



Association between skin disease and anxiety: a logistic analysis and prediction

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Background: Dermatitis has symptoms of flushing, itching, pain, and burning, which causes psychological distress in patients.

Methods: We collected the data of 214 patients from the Wuhan Institute of Dermatology and Venereology from January 2020 to January 2022, including age, gender, diagnosis, Hamilton Anxiety Rating Scale (HAMA), and anxiety. First, descriptive analysis and difference analysis of the included data were carried out. Second, a correlation matrix was used to exclude the confounding factors with strong collinearity. Finally, logistic regression was used to analyze and predict the risk factors of anxiety.

Results: In the anxiety group and nonanxiety group, eczema and generalized eczema accounted for the largest proportion, and there was no difference in the composition of the diagnosis between the 2 groups. Several related analyses proved the accuracy of the logistic model. The results showed that age had a protective effect on the anxiety of patients with skin diseases [odds ratio (OR) =0.8606 with 95% confidence interval (CI): 0.7812, 0.8987]. Neurodermatitis (OR =1.0853 with 95% CI: 1.0115, 1.2512), eczema (OR =1.1358 with 95% CI: 1.0215, 1.2129), generalized eczema (OR =1.3346 with 95% CI: 1.1212, 1.5521), and psoriasis (OR =1.3685 with 95% CI: 1.1728, 1.6215) were associated with the anxiety of patients. Prediction analysis showed that with increase of patients' age, the likelihood of anxiety decreased.

Conclusions: This study demonstrated a strong correlation between skin diseases and anxiety and that the likelihood of anxiety decreases as age increases. Therefore, psychological intervention for patients with skin diseases, especially young patients, is essential.

Keywords: Skin disease; anxiety; logistic; prediction; risk factors

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Introduction

Dermatitis refers to all the diseases that occur on the skin, mucous membrane, and skin appendages. Compared with other organ diseases, it involves symptoms of flushing, itching, pain, and burning, which cause psychological distress (1-3). Patients with vitiligo, psoriasis, and acne usually have different degrees of depression, anxiety, or even suicidal tendencies. Moreover, a negative emotional

state can in turn lead to physiological changes of the skin, aggravate symptoms, and impact the prognosis of patients, thus forming a vicious circle. Chronic skin diseases, including inflammatory and neoplastic skin diseases, can thus lead to both physical and psychological problems (4-6). Interestingly, both skin diseases and psychological problems have been shown to decrease the health-related quality of life (HR-QOL), which includes adverse effects on physical

functions, physical feelings (such as pain or itching), and psychological (such as depression and anxiety) and social functions (7-9).

The brain and skin are interrelated in anatomy and function, a relationship which originates from a common embryonic origin—the ectoderm (10,11). In 2010, it was reported that, among the top 50 diseases worldwide, 5 were skin diseases: pruritus (global prevalence 279,889,120), eczema (global prevalence 229,761,000), impetigo (global prevalence 140,495,000), infectious soft warts/warts (global prevalence 122,601,000), and scabies (global prevalence 100,625,000). Previous reports estimated that 66,5103 people die of bacterial skin infections, including cellulitis, and 30,6103 people die of nonmelanoma skin cancer (NMSC) each year due (12,13). Anxiety disorder is a highly prevalent disease characterized by emotional and cognitive dysregulation. Evidence indicates that certain diseases can lead to anxiety disorders, which in turn can aggravate skin diseases, thus constituting a vicious circle of anxiety disorder and skin disease (14-16). Previous researches (12-15) show that there is a high prevalence of anxiety and depression among Chinese rosacea patients. Younger rosacea patients who have more severe self-reported symptoms and higher disease burden are prone to anxiety and depression. A Cross-Sectional Multicenter Study among Dermatological Out-Patients in 13 European Countries showed that the association with depression and anxiety was highest for patients with psoriasis, atopic dermatitis, hand eczema, and leg ulcers. Psoriasis, atopic dermatitis, acne, steroid-dependent dermatitis, and alopecia have a certain impact on the life quality of most patients, and may cause different degrees of anxiety and depression. In recent years, emerging research has shown that the skin is not only a target for the

regulation of psychological stress signals, but is also actively involved in the local hypothalamus-pituitary-adrenal (HPA) axis, peripheral nerve terminals as well as stress responses and immune cells including keratin-forming cells, mast cells and skin cells (15-17).

