and moderate ones, but not anxiety.[15] Another study in Korea recorded a higher proportion of moderate and severe atopic dermatitis in adult men who experienced depression, but not anxiety in comparison to mild ones.[17] The explanation could probably be that our sample size was not enough to find the distinction. Furthermore, the difference in medical care might play an important role because these two studies were conducted in the United States and South Korea which have a higher standard in the healthcare system, resulting in diagnosing patients with depression sooner.

In subthreshold anxiety patients, there were many factors associated with this condition: edema, scratching, insomnia, SCORAD B score, total SCORAD score (Table 2). However, in the multivariate analysis of the above factors, we did not observe any independent risk factors for subthreshold anxiety. It can be explained that this disorder is influenced by the interaction of a variety of factors mentioned above. In terms of anxiety, results of multivariate logistic regression demonstrated that edema and scratching were related to anxiety disorders (Table 3). Edema can be seen in the acute and subacute stages of atopic dermatitis which are the two main disease stages in the patients of our study. In fact, patients with pruritus and edema are often concerned about the medical conditions that they have heard or read about in the mass media such as fungal diseases, parasitic infections, helminthic infections from dogs, cats, *etc.* It is because of the presumption of these conditions that patients will often develop anxiety and seek medical attention.

In patients with subthreshold depression, multivariate logistic regression analysis between this condition and patient characteristics indicated two independent risk factors, namely comorbidities and SCORAD C (itch and insomnia) score (Table 4). Similarly, with depression, after multivariate analysis, atopic dermatitis patients with a 1-point increase in excoriation score had a 3.22-fold increased risk of developing depression (Table 5). Itching is one of the main symptoms of atopic dermatitis. The relationship between insomnia and pruritus in patients with atopic dermatitis was proved in the study of Kaaz *et al.*[2] When compared with psoriasis patients, the atopic dermatitis group suffered from insomnia and declined sleep quality more, which may give rise to depression.[1,18] Moreover, a variety of studies show that depression and even suicidal ideation in atopic dermatitis patients involve pruritus.[19,20] The more severe the itch is, the higher the risk of depression is.[21] Excoriation and itching symptoms create a pathological circle, leading to the formation of many lesions in atopic dermatitis. Therefore, limiting excoriation is one of the treatment principles in atopic dermatitis. Research using Dupilumab, a monoclonal antibody inhibiting interleukin 4 and interleukin 13, has shown efficacy in the treatment of moderate to severe atopic dermatitis. Not only were the symptoms of atopic dermatitis mitigated but also patients taking Dupilumab experienced an improvement in sleep quality and a reduction in symptoms of anxiety and depression at week 16.[22]

Regarding comorbidities, atopic dermatitis often accompanies a number of allergic and autoimmune diseases such as asthma, allergic rhinitis, and rheumatoid arthritis, and this pattern corresponds to that of our study. These conditions also cause anxiety and depression.[23,24] However, a longitudinal study in Taiwan found no link between depression, asthma, allergic rhinitis, and conjunctivitis.[25] More studies with larger sample sizes are warranted to elucidate the correlation between comorbidities, anxiety and depression disorder in patients with atopic dermatitis.

No significant positive correlation was observed between the severity of the disease based on the total SCORAD score and anxiety and depression disorder. These results provide support for a cross-sectional study conducted in the US in which no association between anxiety, depression, and the severity of atopic dermatitis was observed.[15] However, another research in Germany confirmed a link between severe atopic dermatitis and depression.[26] The study by Lim *et al.* also displayed a significant relationship between the SCORAD score and the level of anxiety-depression based on the HADS scale.[27] Similarly, according to Silverberg *et al.*, the severity of the disease is a major precipitating factor in anxiety and depression disorder.[4] The study by Jacob P. Thyssen *et al.* also recorded that the use of antidepressants and anxiolytic

Table 4. Multivariate logistic regression analysis of the association between subthreshold depression and clinical features (n=208).

Clinical features	P	95% Confidence interval	Odds ratio
Comorbidities	0.047	0.28-0.99	0.52
Edema	0.708	0.63-2.00	1.11
Ooozing/Crusting	0.966	0.58-1.78	1.01
Excoriation	0.263	0.77- 2.6	1.41
SCORAD B	0.14	0.86-2.85	1.57
SCORAD C	0.004	1.11-1.69	1.37
Total SCORAD	0.061	0.76-1.01	0.87

Table 5. Multivariate logistic regression analysis of the association between depression and clinical characteristics (n=208).

Clinical features	P	95% Confidence interval	Odds ratio
Excoriation	0.03	1.12-9.23	3.22
Itching	0.3	0.8-2.1	1.29

drugs in patients with moderate and severe atopic dermatitis was higher than that in the general population, while in the mild atopic dermatitis group, only anxiolytic medication was used.[28] Such variations between studies are attributable to the use of different scales or self-reported psychiatric symptoms but not a clinical diagnosis in evaluating anxiety and depression.

Our study has some limitations. First, our sample size was modest. Second, we only took samples from patients in the dermatology hospital who are more likely to present moderate or severe disease than in the population, so the result is not representative for the entire race to some extent. Last, this was a cross-sectional study so we could not establish a causal relationship in which whether anxiety and depression derive from itching and other cutaneous manifestations or comorbidities or even environmental and socioeconomic factors.

Conclusions

Atopic dermatitis is a chronic, recurrent condition that greatly affects the quality of life through anxiety and depression disorder. Our results showed that patients with severe atopic dermatitis are more prone to anxiety and the symptoms like itching, excoriation, and insomnia are correlated with anxiety and depression. However, more studies with larger sample sizes are recommended to evaluate the correlation between the inflammatory markers, sleep, itching, anxiety, and depression and the effectiveness of the atopic dermatitis treatment such as Dupilumab on anxiety and depression should be further investigated.

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