

---

## The association of atopic dermatitis (AD) with anxiety and depression

Z. Telia<sup>1</sup>, K. Machavariani<sup>2</sup>, A. Telia<sup>2</sup>

<sup>1</sup> MD PhD student of the Department of Allergology and Clinical Immunology of Tbilisi State Medical University

<sup>2</sup> Department of Allergology and Clinical Immunology of Tbilisi State Medical University

---

### Abstract

Atopic dermatitis (AD), a common chronic inflammatory skin disease that may persist into adulthood, is associated with intense itching and a high incidence of sleep disturbances [1, 2]. The worldwide prevalence of AD is 15-20% among children [3] and 1-3% among adults. Psychological distress is a common comorbidity associated with atopic dermatitis and can negatively impact the quality of life [4]. Previous large-scale population-based studies have identified an association between AD and psychiatric illness [5–8]. Children with AD in the United States had a significantly higher prevalence of attention-deficit/hyperactivity disorder (ADHD, depression, anxiety, behavioral disorders, and autism) than children without AD [5]. Other authors [6] found that Taiwanese patients with AD had an increased risk of developing the major depressive disorder (MDD) and anxiety disorders. And also, depressive symptoms were significantly higher in patients with AD than in the control group [7, 8].

This study aimed to evaluate the association of AD with anxiety and depression using a data mining approach to match patients with AD with controls by sex and age.

### Materials and methods

Patients with atopic dermatitis were interviewed at the Allergology and Clinical Immunology Department of the Tbilisi State Medical University clinics. Their medical records (2018-2021 years) were analyzed to determine the coexistence of this disease with anxiety and depression. The study was conducted according to the case-control protocol and included 315 people aged 18 to 69. The "case" and "control" groups consisted of 154 people with chronic atopic dermatitis and 161 randomly selected

healthy individuals (including medical students, their family members, and teaching staff without the presence of asthma, rhinitis, urticaria, seborrheic dermatitis, psoriasis and contact dermatitis). We classified patients by age: 18-29 years old, 30-49 years old, and 50-69 years old. Since the severity of AD is difficult to classify, we assess the severity of the disease based on the drugs used by patients: mild AD (patients used only moisturisers and topical therapy - topical corticosteroids (TCS) short course and topical calcineurin inhibitors (TCIs), moderate AD (patients who received additional oral antihistamines), and severe AD (patients who received other oral immunosuppressants).

Anxiety and depression were identified through appropriate questionnaires GAD-7 (Generalized Anxiety Disorder) and PHQ-9 (Patient Health Questionnaire) by allergists, dermatologists, and general practitioners.

Statistical analysis was performed using software version 25 SPSS and Review Manager 5.4.1. The study was carried out in 4 subgroups according to demographic and clinical characteristics. Odds ratios (ORs) utilised a 95% confidence interval, with a p-value lower than 0.05 considered significant.

## Results

Demographic and clinical parameters of the study population are presented in Table. 1. There were no significant differences in gender; the mean age of patients with AD was 44.26 (SD = 14.76), and the control group was 46.38 (SD = 15.91). The percentage ratio between patients with AD and control was 45.4% vs 46.6% in men and 54.5% vs 53.4% in women. There were no significant differences in the overall number of participants in AD and control (OR = 1.09, 95% CI 0.80-1.49) and gender groups (Case vs Control in male, OR=1.05, 95% CI 0.67-1.63; Case vs Control in female, OR=0.96, 95% CI 0.61-1.49). Significant differences were found in the prevalence of only three (out of six) clinical variables studied (asthma, allergic rhinitis, urticaria, respectively: OR = 0.25, 95% CI 0.07-0.90; OR = 0.18, 95% CI 0.04-0.84; OR = 0.30, 95% CI 0.10-0.96), but not in seborrheic dermatitis, psoriasis, and contact dermatitis.