Therefore, it is necessary to conduct psychological evaluations on patients with skin diseases and further analyze the association between various skin diseases and psychological abnormalities. This study analyzed the relationship between various skin diseases and anxiety, and made further predictions for skin related anxiety. We present the following article in accordance with the TRIPOD reporting checklist (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-6511/rc>).

Methods

Samples

In this study, we collected the data of 214 patients from the Wuhan Institute of Dermatology and Venereology between January 2020 and January 2022, including demographic data, disease diagnosis, Hamilton Anxiety Rating Scale (HAMA) (18), and anxiety outcome. According to the anxiety assessment results of the included samples, patients were divided into an anxiety group (n=50) and a nonanxiety group (n=164). The diagnosis of skin diseases included erysipelas, generalized eczema, parapsoriasis, contact dermatitis, prurigo nodosa, chronic urticaria, dermatitis, neurodermatitis, eczema, atopic dermatitis, urticaria, psoriasis, and palmoplantar pustulosis. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics board of Wuhan Institute of Dermatology and Venereology (No. KY2022-012-011) and informed consent was taken from all the patients.

The HAMA

The HAMA was developed by Hamilton in 1959 and includes 14 items (18,19): (I) anxiety mood; (II) tension; (III) fear; (IV) insomnia; (V) cognitive function; (VI) depression mood; (VII) somatic anxiety (muscle system symptoms); (VIII) sensory system symptoms; (IX) cardiovascular system symptoms; (X) respiratory system symptoms; (XI) gastrointestinal and digestive tract symptoms; (XII) reproductive and urinary system symptoms; (XIII) autonomic nervous system symptoms, and (XIV) behavior when talking to people. In this study, 2 trained assessors

Highlight box

Key findings

- There is strong correlation between skin diseases and anxiety, and the possibility of anxiety decreases as age increases.

What is known and what is new?

- Dermatitis induces symptoms of flushing, itching, pain, and burning, which causes psychological distress in patients;
- We quantitatively analyzed the association between skin diseases and anxiety.

What is the implication, and what should change now?

- Psychological intervention for patients with skin diseases, especially young patients, is essential.

Table 1 Demographic information of the included patients

Variables	Anxiety (n=50)	No anxiety (n=164)	P value
Gender, n (%)			>0.05
Female	19 (38.0)	64 (39.0)	
Male	31 (62.0)	100 (61.0)	
Age (years) (mean ± SD)	67.2±9.43	50.7±13.0	<0.001
HAMA (mean ± SD)	8.52±2.19	3.66±2.02	<0.001
Diagnosis, n (%)			>0.05
Atopic dermatitis	3 (6.0)	12 (7.3)	
Chronic urticaria	1 (2.0)	1 (0.6)	
Contact dermatitis	2 (4.0)	0 (0.0)	
Dermatitis	0 (0.0)	1 (0.6)	
Eczema	22 (44.0)	70 (42.7)	
Erysipelas	0 (0.0)	1 (0.6)	
Generalized eczema	14 (28.0)	43 (26.2)	
Neurodermatitis	1 (2.0)	2 (1.2)	
Palmoplantar pustulosis	2 (4.0)	1 (0.6)	
Parapsoriasis	0 (0.0)	1 (0.6)	
Prurigo nodosa	2 (4.0)	4 (2.4)	
Psoriasis	3 (6.0)	24 (14.6)	
Urticaria	0 (0.0)	4 (2.4)	

HAMA, Hamilton Anxiety Rating Scale; SD, standard deviation.

jointly evaluated patients with the HAMA through conversation and observation. After the evaluation, the 2 assessors scored the patients independently.

