Original Article
Immune and environmental predictors of disease severity in atopic dermatitis: a retrospective cohort study

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Abstract: Objective: To explore the clinical and epidemiologic characteristics of atopic dermatitis (AD) and their correlation with lesion severity. Methods: A total of 3,912 patients with AD were enrolled in this analysis. Statistical analyses included the chi-square test and multivariate logistic regression to identify independent risk factors. Results: The incidence was higher in patients under 10 years old and those with onset in autumn. The primary inducing factors varied with disease severity: hot water bathing (mild cases), seasonal changes/dust mites (moderate cases), and seasonal changes/pet contact (severe cases). The main clinical manifestations were pruritus and xerosis cutis. Elevated eosinophils and increased immunoglobulin E (IgE) levels were observed. Multivariate regression analysis identified elevated IgE levels (OR = 3.41), pet contact (OR = 3.25), elevated eosinophils (OR = 2.95), and seasonal variation (OR = 2.18) as significant independent risk factors for disease exacerbation. Conclusion: AD severity is independently associated with specific immune biomarkers and environmental exposures, targeted intervention, thus offering a basis for risk stratification and targeted clinical management.

Keywords: Atopic dermatitis, disease severity, risk factor, immunoglobulin E, environmental exposure

Introduction

Atopic dermatitis (AD) is a common chronic inflammatory skin disease with an incidence increasing year by year. The disease affects primarily infants and children, and its core clinical manifestations are intense pruritus and characteristic skin lesions. Pruritus can easily induce sleep disorders and thereby impair patients' quality of daily life [1, 2]. Family genetic factors, environmental factors, immune factors, and skin barrier dysfunction are all closely associated with the pathogenesis of AD [3, 4]. The pathophysiologic mechanisms of AD involve the combined effects of impaired skin barrier function, abnormal cell-mediated immune responses, immunoglobulin E (IgE)-mediated hypersensitivity reactions, and environmental factors. AD can induce cytokine imbalance, alter cell-mediated immune responses, and promote the occurrence of IgE-mediated hypersensitivity reactions, thus driving disease progression [5].

The environment is an important factor influencing the onset of AD. Chemical substances in the air, such as formaldehyde, strong detergents, fragrances, and preservatives, may disrupt the acid-base balance of the skin, which in turn triggers downstream changes in enzyme activity and inflammatory responses. Environmental pollutants can simultaneously activate both the innate and adaptive immune responses of the body [6]. In addition, family medical history also affects the risk of developing AD; individuals with a family history of asthma or allergic rhinitis have a significantly higher incidence of AD [7, 8]. Identifying and controlling inducing factors to prevent disease onset holds important clinical value [9, 10].

Clinically, AD severity can be classified according to disease presentation, and patients with different severity levels exhibit significant differences in clinical manifestations and epidemiologic characteristics [11]. Accurate assessment of AD severity is of positive significance for monitoring patients' clinical conditions and evaluating the efficacy of drug therapy [12, 13]. Epidemiology is a discipline that analyzes the distribution patterns and influencing factors of diseases and health status in specific popula-

tions, with the aim of preventing and controlling diseases and improving residents' health. Epidemiological analysis plays a key role in identifying disease-inducing factors, family medical history, and clinical characteristics [14, 15]. Furthermore, analyzing the correlation between the epidemiological characteristics and disease severity of AD helps patients gain a clearer understanding of disease risk factors, actively avoid inducing factors, and thus prevent disease onset and exacerbation [16-18].

This study analyzed the clinical manifestations and epidemiological characteristics of AD patients and their correlation with skin lesion severity. It also explored the inducing factors of AD in patients of different genders and disease severity levels, and compared epidemiologic and clinical indicators among AD patients with disease severity. This may provide a basis for the clinical treatment of AD.

Materials and methods

Case selection

This study was designed as a retrospective study. The study protocol was reviewed and approved by the Ethics Committee of Ningbo No. 6 Hospital. Given the retrospective nature of this study, the requirement for informed consent was waived, and all patient data were anonymized prior to analysis. Medical records from patients treated between From January 2021 to December 2022 were screened, with a total of 3,912 patients diagnosed with AD initially enrolled.

Inclusion criteria were as follows: (1) A confirmed diagnosis of AD in accordance with the Hanifin & Rajka diagnostic criteria or the UK Working Party diagnostic criteria; (2) Availability of complete medical records, including demographic characteristics, detailed clinical history, physical examination findings, and laboratory test results (including complete blood count, eosinophil count, and serum immunoglobulin E [IgE] level); (3) Age ≥ 0 years.

Exclusion criteria were as follows: (1) Comorbidity with other active inflammatory or autoimmune skin diseases (e.g., psoriasis, contact dermatitis, or urticaria); (2) Lack of key clinical or laboratory data required for the

assessment and analysis of disease severity; (3) Current pregnancy or lactation status.