Table 1. Demographic and clinical parameters of the study population

Study or Subgroup	Atopic dermatitis		Control		Odds Ratio (Non-event)	
	Events	Total	Events	Total	M-H, Random, 95% CI	Odds Ratio (Non-event) M-H, Random, 95% CI
<b>1.1.1 Demographic factors</b>						
AD vs Control	154	315	161	315	1.09 [0.80, 1.49]	
Male	70	154	75	161	1.05 [0.67, 1.63]	
Female	84	154	86	161	0.96 [0.61, 1.49]	
<b>1.1.2 Clinical factors</b>						
Asthma	11	154	3	161	0.25 [0.07, 0.90]	
Allergic rhinitis	10	154	2	161	0.18 [0.04, 0.84]	
Urticaria	12	154	4	161	0.30 [0.10, 0.96]	
Seborrheic dermatitis	3	154	2	161	0.63 [0.10, 3.84]	
Psoriasis	1	154	1	161	0.96 [0.06, 15.42]	
Contact dermatitis	2	154	1	161	0.47 [0.04, 5.29]	

Odds ratios for the association between atopic dermatitis (AD), anxiety, and depression stratified by age and sex, are demonstrated in Table 2. Anxiety was nearly 1.5 times more prevalent in the AD group than in the controls (33.7% vs 21.7%; OR 1.84, 95% CI 1.11–3.03,  $p < 0.001$ ). Anxiety prevalence also was higher in women (OR = 2.27, 95% CI 1.02–5.07,  $p < 0.001$ ) and two age groups: 30-49 y, 50-60 y (respectively OR = 3.93, 95% CI 1.04–14.90,  $p < 0.001$ ; OR = 3.44, 95% CI 1.04–11.39,  $p < 0.001$ ).

There was no difference between the prevalence of depression in men and women. (31.2% vs 39.7%; OR 0.69, 95% CI 1.11–3.03,  $p < 0.001$ ). However, depression was more prevalent in the following age groups (30-49 y, 50-69 y; OR = 2.78, 95% CI 1.09–7.06, OR = 3.99, 95% CI 1.71–9.28 respectively) of both sexes.

Table 2. Association between Atopic Dermatitis (AD), anxiety and depression

Study or Subgroup	Atopic dermatitis		Control		Odds Ratio M-H, Random, 95% CI	Odds Ratio M-H, Random, 95% CI
	Events	Total	Events	Total		
<b>1.2.1 Anxiety in AD vs Control</b>						
Anxiety AD vs Control	52	154	35	161	1.84 [1.11, 3.03]	
Male	31	70	24	75	1.69 [0.86, 3.32]	
Female	21	84	11	86	2.27 [1.02, 5.07]	
age 18-29	14	52	8	35	1.24 [0.46, 3.38]	
age 30-49	14	52	3	35	3.93 [1.04, 14.90]	
age 50-69	16	52	4	35	3.44 [1.04, 11.39]	
<b>1.2.2 Depression AD vs Control</b>						
Depressino AD vs Control	48	154	64	161	0.69 [0.43, 1.09]	
Male	36	70	31	75	1.50 [0.78, 2.90]	
Female	28	84	22	86	1.45 [0.75, 2.82]	
age 18-29	10	48	12	64	1.14 [0.45, 2.91]	
age 30-49	15	48	9	64	2.78 [1.09, 7.06]	
age 50-69	23	48	12	64	3.99 [1.71, 9.28]	

## Discussion

Previous research on the relationship between anxiety/depression and atopic dermatitis has been inconsistent. Several studies have reported no significant difference in anxiety levels between AD patients and controls [1, 2] and no significant correlation between AD severity and anxiety [10]. However, other studies have shown that AD patients are more likely to experience anxiety than healthy individuals [5, 6]. A recent large population-based study showed that moderate to severe AD is significantly associated with an increased risk of using anxiolytics and antidepressants [11].

Anxiety and depression are the primary disorders associated with chronic skin diseases. This disease can contribute significantly to psychological distress and is often associated with other atopic conditions such as allergic rhinitis (AR) and asthma.

Our study confirmed the association between AD and some mental illnesses (depression and anxiety) in the 30-69 age group compared to healthy individuals; It was also revealed that patients with atopic dermatitis suffer more often from diseases such as bronchial asthma, allergic rhinitis and urticaria.