Statistical analysis

This study included 3 steps. First, descriptive analysis and difference analysis of the included data were conducted. Second, a correlation matrix was used to exclude the confounding factors with strong collinearity. Finally, logistic regression was used to analyze and predict the risk factors of anxiety. All the analyses were conducted in R software 4.1.2 (The R Foundation for Statistical Computing). A two-sided P value <0.05 was considered statistically significant.

Logistic regression

Logistic regression is a supervised learning algorithm

used to predict a dependent categorical target variable. Essentially, logistic regression is used in categorizing large sets of data (20).

Meanwhile, binary logistic regression estimates the likelihood that a characteristic of a binary variable is present, given the values of the covariates. Suppose Y is a binary response variable where $Y_i = 1$ if the character is present and $Y_i = 0$ if the character is absent and the data $[Y_1, Y_2, \dots, Y_n]$ are independent, with π_i being the probability of success. Additionally, consider $x = (x_1, x_2, \dots, x_p)$ as a set of explanatory variables which can be discrete, continuous, or a combination of both discrete and continuous. Then, the logistic function for π_i is given as follows:

$$\text{logit}(\pi_i) = \log\left(\frac{\pi_i}{1-\pi_i}\right) = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \dots + \beta_p x_{ip} \quad [1]$$

Here, π_i denotes the probability that a sample is in a given category of the dichotomous response variable, commonly called the “success probability” and thus $0 \leq \pi_i \leq 1$. $\left(\frac{\pi_i}{1-\pi_i}\right)$ is the odds ratio (OR) or relative risk.

Results

According to the anxiety assessment results of the included samples, patients were divided into an anxiety group (n=50) and a nonanxiety group (n=164). In both groups, there were more men than women, and there was no difference in gender composition. The mean value of patients' age in the anxiety group was higher than that in nonanxiety group, and the mean HAMA score of the anxiety group was much higher than that of the nonanxiety group. In the anxiety group and nonanxiety group, eczema and generalized eczema accounted for the largest proportion, and there was no difference in the composition of the diagnosis between the 2 groups (Table 1).

Based on the descriptive results, we analyzed the influencing factors of anxiety. Prior to this, we conducted a correlation matrix analysis to remove the factors that were highly correlated with the anxiety results. From the results, we found that the HAMA was highly correlated with anxiety, and it was thus removed (Figure 1). Based on correlation analysis, we set age, sex, and diagnosis as risk factors into logistic regression to analyze the relevant risk factors.

Logistic regression was performed on the binary anxiety results. The reference of the diagnosis results was short-term acute disease contact dermatitis. The results showed

that age had a protective effect on the anxiety of patients with skin diseases (OR =0.8606 with 95% CI: 0.7812, 0.8987). Neurodermatitis (OR =1.0853 with 95% CI: 1.0115, 1.2512), eczema (OR =1.1358 with 95% CI: 1.2129), generalized eczema (OR =1.3346 with 95% CI: 1.1212, 1.5521), and psoriasis (OR =1.3685 with 95% CI: 1.1728, 1.6215) were associated with anxiety in patients. Meanwhile, the gender, erysipelas, parapsoriasis, prurigo

nodosa, chronic urticaria, dermatitis, neurodermatitis, atopic dermatitis, urticaria, and palmoplantar pustulosis showed no significant associations with patient anxiety (Table 2).

In order to ensure the accuracy of the logistic regression, we systematically evaluated the model. A residuals *vs.* fitted chart showed that the residual was independent of the estimated value, indicating that the model had good accuracy. A normal QQ chart showed that the included data were not subject to normality and that the model was accurate. A scale location graph showed no variance homogeneity, which did not affect the accuracy of the model. A residuals *vs.* leverage chart showed that there were 2 extreme values but that these did not affect the accuracy of the model (Figure 2).