After screening, a total of 3,192 patients (1,677 males and 1,515 females) met the eligibility criteria and were included in the final analysis.

Data collection

Data were extracted from the hospital electronic medical record system using standardized data collection forms. The collected information was categorized as follows:

Epidemiologic and baseline characteristics: Age and sex at enrollment, season of onset (defined as the season when the patient first reported symptom exacerbation leading to medical consultation), family history of atopic diseases (AD, asthma, allergic rhinitis), lifestyle factors (smoking, alcohol consumption), and living environment (pet contact, frequent carpet use).

Triggering factors: Factors reported by patients or identified by physicians as associated with symptom onset or exacerbation were documented as binary variables (present/absent). These included hot-water bathing, seasonal changes (patient-reported symptom worsening associated with weather fluctuations), dust mite exposure (based on medical history and/or positive skin prick test or specific IgE results), pet contact (presence of furry pets in the household), and alcohol consumption.

Clinical manifestations: Presence or absence of signs and symptoms recorded during clinical visits, including pruritus, xerosis cutis, erythema, urticaria, scalp scaling, edema, and eczematous rash.

Disease severity: Based on clinical guidelines, AD severity was comprehensively assessed by physicians and classified into three grades (mild, moderate, severe), integrating the extent and severity of eczema, disease severity index scores, and impact on quality of life. The severity classification was independently determined by two dermatologists through medical record review, and any discrepancies were resolved through consensus.

Laboratory values: The following laboratory data were recorded: Eosinophil count: Elevated

Table 1. General characteristics of AD patients

Category	Number of cases	Percentage
Gender		
Male	1677	52.54
Female	1515	47.46
Age (years)		
< 2	1914	59.96
2-10	915	28.67
10-18	102	3.20
> 18	261	8.18
Previous treatment modalities		
Topical corticosteroids	1500	46.99
Calcineurin inhibitors	800	25.06
Systemic medications	400	12.53
Lifestyle habits		
Smoking history	51	1.60
Alcohol consumption history	90	2.82
Living environment		
Pet ownership	700	21.94
Frequent carpet use	500	15.66
Exposure to suspected allergens		
Dust mites	1000	31.39
Pollen	700	21.94
Animal dander	500	15.66
Onset season		
Spring	575	18.01
Summer	606	18.98
Autumn	1181	37.00
Winter	830	26.00
Family medical history		
Family history of AD	532	16.67
Family history of asthma	583	18.26
Family history of allergic rhinitis	1589	49.78

AD: atopic dermatitis.

Statistics version 20.0. Continuous variables conforming to a normal distribution were expressed as mean ± standard deviation $(X \pm S)$ and inter-group comparisons were performed using the independent samples t-test or one-way analysis of variance (ANOVA). Categorical variables were presented as counts and percentages (n, %) and inter-group comparisons were conducted using the chi-square (χ^2) test.

To identify independent risk factors associated with AD exacerbation, variables with significant differences in univariate analyses between different severity groups were included in a multivariate ordinal logistic regression model. Disease severity (mild, moderate, severe) was designated as the ordered dependent variable, with "mild" as the reference category. Results of the regression analysis were reported as odds ratios (ORs) with corresponding 95% confidence intervals (95% CIs). A two-tailed test was applied, and a *P* value < 0.05 was considered significant.

Results

if the proportion of eosinophils among total leukocytes was > 5% or the absolute count was > 0.5×10^9/L; Serum total IgE level: Elevated if the level was > 100 IU/mL.

Prior treatment history: Treatments received by patients before the study visit, including topical corticosteroids, topical calcineurin inhibitors, and systemic medications.

Statistical analysis

Data collation and documentation were performed using Microsoft Excel 2016. All statistical analyses were conducted with IBM SPSS

