Increased Risk of Suicide Attempt in Patients With Atopic Dermatitis:

A Nationwide Population-Based Cohort Study

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Abstract

Introduction: Atopic dermatitis (AD) is associated with an increased risk of mental illness. However, few studies have explored the association between AD and suicidal risk. This study aimed to investigate the risk of suicide attempts in patients with AD.

Methods: Between 1997–2013, 5,169 patients with AD and 20,676 controls (1:4) matched according to age, sex, socioeconomic status, and selected comorbidities were enrolled from the Taiwan's National Health Insurance Research Database to analyze the risk of suicide attempt.

Results: Individuals with AD were found to have an elevated risk of suicide attempts, with an adjusted hazard ratio of 3.44 (95% CI, 1.83–6.46), compared to the control group. In the stratification analysis, the risk of suicide remained significantly higher in patients with AD of younger age, female sex, and those with cumulative systemic corticosteroid use for <30 days.

Conclusions: Dermatologists must recognize the potential increased suicidal risk in patients with AD, especially in vulnerable groups and those with certain comorbidities. Furthermore, patients with mild AD did not have a reduced suicidal risk.

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Atopic dermatitis (AD) is a chronic inflammatory skin condition characterized by recurrent eczematous rashes with intense pruritus that affects approximately 20% of children and between 2.1–4.9% of adults globally.[1] The pathogenesis of AD involves intricate interactions between genetic predisposition, skin barrier dysfunction, environmental exposures, and immune dysregulation.[2,3] Management of AD focuses on restoring the integrity of the skin barrier, controlling inflammation, and relieving pruritus, with treatment strategies, including emollients, phototherapy, topical and systemic immunomodulators, biologics, and Janus kinase (JAK) inhibitors. Despite advances in treatment, AD remains a challenging condition, owing to its chronic relapsing nature, economic burden of biologics and JAK inhibitors, and potential side effects of long-term therapy.[4,5]

In addition to the discomfort associated with skin lesions, AD also imposes a significant psychological burden on patients.[6] The chronic and often visible nature of the disease can lead to stigma, social withdrawal, and decreased self-esteem, contributing to increased rates of psychological disorders, such as depression and anxiety.[7] Furthermore, the persistent and intense itching can lead to sleep disturbances, which further exacerbates preexisting mental health issues, particularly in those with moderate and severe AD.[8] Recent studies have explored the relationship between AD and suicidal ideation and behavior, revealing a concerning link, particularly in females, adolescents, and young adults.[9–11] However, most of these existing studies were cross-sectional in design and limited by relatively small sample sizes. The influence of disease severity and comorbidities is also under explored.

To test the hypothesis that AD increases the risk of suicide attempts, a cohort study with an adequate follow-up period and adjustment of potential confounding factors is needed. Therefore, we conducted this nationwide, population-based cohort study to investigate the association.

Editor's Note
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Clinical Points

- Individuals with atopic dermatitis (AD) have an elevated risk of suicide.
- In the stratification analysis, the risk of suicide attempts remained significant among younger and female patients with AD.

MATERIALS AND METHODS

Data Source

Established in 1995, Taiwan's National Health Insurance (NHI) program is a mandatory health insurance system with 99.9% coverage of the population.[12] The NHI Research Database (NHIRD) comprises anonymized information encompassing demographic information (such as date of birth, sex, and residency), diagnosis codes, and claims data of insured individuals.[13] As the database contains comprehensive, patient-level information, it has been utilized extensively in epidemiological studies.[14–16] This study was approved by the Institutional Review Board of Taipei Veterans General Hospital (2018-07-016AC).

Study Cohort and Controls

Patients diagnosed with AD (*ICD-9-CM* code 691.8) between January 1, 1997, and December 31, 2013, were included in the study. To ensure the accuracy of the diagnosis, only patients diagnosed with AD >3 times during outpatient visits or at least once in an inpatient setting by board-certified dermatologists were included. Patients aged <10 years were excluded.