Based on the construction of Logistic regression, we predicted anxiety by age and skin diseases (Figure 3). It could be seen from the figures that the possibility of anxiety gradually decreases with the increase of age, which also confirmed that age was a protective factor for anxiety. However, this decreasing trend had nothing to do with the dermatosis diagnosed.

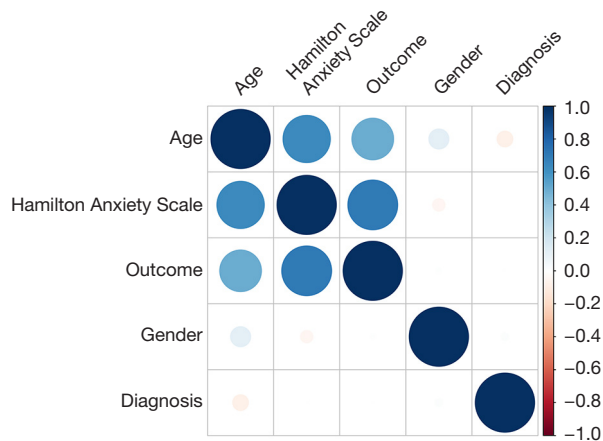


Figure 1 Correlation matrix of the included variables.

Discussion

This study found that age was related with the anxiety of

Table 2 Logistic regression of risk factors for anxiety among patients with dermatosis

Variables	β	Standard error	Z	OR	P value
Gender	0.10053	0.43933	0.229	1.1058	0.819
Age	-0.15014	0.02539	-5.912	0.8606	0.001*
Neurodermatitis	-2.46139	1.36083	-1.809	1.0853	0.0405*
Eczema	14.74252	3956.18	0.004	1.1358	0.0099*
Generalized eczema	0.28863	0.48596	0.594	1.3346	0.0352*
Psoriasis	0.31369	1.19934	0.262	1.3685	0.0196*
Palmoplantar pustulosis	-1.63832	1.26729	-1.293	0.1943	0.725
Erysipelas	-0.18272	0.95857	-0.191	56	0.8488
Prurigo nodosa	-0.09609	1.08015	-0.089	0.9084	0.9291
Dermatitis	-0.09621	1.45575	-0.066	25	0.9473
Urticaria	14.55928	1.83E+03	0.008	21	0.9937
Atopic dermatitis	-19.5658	2713.954	-0.007	0.833	0.9942
Chronic urticaria	15.54283	3956.18	0.004	0.9083	0.9969
Parapsoriasis	11.03861	3956.18	0.003	62	0.9978

*, $P < 0.05$. OR, odds ratio.