Statistical analysis of epidemiologic characteristics of AD patients

A total of 3192 patients with AD were enrolled in this study, including 1677 males (52.54%) and 1515 females (47.46%). The patient cohort was composed mainly of infants under 2 years of age, accounting for 59.96%, followed by children aged 2-10 years, who made up 28.67%. Autumn was the most frequent season of onset (37.00%), followed by winter (26.00%). Notably, among the family history of AD patients, the proportion of a positive family history of allergic rhinitis was the highest, reaching 49.78%. In addition, the proportions
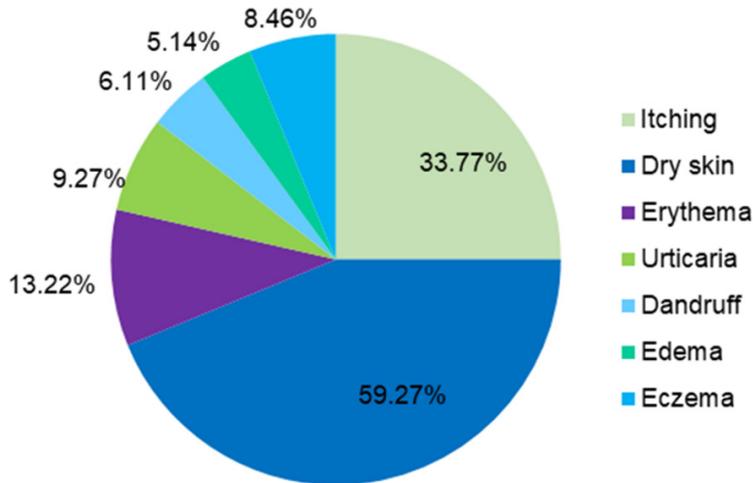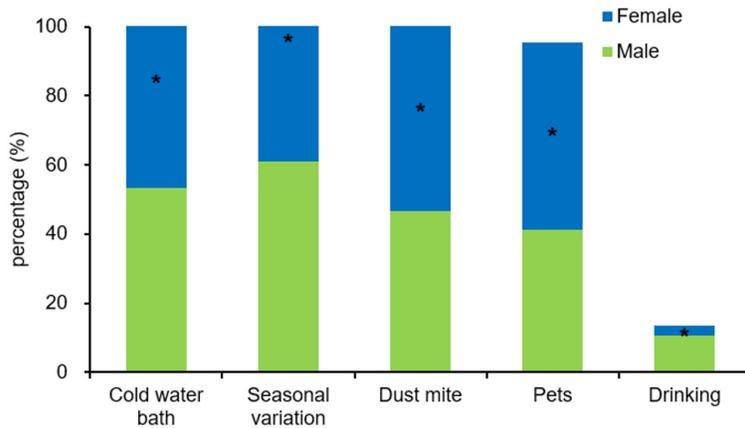
Figure 1. Clinical symptoms of AD patients. AD: atopic dermatitis.

Figure 2. Statistical analysis of predisposing factors in AD patients of different sexes. * indicates: compared to males, *P* < 0.05. AD: atopic dermatitis.
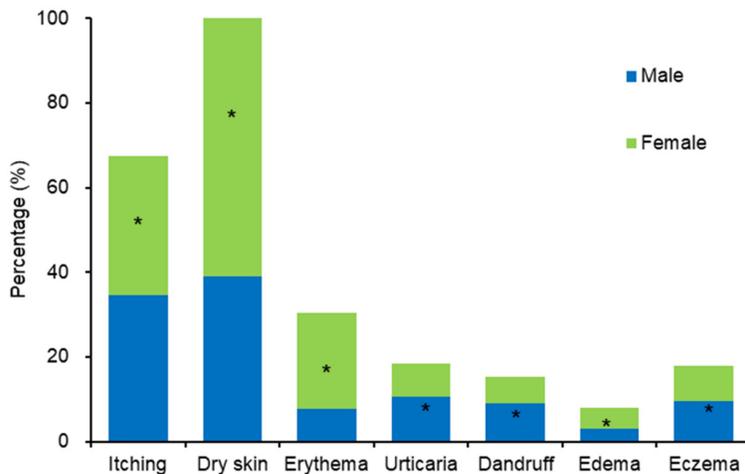

Figure 3. Statistical analysis of clinical manifestations in AD patients of different sexes. * indicates: compared to males, *P* < 0.05. AD: atopic dermatitis.

of male patients, those under 10 years old, and those with onset in autumn were significantly higher (both *P* < 0.05). Detailed demographic and clinical characteristics are presented in **Table 1**.

Clinical manifestations of AD patients

Among patients with AD, xerosis cutis was the most frequent symptom, with an incidence rate of 59.27%, followed by pruritus (33.77%) and erythema (13.22%). Other clinical manifestations, including urticaria, dandruff, edema, and eczematous rash, were relatively rare. The specific distribution of clinical symptoms is presented in **Figure 1**.

Analysis of precipitating factors and clinical manifestations of AD by gender

The prevalence of precipitating factors such as hot-water bathing, seasonal changes, dust mite exposure, and pet contact was significantly higher in female patients than in male patients (P < 0.05), whereas alcohol consumption as a precipitating factor was significantly less common in females (**Figure 2**).

Regarding clinical manifestations, the main symptoms in male patients were pruritus (34.47%) and xerosis cutis (39.12%), while the prevalence of xerosis cutis was markedly higher in female patients (81.58%, *P* < 0.05) (**Figure 3**).