Many authors failed to confirm the hypothesis that the severity and duration of dermatitis affect depression because they couldn't find a correlation, probably due to the shortage of observed individuals in the respective groups. Some publications claim that depressive symptoms in

dermatological patients are associated with cosmetic malformations and body image problems [12, 13] and that most pruritic depressive skin diseases include psoriasis and chronic idiopathic urticaria [14]. The mechanisms underlying mental illness and AD are unknown. One theoretical tool is that mental illness may be a common consequence of many chronic illnesses, including AD. Blackman et al. [15] found that children with chronic illnesses are at increased risk of emotional and behavioural problems. The link between mental illness and AD can be explained by elevated levels of pro-inflammatory cytokines in AD, which can lead to depression, anxiety, and autism [15,16]. Schmitt et al. [17] suggested that sustained overexpression of inflammatory mediators released during atopic reactions may influence brain circuits.

Several candidate genes encoding significant elements of the immune system and proteins involved in regulating Th1/Th2 cell differentiation and effector function for atopic traits have been identified [18]. In particular, genetic variants in the gene encoding signal transducer and activator of transcription 6 (Stat6), a key regulatory element of Th2 immune response, have been associated with atopy-related traits [19].

Activator of transcription 6 (Stat 6) is also highly expressed in the central nervous system and is suggested to play a significant role in Attention deficit hyperactivity disorder (ADHD) pathogenesis [19]. In addition, previous research on the association between atopy and behavioural symptoms in twins has supported the hypothesis of shared genetic factors influencing the risk for atopic and behavioural disorders [18].

## Conclusion

Our study has shown that concomitant diseases (bronchial asthma, allergic rhinitis and urticarial) were more often observed in patients with atopic dermatitis; Depression and anxiety are also more common in this condition in the 30-69 age group.

The association of depression and anxiety with chronic AD is not well understood. Future studies recommend exploring the inverse relationship between atopic dermatitis and psychiatric disorders (depression and anxiety).

## Reference

1. Silverberg JI, Garg NK, Paller AS, Fishbein AB, Zee PC. According to a US population-based study, sleep disturbances in adults with eczema are associated with impaired overall health. *J Invest Dermatol.* 2015; 135:56–66. doi:10.1038/jid.2014.325;
2. Kim JP, Chao LX, Simpson EL, Silverberg JI. Persistence of atopic dermatitis (AD): a systematic review and meta-analysis. *J Am Acad Dermatol.* 2016; 75:681–7.e11. doi:10.1016/j.jaad.2016.05.028;
3. Asher MI, Montfort S, Bjorksten B, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC phases one and three repeat multicounty cross-sectional surveys. *Lancet.* 2006; 368:733–743. doi:10.1016/S0140-6736(06)69283-0;