For each AD patient, 4 matched controls were randomly selected from the Longitudinal National Health Insurance Database. Controls were matched for age, sex, monthly insurance premiums, residence, and selected comorbidities. Monthly premiums were classified into 3 categories: $0–$500, $501–$800, and >$801 USD. Residence was divided into 5 levels, with level 1 indicating the most urbanized area, and level 5 indicating the least urbanized area. Monthly premiums and the degree of urbanization of residences were used as indicators of socioeconomic status.

Comorbidities

In this study, certain comorbidities related to suicide attempts were matched to reduce bias, which was determined using *ICD-9-CM* codes from the NHIRD. These selected comorbidities encompassed hypertension (*ICD-9-CM* codes 401–405), diabetes mellitus (*ICD-9-CM* code 250), hyperlipidemia (*ICD-9-CM* code 272), cerebrovascular disease (*ICD-9-CM* codes 430–438), traumatic brain injury (TBI) (*ICD-9-CM* code 959.01), major depressive disorder (*ICD-9-CM* codes 296.2 and 296.3), substance abuse disorder (*ICD-9-CM* codes 304 and 305), and alcohol-related disorders (*ICD-9-CM* codes 291, 303, 305.0, 357.5, 425.5, 535.3, 571.0, 571.1, 571.2, and 571.3). These diagnoses were recorded at least thrice in an outpatient setting or once during hospital admission.

Primary Outcome

The primary end point in this study was the first recorded suicide attempt identified using *ICD-9-CM* codes E950–958 in the NHIRD, which included suicide and self-inflicted poisoning by solid or liquid substances, by gases in domestic use, by other gases and vapors, by submersion, by firearms air guns and explosives, by cutting and piercing instrument, by jumping from high place, and by other and unspecified means. The index date for individuals in an AD group was their initial AD diagnosis date, and for control participants, it was the corresponding AD diagnosis date for their matched AD patients. Patients with a prior record of *ICD-9-CM* codes E950–E958, indicating a history of attempted suicide before the index date, were excluded from the study. All participants were followed from the index date until the first suicide attempt documented in medical records, withdrawal from the National Health Insurance (NHI) program, or December 31, 2013.

Stratification analysis was performed based on age, sex, and duration of systemic corticosteroid use. As systemic corticosteroids are commonly used during AD acute flare-ups, their use may serve as a proxy for disease severity. The duration of systemic corticosteroid use was defined as the cumulative number of days of exposure to at least 1 oral or intravenous systemic corticosteroid prescribed by a licensed physician during the follow-up period. The duration of use was further divided into <30 days and ≥30 days, with usage ≥30 days indicating moderate to severe disease.

Statistical Analysis

We employed conditional Cox proportional hazards regression to evaluate the association between the collected variables and suicidal attempts. Significant factors identified by univariate analyses (P value < .1) were incorporated into the multivariable backward stepwise regression models with the entry criteria of a significance level of 0.05 and exit criteria of 0.10 to determine independent explanatory factors and to calculate adjusted hazard ratios (aHRs) and 95% CIs for suicidal attempts. Proportional hazards assumptions were visually confirmed using log-minus-log plots.[17] Kaplan-Meier methods and log-rank tests were used to compare the cumulative incidence of study outcomes between the 2 groups.

Table 1.