Distribution of AD patients by disease severity

Among all patients, 478 cases (14.97%) were classified as mild, 2234 cases (69.99%) as moderate, and 480 cases
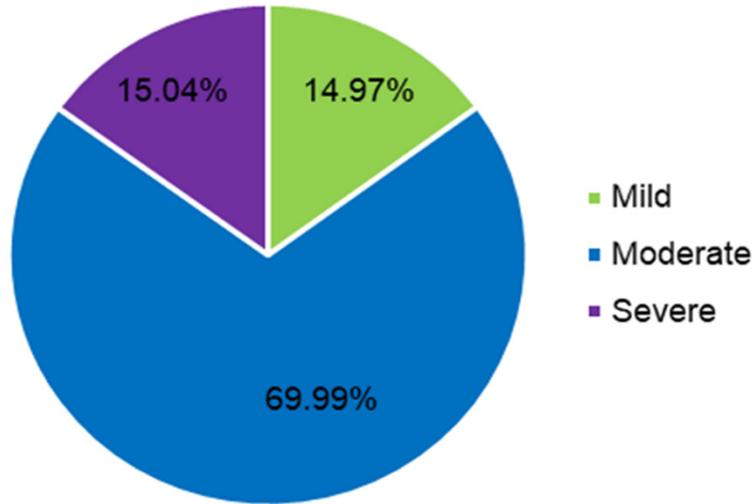
Figure 4. Distribution of AD patients by disease severity. AD: atopic dermatitis.
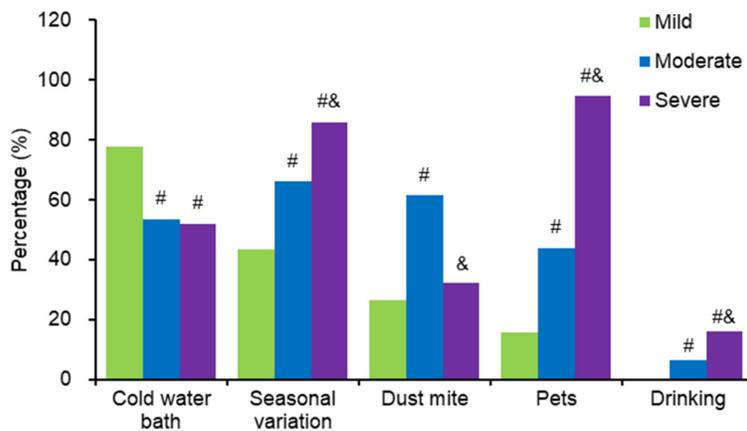

Figure 5. Statistical analysis of predisposing factors in patients with AD of various severities. # indicates compared to the mild group, *P* < 0.05; & indicates compared to the moderate group, *P* < 0.05. AD: atopic dermatitis.
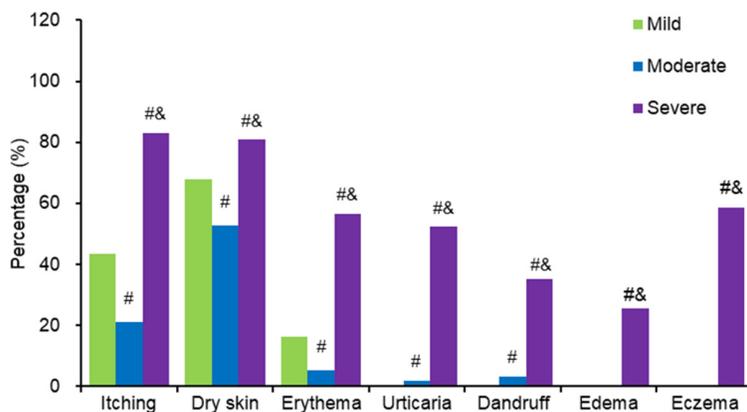

Figure 6. Statistical analysis of clinical manifestations in patients with AD of various severities. # indicates compared to the mild group, *P* < 0.05; & indicates compared to the moderate group, *P* < 0.05. AD: atopic dermatitis.

(15.04%) as severe, indicating that the majority of patients presented with moderate AD (**Figure 4**).

Analysis of precipitating factors and clinical manifestations in AD patients by disease severity

Analysis of precipitating factors revealed that hot-water bathing was the primary trigger in mild cases; seasonal changes and dust mite exposure were the most common triggers in moderate cases; in contrast, seasonal changes and pet contact were the predominant triggers in severe cases (both *P* < 0.05) (**Figure 5**).

Clinical manifestations varied with disease severity: pruritus and xerosis cutis frequently co-occurred in mild and severe patients, whereas isolated xerosis cutis was the most common presentation in moderate patients (*P* < 0.05) (**Figure 6**).