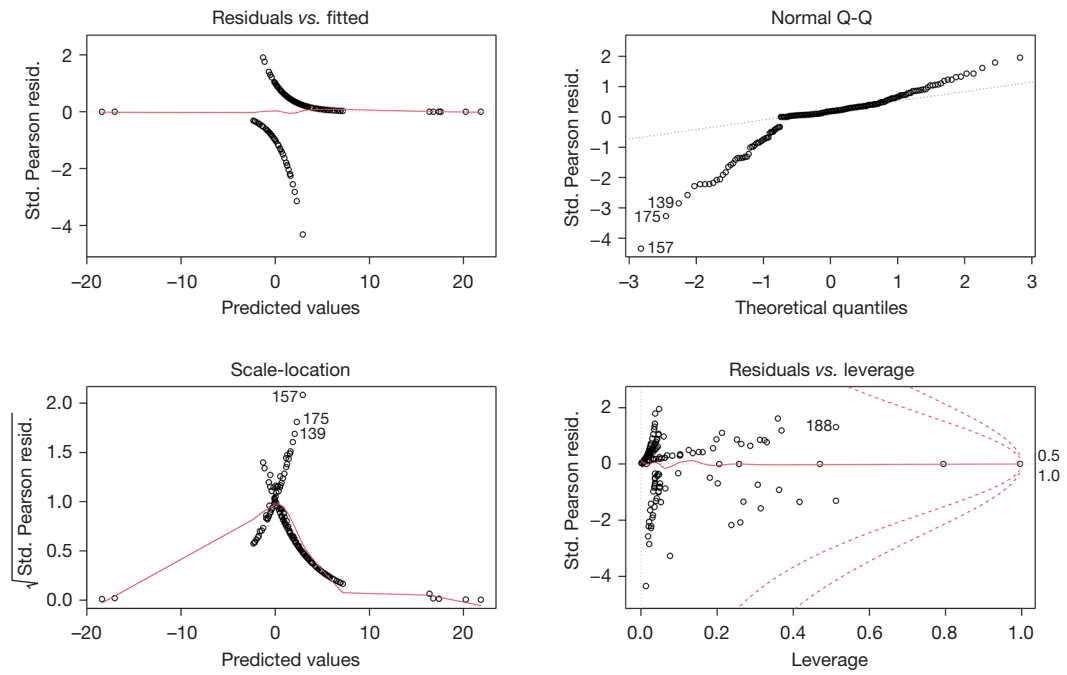


Figure 2 Evaluation of the logistic model. Resid., residuals; Std., standard.

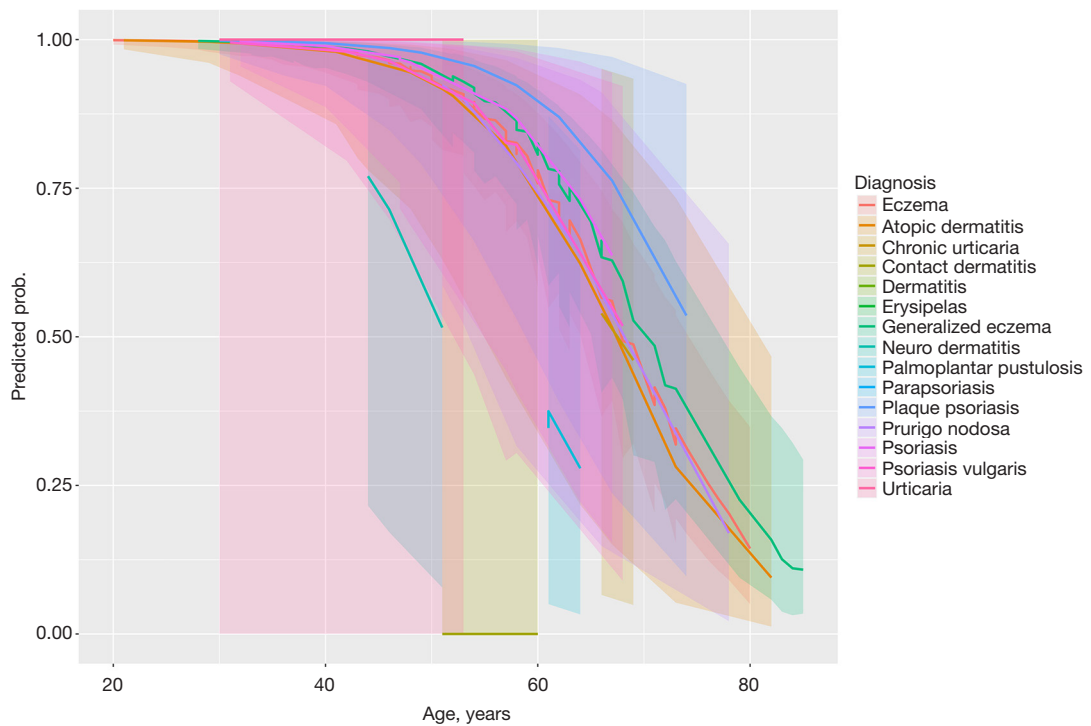


Figure 3 Prediction of anxiety based on age and diagnosis in logistic model. Prob, probability.