4. Wittkowski A, Richards HL, Griffiths CE, et al. The impact of psychological and clinical factors on quality of life in individuals with atopic dermatitis. *J Psychosom Res.* 2004; 57:195–200. doi:10.1016/j.jpsychores.2004.04.371;
5. Yaghmaie P, Koudelka CW, Simpson EL. Mental health comorbidity in patients with atopic dermatitis. *J Allergy Clin Immunol.* 2013; 131:428–433. doi:10.1016/j.jaci.2012.10.041;
6. Cheng CM, Hsu JW, Huang KL, et al. Risk of developing the major depressive disorder and anxiety disorders among adolescents and adults with atopic dermatitis: a nationwide longitudinal study. *J Affect Disord.* 2015; 178:60–65. doi:10.1016/j.jad.2015.02.025;
7. Kim S, Lee JY, Oh JY, Chekal L, Lee DC. The association between atopic dermatitis and depressive symptoms in Korean adults: the fifth Korea national health and nutrition examination survey, 2007–2012. *Korean J Fam Med.* 2015; 36:261–265. doi:10.4082/kjfm.2015.36.6.261;
8. Lee S, Shin A. Association of atopic dermatitis with depressive symptoms and suicidal behaviours among adolescents in Korea: the 2013 Korean youth risk behaviour survey. *BMC Psychiatry.* 2017; 17:3. doi:10.1186/s12888-017-1489-6;
9. Gupta MA, Gupta AK. The use of antidepressant drugs in dermatology. *J Eur Acad Dermatol Venereol.* 2001; 15:512–518. doi:10.1046/j.1468-3083.2001.00278.x;
10. Linnet J, Jemec GB. An assessment of anxiety and dermatology life quality in patients with atopic dermatitis. *Br J Dermatol.* 1999; 140:268–272. doi:10.1046/j.1365-2133.1999.02661.x;
11. Thyssen JP, Hamann CR, Linneberg A, et al. Atopic dermatitis is associated with anxiety, depression, and suicidal ideation, but not with hospitalisation or suicide. *Allergy.* 2017. doi:10.1111/all.13231;
12. Gupta MA, Gupta AK. Depression and suicidal ideation in dermatology patients with acne, alopecia areata, atopic dermatitis and psoriasis. *Br J Dermatol.* 1998; 139:846–850;
13. Klockklokk M, Gotestam KG, Mykletun A. Factors accounting for the association between anxiety and depression, and eczema: the Hordaland health study (HUSK). *BMC Dermatol.* 2010; 10:3. doi:10.1186/1471-5945-10-3;
14. Holloway JW, Holgate ST. Genetics of allergic disease. *J Allergy Clin Immunol.* 2010; 125:S81–S94. doi:10.1016/j.jaci.2009.10.071;
15. Lau M, Tsantikos E, Maxwell MJ, Tarlinton DM, Anderson GP, Hibbs ML. Loss of STAT6 promotes autoimmune disease and atopy on a susceptible genetic background. *J Autoimmun.* 2012; 39:388–397. doi:10.1016/j.jaut.2012.06.003
16. Lau M, Tsantikos E, Maxwell MJ, Tarlinton DM, Anderson GP, Hibbs ML. Loss of STAT6 promotes autoimmune disease and atopy on a susceptible genetic background. *J Autoimmun.* 2012; 39:388–397. doi:10.1016/j.jaut.2012.06.003;
17. Yukawa K, Kishino M, Goda M, et al. STAT6 deficiency inhibits tubulointerstitial fibrosis in obstructive nephropathy. *Int J Mol Med.* 2005;15:225–230;
18. Thomsen SF, Kyvik KO, Backer V. Etiological relationships in atopy: a review of twin studies. *Twin Res Hum Genet.* 2008; 11:1112–1120. doi:10.1375/twin.11.2.112;

19. Miyazaki C, Koyama M, Ota E, et al. Allergic diseases in children with attention deficit hyperactivity disorder: a systematic review and meta-analysis. BMC Psychiatry. 2017; 17:120. doi:10.1186/s12888-017-1489-6.

## **Связь атопического дерматита (АД) с тревогой и депрессией**

**З. Телиа<sup>1</sup>, К. Мачавариани<sup>2</sup>, А. Телиа<sup>2</sup>**

<sup>1</sup> докторант департамента аллергологии и клинической иммунологии Тбилисского Государственного Медицинского Университета

<sup>2</sup> департамент аллергологии и клинической иммунологии Тбилисского Государственного Медицинского Университета

Атопический дерматит (АД), распространенное хроническое воспалительное заболевание кожи, которое может сохраняться во взрослом возрасте, связано с интенсивным зудом, высокой частотой нарушений сна и низким качеством жизни. Распространенность АД среди детей составляет 15–20%, и 1-3% среди взрослых во всем мире. Психологический дистресс является одним из распространенных сопутствующих заболеваний, связанных с атопическим дерматитом, и может негативно влиять на качество жизни. Предыдущие крупномасштабные популяционные исследования выявили связь между АД и психическими заболеваниями. Целью нашего исследования было провести всестороннее сравнение психических заболеваний во всех возрастных группах пациентов с АД среди Грузинского населения.

Исследование проводилось по протоколу случай-контроль и включало 315 человек в возрасте от 18 до 69 лет. В основную и контрольную группы вошли 154 человек с хроническим атопическим дерматитом и 161 произвольно выбранных здоровых лиц (включая студентов-медиков, членов их семьи и преподавателей). Пациенты были стратифицированы по демографическим (пол и возраст) и клиническим характеристикам (астма, аллергический ринит, крапивница, себорейный дерматит, псориаз и контактный дерматит). Мы классифицировали пациентов по возрасту: 18-29 лет; 30-49 лет и 50-69 лет.

Статистический анализ проводили с использованием программного обеспечения версии 25 SPSS и Review Manager 5.4.1. Отношения шансов (OR) использовали 95% доверительный интервал, при этом р-значение ниже 0.05 считалось значимым. Анализ проводился в 4 подгруппах по демографическим и клиническим характеристикам. Наши исследования показали, что у больных с атопическим дерматитом, по сравнению со здоровыми лицами в возрасте 30-69 лет частота депрессии и тревоги была выше. У больных атопическим дерматитом коморбидные заболевания, такие как бронхиальная астма, аллергический ринит, крапивница, также наблюдались чаще, чем в контрольной группе.