Comparative analysis of epidemiology and clinical indexes in patients with AD

Patients over 18 years of age had a significantly increased risk of progressing to severe AD (*P* < 0.05). As disease severity progressed, the proportion of patients with normal eosinophil counts decreased markedly (mild: 79.29%, moderate: 61.50%, severe: 29.17%; P < 0.05). Similarly, the proportion of patients with normal total serum IgE levels also decreased significantly with increasing disease severity (mild: 68.41%, moderate: 26.63%, severe: 23.96%; P < 0.05) (**Figure 7**).
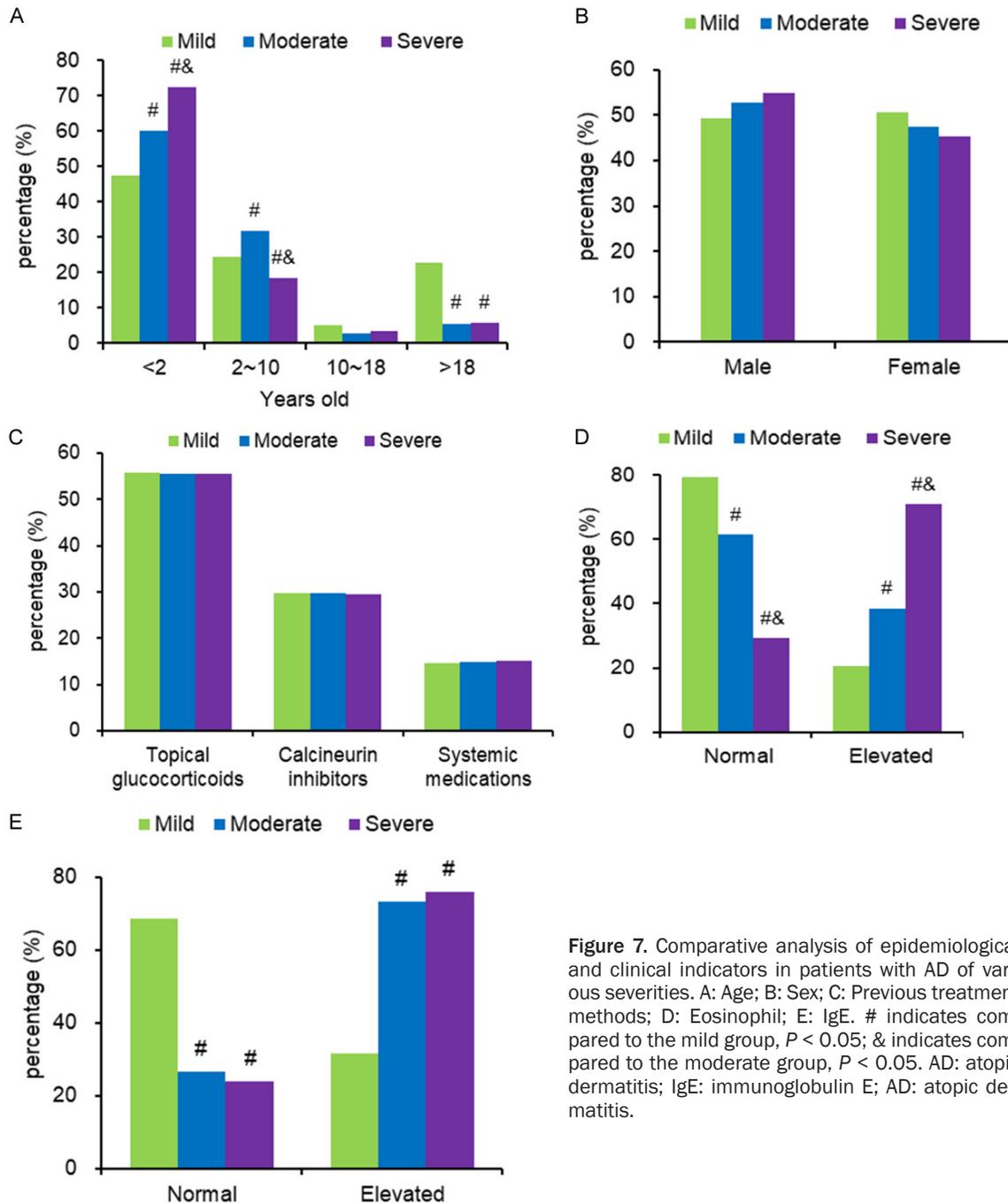
Figure 7. Comparative analysis of epidemiological and clinical indicators in patients with AD of various severities. A: Age; B: Sex; C: Previous treatment methods; D: Eosinophil; E: IgE. # indicates compared to the mild group, $P < 0.05$; & indicates compared to the moderate group, $P < 0.05$. AD: atopic dermatitis; IgE: immunoglobulin E; AD: atopic dermatitis.

Multivariate logistic regression analysis of factors independently associated with AD severity

Multivariate ordered logistic regression analysis revealed that after adjusting for other confounding factors, age (10-18 years and > 18 years), autumn onset, positive family history of allergic rhinitis, pet contact, dust mite exposure, seasonal changes, elevated eosinophil counts, and increased serum total IgE levels were all independent risk factors for AD exacerbation (all P < 0.05).