Demographic Data of Patients With Atopic Dermatitis and Controls

	AD (n = 5,169)	Controls (n = 20,676)	*P*
Age at enrollment (years), median (IQR)	25.0 (15.0–39.0)	25.0 (15.0–39.0)	.7488
Sex, n (%)			1.0000
Male	2,179 (42.2)	8,716 (42.2)	
Female	2,990 (57.8)	11,960 (57.8)	
Monthly insurance premium (USD), n (%)			1.0000
$0–$500	3,036 (58.7)	12,144 (58.7)	
$501–$800	1,041 (20.1)	4,164 (20.1)	
≥ $801	1,092 (21.1)	4,368 (21.1)	
Residence, n (%)			1.0000
1 (urbanized)	804 (15.6)	3,216 (15.6)	
2	1,113 (21.5)	4,452 (21.5)	
3	317 (6.1)	1,268 (6.1)	
4	417 (8.1)	1,668 (8.1)	
5 (rural)	2,518 (48.7)	10,072 (48.7)	
Comorbidity, n (%)			
Hypertension	521 (10.1)	2,084 (10.1)	1.0000
Diabetes mellitus	201 (3.9)	804 (3.9)	1.0000
Hyperlipidemia	386 (7.5)	1,544 (7.5)	1.0000
Cerebrovascular disease	146 (2.8)	584 (2.8)	1.0000
Traumatic head injury	87 (1.7)	348 (1.7)	1.0000
Major depressive disorder	204 (4.0)	816 (4.0)	1.0000
Substance use disorder	78 (1.5)	312 (1.5)	1.0000
Alcohol use disorder	43 (0.8)	172 (0.8)	1.0000
Tobacco use disorder	77 (1.5)	308 (1.5)	1.0000
Obesity	98 (1.9)	392 (1.9)	1.0000
Asthma	1,306 (25.3)	5,224 (25.3)	1.0000
Allergic conjunctivitis	1,686 (32.6)	6,744 (32.6)	1.0000
Allergic rhinitis	2,811 (54.4)	11,244 (54.4)	1.0000
Duration of systemic corticosteroids (days), n (%)			<.0001
<30	4,073 (78.8)	20,427 (98.8)	
30–179	816 (15.8)	187 (0.9)	
≥180	280 (5.4)	62 (0.3)	
Annual outpatient visits, n (%)			<.0001
<5	385 (7.5)	2,666 (12.9)	
6–9	417 (8.1)	1,741 (8.4)	
≥10	4,367 (84.5)	16,269 (78.7)	

Abbreviations: AD = atopic dermatitis, IQR = interquartile range, USD = United States Dollar.

RESULTS

Demographics of Participants

In this study, 5,169 patients with AD and 20,676 controls were enrolled. Age, sex, monthly premium, urbanization level of residential area, and selected comorbidities were matched without intergroup differences (Table 1). Median age for both cohorts was 25 years old (interquartile range, 15.0–39.0 years old), and 57.8% were females. Notably, participants with AD had a significantly longer duration of systemic corticosteroid use ($P < .0001$) and a higher number of annual outpatient visits ($P < .0001$).

Cumulative Incidence of Suicide Attempt

A significantly higher cumulative incidence of suicide attempts was observed in the AD group than that in the control group ($P < .0001$) (Figure 1).

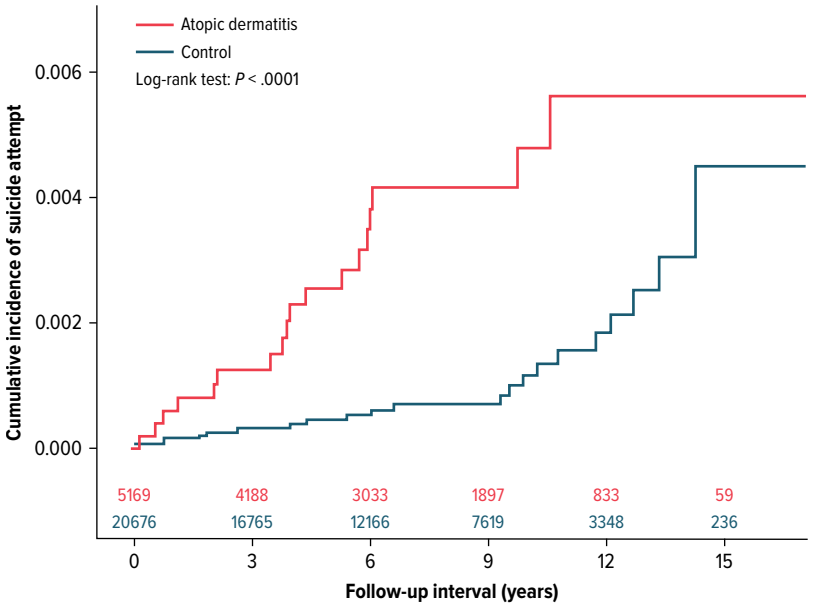
Multivariate Regression Analysis of Suicide Attempts

Eighteen individuals in the AD group and 21 in the control group attempted suicide during the follow-up period. The median age at first suicide attempt was 28.7 years (interquartile range, 18.9–48.0 years) in the AD group and 44.7 years (interquartile range, 30.0–65.4 years) in the control group. The duration between the index date and first suicide attempt showed no significant difference ($P = .8084$).