Наше исследование показало, что у больных атопическим дерматитом чаще

наблюдались сопутствующие заболевания по сравнению с контрольной группой в виде бронхиальной астмы, аллергического ринита и крапивницы; Депрессия и тревога также чаще встречаются при АД. Поскольку нам не удалось сопоставить проявления депрессии и тревоги с тяжестью атопического дерматита, необходимы дальнейшие исследования для уточнения этих взаимосвязей.

## ატოპიური დერმატიტის (AD) კავშირი შფოთვისთან და დეპრესიასთან

ზ. თელია<sup>1</sup>, ქ. მაჭავარიანი<sup>2</sup>, ალ. თელია<sup>2</sup>

<sup>1</sup> თბილისის სახელმწიფო სამედიცინო უნივერსიტეტის ალერგოლოგიისა და კლინიკური იმუნოლოგიის დეპარტამენტის დოქტორანტი

<sup>2</sup> თბილისის სახელმწიფო სამედიცინო უნივერსიტეტის ალერგოლოგიისა და კლინიკური იმუნოლოგიის დეპარტამენტი

ატოპიური დერმატიტი (AD), კანის გავრცელებული ქრონიკული ანთებითი დაავადებაა, რომელიც შეიძლება გაგრძელდეს ზრდასრულ ასაკშიც. ეს დაავადება მნიშვნელოვნად აქვეითებს ადამიანის ცხოვრების ხარისხს. უკანასკნელი კვლევების თანახმად ატოპიური დერმატიტი შესაძლოა იწვევდეს სხვადასხვა ფსიქოლოგიურ დისტრესულ მდგომარეობებს. ჩვენი კვლევის მიზანი იყო შეგვესწავლა ფსიქიკური დაავადებების (შფოთვა და დეპრესია) თანაარსებობა ატოპიური დერმატიტით დაავადებულ სხვადასხვა ასაკის და სქესის პირებში.

კვლევა ჩატარდა საცდელ-საკონტროლო პროტოკოლით და მოიცავდა 18-დან 69 წლამდე ასაკის 315 პირს. საკვლევ და საკონტროლო ჯგუფებში შევიდა 154 ქრონიკული ატოპიური დერმატიტით დაავადებული და 161 შემთხვევით შერჩეული ჯანმრთელი ინდივიდი. საკვლევ სუბიექტების დაჯგუფება მოხდა დემოგრაფიული და კლინიკური მახასიათებლების მიხედვით (ასთმა, ალერგიული რინიტი, ჭინჭრის ციება, სეზონური დერმატიტი, ფსორიაზი და კონტაქტური დერმატიტი) მიხედვით.

სტატისტიკური ანალიზი ჩატარდა 25 SPSS და Review Manager 5.4.1 სტატისტიკური პროგრამების საშუალებით. შანსების კოეფიციენტები (ORs) გამოთვლა განხორციელდა 95% ნდობის ინტერვალით, 0.05-ზე. მონაცემების ანალიზი ჩატარდა 4 ქვეჯგუფში დემოგრაფიული და კლინიკური მახასიათებლების მიხედვით.

ჩვენმა კვლევამ აჩვენა, რომ ატოპიური დერმატიტის მქონე (30-69 წლის) პაციენტებში, ამავე ასაკის ჯანმრთელ პირებთან შედარებით, დეპრესიისა და შფოთვის სიხშირე უფრო მაღალი იყო. ატოპიური დერმატიტის მქონე პირებში საკონტროლო ჯგუფთან შედარებით ასევე უფრო ხშირად აღინიშნებოდა თანმხლები დაავადებები, როგორცაა ბრონქული ასთმა, ალერგიული რინიტი, ჭინჭრის ციება. ვინაიდან ჩვენ ვერ შევძელით დეპრესიისა და შფოთვის გამოვლინებების კორელაციის შესწავლა ატოპიური დერმატიტის სიმძიმესთან, მიზანშეწონილია შემდგომი კვლევების ჩატარება ამ ურთიერთობების დასადგენად.