Among these factors, increased serum total IgE levels (OR = 3.41) and pet contact (OR = 3.25) demonstrated the strongest correlations with disease severity, followed by elevated eosinophil counts (OR = 2.95) and seasonal

Table 2. Multivariate ordinal logistic regression analysis of disease severity in AD patients

Variable	Category	OR value	95% CI	P
Age group	2-10 years (vs. < 2 years)	1.12	(0.91-1.38)	0.289
	10-18 years (vs. < 2 years)	1.85	(1.15-2.98)	0.012
	18 years (vs. < 2 years)	2.41	(1.72-3.38)	0.001
Sex	Male (vs. Female)	1.08	(0.92-1.27)	0.346
Onset season	Autumn (vs. Spring)	1.52	(1.22-1.89)	0.001
Family history	Allergic rhinitis (vs. None)	1.31	(1.10-1.55)	0.002
Precipitating factors	Pet contact (vs. None)	3.25	(2.68-3.94)	0.001
	Dust mite exposure (vs. None)	1.48	(1.25-1.75)	0.001
	Seasonal variation (vs. None)	2.18	(1.84-2.58)	0.001
Laboratory values	Elevated eosinophils (vs. Normal)	2.95	(2.47-3.52)	0.001
	Elevated IgE (vs. Normal)	3.41	(2.85-4.08)	0.001

Note: OR > 1 indicated the factor is a risk factor for increased disease severity. *P* < 0.05 was considered statistically significant. OR: Odds Rati; CI: Confidence Interval. IgE: immunoglobulin.
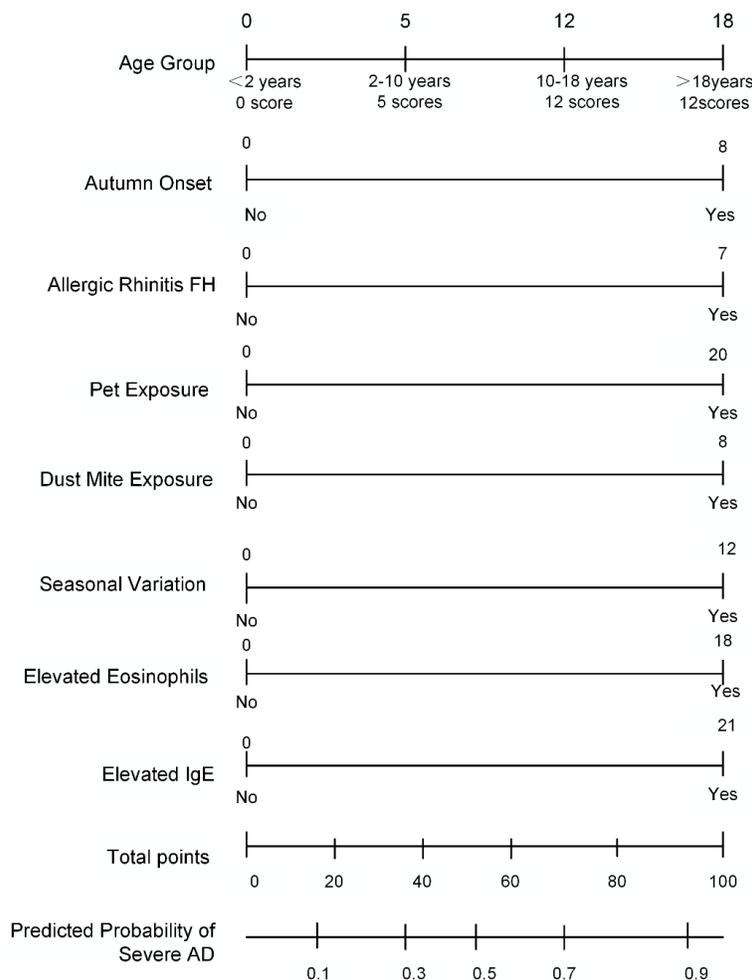

Figure 8. Nomogram for predicting the severity of atopic dermatitis. FH: family history; IgE: immunoglobulin E; AD: atopic dermatitis.

dent influencing factor for AD severity (**Table 2**).

Construction and validation of a nomogram for predicting AD severity

Based on the independent risk factors identified by the multivariate ordered logistic regression analysis - including age, autumn onset, positive family history of allergic rhinitis, pet contact, dust mite exposure, seasonal changes, elevated eosinophil counts, and increased serum total IgE levels - a nomogram was constructed to predict AD severity (mild, moderate, severe) in patients (**Figure 8**). This model integrated the aforementioned clinical and laboratory indicators, allowing the calculation of a total score for each patient, which could be directly converted into a predicted probability of progression to severe AD.