After adjusting for potential confounders, individuals with AD had a significantly higher risk of suicide attempt than that in the control group (aHR: 3.44; 95% CI, 1.83–6.46) (Table 2). We also found that age (aHR: 1.04), TBI (aHR: 6.07), major depressive disorder (aHR: 4.86), and asthma (aHR: 2.37) exhibited an elevated risk of suicide attempts in the Cox proportional hazard regression analysis (Table 2).

Figure 1.

Cumulative Incidence of Suicide Attempt Comparing Patients With Atopic Dermatitis to the Control Group



Stratification Analysis

In the stratification analysis, the association between AD and suicide attempt remained significant among younger populations (age <20 and 20–39 years), females, and systemic corticosteroid use for <30 days (Table 3).

DISCUSSION

In this study, we found an increased risk of suicide attempts in individuals with AD compared with that in the matched controls. In the stratification analysis, the association remained significant in females, patients aged <40 years, and those with systemic corticosteroid use for <30 days. Our study among the Taiwanese population corroborated previous studies showing that young female patients face an elevated suicide risk. Given the high prevalence of AD in children and its significant lifelong chronic effect, identifying factors that increase the risk of suicide attempts is crucial for effective suicide prevention.[2]

Numerous hypotheses support the link between AD and suicidal attempt. These include (1) sleep disturbances that lead to a higher rate of depression and chronic stress; (2) potential genetic overlaps between AD and depression; (3) stigmatizing nature of AD leading to low self-esteem and social isolation; and (4) chronic inflammatory status.[18,19] First, patients with AD often experience sleep disturbances due to nocturnal chronic pruritus, dry skin, and comorbid conditions, such as airway diseases and autoimmune disorders.[20,21] These factors also contribute to daytime impulsivity, mental burden, and a diminished quality of life, leading to increased suicidality. Second, a causal effect of genetic liability has been proposed between major depressive disorder and atopic skin disease.[22] The underlying etiologies include genetic molecular bases, interactions between neurons and the immune system, and cutaneous microbiota.[23] Consequently, routine screening for anxiety and depression symptoms is recommended in younger AD populations to facilitate early psychiatric intervention and support. Third, younger individuals may be more concerned with changes in body image, especially due to the influence of social media.[24] Thus, younger individuals with AD might suffer more intensely from the psychological burden of skin disruption, potentially leading to the development of neuropsychiatric disorders and suicidality.[25,26] Fourth, several studies have linked the elevated levels of proinflammatory cytokines in autoimmune skin diseases, including psoriasis, vitiligo, alopecia areata, and systemic lupus erythematosus, with the pathogenesis of suicide.[27,28] These cytokines, such as interleukin-6 (IL-6), tumor necrosis factor-alpha, and IL-1 beta, are thought to contribute to neuroinflammation, alterations in neurotransmitter systems, and dysregulation of the hypothalamic-pituitary-adrenal axis, all of which are associated with suicidal behaviors.[29,30] In addition, cytokine-targeted therapies, particularly those inhibiting

Table 2.