patients with dermatosis and that older age was a protective factor of anxiety. As age increased, the possibility of anxiety decreased. In addition, neurodermatitis (OR =1.0853), eczema (OR =1.1358), generalized eczema (OR =1.3346), and psoriasis (OR =1.3685) were associated with patient anxiety. A few studies have analyzed the psychological status of middle-aged and young patients with dermatosis; generally, young patients pay more attention to appearance, and their emotional state is more linked to changes in appearance (20). It was reported that old patients with skin pruritus mostly showed type A behavior, who were prone to being nervous and anxious, and were not able to cope with this situation (21,22). Pruritus is an unpleasant feeling of the skin or mucous membrane that causes a desire to scratch. As pruritus causes scratching, it in turn stimulates the synthesis and release of inflammatory factors (23). There are a large number of inflammatory cells in the allergic reaction site, which promotes an inflammatory reaction and itching, thus leading to irritability, compulsion, and anxiety, forming a vicious cycle (24-26). These conclusions were consistent with our research results. Moreover, some studies (23-24) have reported that the average scores of depression and anxiety in the psoriasis group had a medium degree of severity, further proving that patients with psoriasis are prone to having a negative psychological state, which is closely related to psychological disorders in dermatological diseases.

It has been reported that the association between psoriasis and anxiety involves the increase of tumor necrosis factor α (TNF- α), interleukin (IL)-17A, and IL-23, which can reflect the anxiety and depression of those with psoriasis (27,28). These results revealed the effectiveness of proinflammatory cytokine measurement in monitoring and even preventing anxiety and depression in patients with psoriasis. Inflammatory cytokines were shown to mediate anxiety and depression in a variety of ways, including via immunity, inflammation, and the HPA axis (29,30). Our study aimed to further clarify the association between the levels of common proinflammatory cytokines and anxiety with depression in patients with psoriasis. However, the analysis of neurodermatitis, eczema, generalized eczema, and anxiety was limited and should be studied further.

It was reported that social anxiety disorder (62.9%), health anxiety disorder (18.1%) and generalised anxiety disorder (32.5%) were positive for social anxiety disorder. Consistent with the hypothesis, each anxiety syndrome was indirectly associated with skin-related impairment through anxiety sensitivity. Overall, these findings highlight

the importance of anxiety symptoms in dermatological outcomes (31).

Research has attempted to uncover the mechanism underlying the relationship between skin diseases and anxiety (32,33). The mechanism of mental factors causing skin diseases might be related to the increase of amygdala activity caused by stress, which can lead to the degeneration of the prefrontal cortex and hippocampus, in turn affecting emotional regulation, cognitive function, anxiety, and depression (34). The increased activity of the amygdala also activates the HPA axis, stimulates the release of corticotropin-releasing hormone, induces skin inflammation through mast cell degranulation, and enhances vascular permeability. Stress could also activate dendritic cells in the skin, leading to the release of neurotransmitters and catecholamines through nerve endings in the skin, aggravating skin diseases (35-40).

Conclusions

This study found there to be a strong correlation between skin diseases and anxiety, with the possibility of anxiety decreasing as age increases. Therefore, psychological intervention for patients with skin diseases, especially young patients, is critical. However, this study was limited by a few factors. First, there were insufficient data concerning other risk factors, such as economic status. Second, this study was a cross-sectional study, and a causal relationship cannot be assumed. Finally, in addition to the psoriasis and anxiety, some reports (33,34) suggest that vitiligo has a strong correlation with anxiety, but patient data on vitiligo were not included in this study.

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Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at <https://atm.amegroups.com/article/view/10.21037/atm-22-6511/rc>

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-6511/icoi>)

amegroups.com/article/view/10.21037/atm-22-6511/coif.
The authors have no conflicts of interest to declare.

Ethical Statement: The authors are 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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics board of Wuhan Institute of Dermatology and Venereology (No. KY2022-012-011) and informed consent was taken from all the patients.

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