The performance of the nomogram was evaluated by internal validation: Discrimination was evaluated using the concordance index (C-index), which was 0.82 (95% CI: 0.79-0.85), indicating that the model had a good ability to distinguish patients with different disease severities.

changes (OR = 2.18). Neither sex nor the 2-10 year age group was identified as an indepen-

A

Calibration Curve
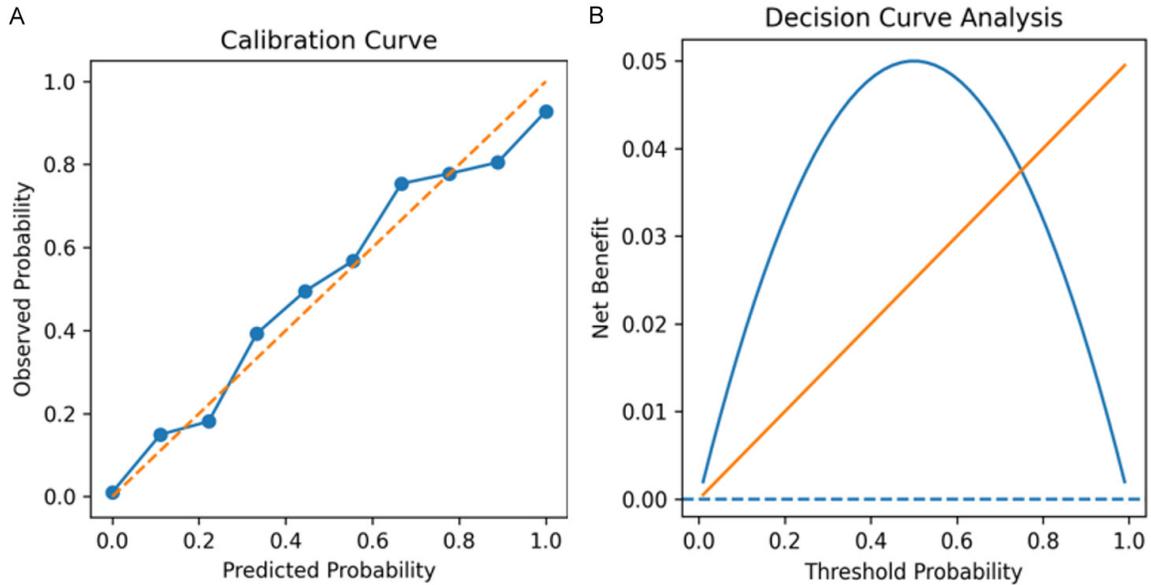
B

Decision Curve Analysis

Figure 9. Validation of the predictive model for atopic dermatitis severity. A: Calibration curve of the model; B: Decision curve.

Calibration was evaluated using calibration curves (**Figure 9A**), which showed a good agreement between the predicted probability of disease severity and the actual distribution (Hosmer-Lemeshow test, P = 0.214).

Clinical use was evaluated using decision curve analysis (**Figure 9B**), which showed that across a wide range of threshold probabilities, the net benefit of using this nomogram to guide clinical decision-making was higher than that of the strategies of "treating all patients" or "treating no patients".

Discussion

Atopic dermatitis (AD) is a chronic, recurrent inflammatory skin disease that affects both children and adults, with a higher incidence rate in the pediatric population. This condition impairs patients' quality of life, necessitating prompt implementation of high-efficacy skin care interventions and pruritus relief [19, 20]. The core pathogenesis of AD lies in impaired skin barrier function. As the body's first line of mechanical and immunological defense, structural damage and functional abnormalities of the skin are key factors triggering and driving the development and progression of AD. When the skin barrier is compromised, environmental allergens can penetrate the skin more easily, thereby promoting interactions between antigen-presenting cells and immune effector cells, and inducing the transformation of IgE-mediated sensitization system from a non-allergic state to allergic state, ultimately leading to disease onset. By conducting an in-depth analysis of clinical and epidemiologic data from 3,192 AD patients, this study not only clarified the basic characteristics of the study cohort but, more importantly, identified key independent risk factors associated with disease severity using univariate and multivariate logistic regression models. These findings provide an important clinical reference for individualized diagnosis, treatment, and prevention of more severe AD.