Cox Regression Analyses of Confounding Factors Associated With the Risk of Suicide Attempt

	AD vs Controls					
	Crude hazard ratio	95% CI	*P*	Adjusted hazard ratio[a]	95% CI	*P*
AD vs control	3.44	1.83–6.45	.0001	3.44	1.83–6.46	.0001
Age, y	1.03	1.02–1.05	<.0001	1.04	1.02–1.05	<.0001
Sex, male vs female	1.16	0.62–2.17	.6517	1.06	0.55–2.04	.8607
Monthly insurance premium (USD)			.3461			.2391
$501–$800 vs $0-$500	1.22	0.59–2.56	.5911	0.82	0.38–1.77	.6096
≥$801 vs $0–$500	0.56	0.21–1.45	.2309	0.43	0.16–1.15	.0910
Residence			.3668			.2401
2 vs 1	1.08	0.38–3.02	.8901	0.94	0.33–2.66	.9100
3 vs 1	2.19	0.67–7.18	.1956	2.01	0.61–6.64	.2525
4 vs 1	1.31	0.37–4.63	.6782	1.21	0.34–4.31	.7742
5 vs 1	0.77	0.30–2.00	.5964	0.62	0.24–1.62	.3314
Comorbidity						
Hypertension	2.54	1.17–5.54	.0187	0.63	0.20–1.97	.4225
Diabetes mellitus	4.43	1.73–11.38	.0020	2.32	0.69–7.85	.1762
Hyperlipidemia	1.49	0.53–4.18	.4535	0.64	0.19–2.15	.4682
Cerebrovascular disease	2.14	0.52–8.90	.2939	0.47	0.10–2.31	.3510
Traumatic head injury	4.91	1.51–15.96	.0081	6.07	1.85–19.91	.0029
Major depressive disorder	4.66	2.06–10.56	.0002	4.86	2.14–11.06	.0002
Substance use disorder	1.73	0.24–12.61	.5879	–	–	.9997
Alcohol use disorder	4.41	0.60–32.17	.1439	4.45	0.57–34.64	.1537
Tobacco use disorder	1.77	0.24–12.88	.5739	–	–	.9997
Obesity	–	–	.9863	–	–	.9974
Asthma	1.79	0.94–3.42	.0761	2.37	1.23–4.57	.0098
Allergic conjunctivitis	0.69	0.33–1.41	.3030	0.81	0.38–1.72	.5834
Allergic rhinitis	1.05	0.56–1.98	.8798	1.10	0.54–2.25	.7923
Annual outpatient visits			.9997			.9999
6–9 vs <5	–	–	1.0000	–	–	.9997
≥10 vs <5	–	–	.9863	–	–	.9917

[a]Adjusted for age, traumatic head injury, major depressive disorder, and asthma.
Abbreviations: AD = atopic dermatitis, aHR = adjusted hazard ratio, cHR = crude hazard ratio, USD = United States Dollar.

IL-4 and IL-13 activity, have demonstrated efficacy in reducing symptoms of depression and anxiety in patients with AD.[31]

The effect of AD severity on suicide risk was also an issue with importance. In our study, we defined the duration of systemic corticosteroid use, which is a commonly used medication for acute flare-ups, as a proxy for AD severity. Our findings align with those of prior studies, which indicated that suicidality and psychiatric comorbidities were significantly increased, even in patients with mild-to-moderate AD severity.[32] These findings suggested that even milder disease severity should not diminish vigilance regarding patient suicide risk.

Our study also revealed that some comorbidities, including TBI, depression, and asthma, may be associated with higher suicide attempt rates. TBI, in previous studies, has been found to be a risk factor for suicidal ideation, suicide attempts, and completed suicide.[33,34] Patients with TBI often exhibit persistent neuropsychiatric sequelae, such as neurological and cognitive deficits, increased feelings of hopelessness and despair from physical and emotional pain, social isolation, and post-traumatic stress disorder, all of which elevate their risk of suicidality.[35,36] In individuals with serious mental illness such as bipolar disorder, major depression, or schizophrenia, the risk of suicide attempt is known to be higher compared to the general population. In one recent meta-analysis, the pooled suicide rate was 534.3 per 100,000 person-years among patients with major depression.[37,38] As to asthma, previous systematic reviews have also suggested it as a potential risk factor for suicide.[39–41] The link between asthma and suicide risk may be mediated by brain-derived neurotrophic factor (BDNF), a neurotrophin involved in major depressive disorder and implicated in regulating airway smooth muscle and inflammatory processes.[42–45] Studies have also shown that BDNF gene polymorphism may increase susceptibility to bronchial asthma in children.[46–48] Further studies are needed to clarify the specific pathways

Table 3.