The immunologic feature of AD is a T-helper 2 (Th2)-type immune response. Interleukin (IL)-4, IL-13, and IL-31 are the core cytokines mediating Th2 inflammation. IL-4 and IL-13 can activate B cells to produce IgE antibodies and mediate allergic reactions [21, 22]. AD is characterized by a predominant Th2 immune response; driven by key cytokines such as IL-4, IL-13, and IL-31, the body exhibits a series of pathological manifestations including increased IgE production, eosinophil activation, and pruritus [23, 24]. The most prominent finding of this study is that the immune biomarkers-serum IgE levels and eosinophil counts-are the

strongest independent predictors of AD severity. Multivariate analysis results indicated that elevated IgE levels (OR = 3.41) and eosinophilia (OR = 2.95) were both significantly positively correlated with disease severity, which is consistent with the core Th2-dominant immune mechanism of AD [25, 26]. Specifically, IgE-mediated hypersensitivity and eosinophil activation can synergistically drive chronic skin inflammation and the "itch-scratch cycle", directly leading to disease exacerbation and chronic persistence [27]. Therefore, monitoring serum IgE levels and eosinophil counts is of great significance for assessing disease status and predicting the risk of progression to moderate-to-severe AD in patients.

Among environmental triggering factors, pet contact (OR = 3.25) was identified as the strongest environmental risk factor, with an effect size exceeding that of well-established risk factors such as dust mite exposure and seasonal changes. This suggests that pet contact and fur may act as potent and persistent sources of allergens and irritants for AD patients with specific genetic backgrounds or immune profiles, a notion supported by previous studies on environmental allergen exposure. The results indicate that in clinical practice, clinicians should proactively inquire about household pet ownership in patients with moderate-to-severe AD and recommend "pet avoidance" as a core environmental management strategy. Furthermore, seasonal changes (particularly autumn onset) were also confirmed as an independent risk factor for disease exacerbation (OR = 2.18) [28]. Dry climatic conditions and significant diurnal temperature fluctuations in autumn may exacerbate skin barrier damage; meanwhile, altered concentrations of environmental allergens such as mold and weed pollen may synergistically induce or aggravate inflammatory responses in AD [29].

This study also found an independent association between age and AD severity. Compared to patients with infantile-onset AD (< 2 years old), those with adult-onset AD (> 18 years old) had a significantly higher risk of developing a severe disease phenotype (OR = 2.41). This is consistent with the emerging academic consensus that adult-onset or persistent AD is often associated with more refractory skin lesions, a higher risk of complications (e.g.,

ocular involvement, psychological disorders), and a heavier disease burden [30, 31]. The underlying pathophysiological mechanisms may involve more complex immune pathways (including activation of Th1/Th17 responses in addition to Th2 responses) and more severe skin barrier dysfunction [32, 33]. This finding highlights the need for more aggressive and comprehensive treatment and management strategies for adult AD patients. It is worth noting that gender, which showed a distribution difference in univariate analysis, did not exhibit an independent correlation by multivariate analysis. This indicates that the effect of gender on disease severity may be indirect, mediated through interactions with other factors, rather than serving as a direct independent driver. This also underscores the indispensable value of multivariate statistical methods in controlling confounding biases and revealing true correlations [34].

The results of this study have clear clinical translational significance. The study established a risk factor checklist encompassing high-risk environmental exposures (pet contact), specific disease onset seasons (autumn), and objective laboratory markers (IgE levels, eosinophil counts). Clinicians can use this checklist to rapidly perform risk stratification during patients' initial diagnosis or follow-up visits, identify high-risk populations prone to progression to moderate-to-severe disease, and implement early interventions and close monitoring accordingly. This study provides an evidence-based foundation for targeted patient education; it strongly recommends that patients with severe AD avoid keeping furry pets and emphasizes the importance of enhancing skin moisturization and environmental protection during autumn.

This study has several limitations. As a single-center cross-sectional study, the predictive efficacy of the aforementioned risk factors needs to be further validated by future multi-center prospective cohort studies. Although various common influencing factors were included in this study, potential triggers such as diet, exposure to specific microorganisms, and psychological stress were not incorporated into the analysis. In addition, regarding pet contact, this study did not distinguish between pet species or the individual sensitization status of patients,

warranting more refined investigations in future research. Recent studies have revealed a strong association between AD and skin microbiome dysbiosis, which is characterized by decreased bacterial diversity, increased abundance and colonization rate of Staphylococcus aureus, and bidirectional regulatory interactions with immune dysfunction, representing a key link in the pathogenesis of AD [35, 36]. Future research should integrate multiomics data, including genomics, epigenomics, and exposomics, to comprehensively elucidate the complex interactions between AD and host-related factors, thereby providing novel strategies for disease prevention and therapeutic intervention.

Conclusion

This study confirmed that the main clinical manifestations of AD are pruritus and xerosis cutis, and disease severity is significantly correlated with immune biomarkers (elevated IgE levels, eosinophilia) and environmental exposure factors (pet contact, seasonal changes). Multivariate analysis further verified that these factors are all independent risk factors for AD exacerbation. The findings indicated that serum IgE levels, eosinophil counts, and pet contact history can serve as core indicators for AD risk stratification. These can help identify high-risk patients, enabling targeted prevention and management.

Disclosure of conflict of interest

None.

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