Hazard Ratios of Suicide Attempt Among Patients With Atopic Dermatitis Stratified According to Age, Sex, and Duration of Systemic Corticosteroids

	AD vs Controls					
	Crude hazard ratio	95% CI	*P*	Adjusted hazard ratio[a]	95% CI	*P*
Total	3.44	1.83–6.45	.0001	3.44	1.83–6.46	.0001
Age group (years)						
<20	4.04	1.30–12.54	.0155	4.11	1.32–12.78	.0147
20–39	5.55	1.76–17.48	.0034	5.49	1.74–17.31	.0037
40–59	1.99	0.37–10.88	.4258	2.03	0.37–11.12	.4129
≥60	2.05	0.51–8.20	.3096	2.00	0.50–7.99	.3278
Sex						
Male	1.54	0.55–4.33	.4091	1.55	0.55–4.35	.4053
Female	6.52	2.70–15.72	<.0001	6.53	2.71–15.75	<.0001
Duration of systemic corticosteroids (days)						
<30	2.64	1.23–5.63	.0124	2.75	1.29–5.89	.0090
≥30	2.09	0.26–16.73	.4871	3.20	0.39–26.27	.2790

[a]Adjusted for age, traumatic head injury, major depressive disorder, and asthma.
Abbreviation: AD = atopic dermatitis, aHR = adjusted hazard ratio, cHR = crude hazard ratio.

linking asthma, major depression, and suicide.[49,50] However, contrary to previous studies, our analysis did not identify type 2 diabetes mellitus (T2DM) as a significant risk factor for suicide.[51] Since the enrolled participants in this study were relatively young and had a low prevalence of T2DM, the impact of T2DM on suicide risk may have been underestimated.

Promoting communication and collaboration between dermatologists and psychiatrists is crucial, as the complex relationship between skin diseases and suicide attempts often stems from factors such as an individual's desire to escape life, search for answers, internal turmoil, and societal pressures.[52] Research on social support indicates that personalized care in various forms—such as face-to-face interactions, telephone calls, mail, online communication, and virtual interactions—can effectively reduce suicide risk among at-risk populations.[53] As frontline supporters of patients, dermatologists can benefit from learning empathetically understanding techniques, as many individuals with suicidal ideation often convey their distress through verbal or nonverbal cues.

Our study provided evidence based on a population-based cohort of Asian individuals. It spans adolescence to adulthood and offers a detailed analysis using 20-year age intervals. However, this study has some limitations. First, this study did not enroll patients with AD <10 years of age who exhibited a higher AD prevalence and may have distinct risk factor patterns. Second, suicidal behavior is a complex issue highly related to cultural context, societal norms, and welfare systems.[54,55] As the enrolled participants were mostly Taiwanese, the generalizability to other ethnicities may be a concern. Third, our study did not include the use of immunosuppressants, biologics, or phototherapy in the analysis, which were typically used for patients with moderate to severe AD. However, factors such as potential side effects, out-of-pocket cost, and treatment accessibility may influence patients' treatment choices. Therefore, we used the duration of systemic steroid use as a proxy for AD severity, as systemic steroids are more commonly prescribed during acute flare-ups. Fourth, the NHI database may contain potential coding errors. Therefore, we required at least 1 inpatient or 3 outpatient diagnoses by certified dermatologists to enroll the selected individuals.

In conclusion, vigilance for potential suicidality is crucial in younger female patients with AD and specific comorbidities. Furthermore, neither mild AD severity nor short-term systemic steroid use guarantees a reduced suicide risk. Enhanced collaboration between dermatologists and multidisciplinary specialists, involving referral, consultation, and cooperation, is recommended to promote comprehensive care and suicide prevention.

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Ethics Approval: This study was reviewed and approved by the Institutional Review Board of Taipei Veterans General Hospital, approval number 2018-07-016AC. As this is a retrospective review of patient data, written informed consent was not required in accordance with local/national guidelines.

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