# ZAZA TELIA, KETEVAN MACHAVARIANI, ALEXANDER Z. TELIA, ALEXANDER A. TELIA INSOMNIA IN PATIENTS WITH URTICARIA AND ATOPIC DERMATITIS

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გამა თელია, ქეთევან მაჭავარიანი, ალექსანდრე 8. თელია, ალექსანდრე ა. თელია ატოპიური დერმატიტის და ქრონიკული ურტიკარიის გავლენა უძილობაზე თბილისის სახელმწიფო სამედიცინო უნივერსიტეტის ალერგოლოგიისა და კლინიკური იმუნოლოგიის დეპარტამენტი, თბილისი, საქართველო

## რეზიუმე

უძილობა მთელს მსოფლიოში აწუხებს ადამიანთა მნიშვნელოვან რაოდენობას (10-20%). ის შეიძლება გამოწვეული იყო მრავალი პირველადი დაავადებით, მათ შორის, ატოპიური დერმატიტითა და ქრონიკული სპონტანური ურტიკარიით. ჩვენ მიზნად დავისახეთ შეგვესწავლა კავშირი უძილობასა და ამ ორ დაავადებას შორის. კვლევა ჩატარდა 2020-2021 წ.წ. თბილისის სახელმწიფო სამედიცინო უნივერსიტეტის კლინიკებში; ის მოიცავდა სულ 180 პაციენტს (მამაკაცი 56, ქალი 124): 74-ს ატოპიური დერმატიტით (AD) და 106-ს ქრონიკული ურტიკარიით (CSU); ჩატარებული გამოკვლევით ვერ იქნა დადასტურებული წინასწარ გენერირებული ნულოვანი ჰიპოთეზა ამ მდგომარეობათა შორის სავარაუდო კავშირის არარსებობის შესახებ. გამოვლინდა, რომ AD-ისა და CSU-ის მქონე პირებს საკონტროლო ჯგუფთან შედარებით ჰქონდათ ძილის მნიშვნელოვანი დარღვევები.

#### Introduction

Insomnia affects a considerable number (10-20%) of people worldwide [18]. The cause of this disease is still unknown. Described only its clinical forms: occurrence falling asleep, staying asleep, waking up early or a lack of sleep despite opportunities to sleep [2, 4]. Many primary clinical diseases may underlie the occurrence of these symptoms. Among them may be atopic dermatitis and chronic spontaneous urticaria [13, 14], which, in turn, are multifactorial conditions and are determined by many hormonal fluctuations, psychological stress, infectious diseases and triggers [12]. Atopic dermatitis and chronic urticaria worldwide affect 10 and 30% of the population.

Many recent studies confirm that chronic urticaria and atopic dermatitis is often accompanied by neuropsychiatric problems such as anxiety, depression and insomnia [1]. However, a causal relationship between these two pathological conditions has not yet been established [7]. Our recent logistic regression studies confirmed that anxiety and depression could be predictive risk factors for developing atopic dermatitis and chronic urticaria [19].

Therefore, in this study, we were tasked with studying the relationship between sleep disorders, atopic dermatitis, and chronic urticaria and determining the feasibility of adding this risk factor to the previous two (anxiety and depression) to increase their combined predictive power.

#### Methods

To achieve this goal, we formulated a null hypothesis: atopic dermatitis and chronic urticaria are not associated with sleep disorders. This hypothesis was tested according to a case-control protocol. Randomly selected subjects were divided into three groups.

The control group consisted of persons without acute and chronic skin diseases. And the second group consisted of people suffering from atopic dermatitis and chronic urticaria. The medical records of all subjects were carefully reviewed and interviewed using standardized questionnaires to assess the nature and severity of their insomnia.

The Insomnia Severity Index (ISI) was assessed on three dimensions. The ISI is a 7-item self-report questionnaire assessing the nature, severity, and impact of insomnia: Severity of sleep onset, sleep maintenance and problems with early morning awakenings, sleep dissatisfaction, interference of sleep problems with daytime functioning, visibility of sleep problems by others, and distress caused by sleep problems. Each item is scored on a 5-point Likert scale (e.g., 0 = no problem; 4 = very serious problem), giving an overall score from 0 to 28. The total score is interpreted as follows: no insomnia (0-7); subthreshold insomnia (8-14); moderate insomnia (15-21); and severe insomnia (22-28) [15, 16]. To

measure the severity of itching, patients were asked to rate their itching on a visual analogue scale (VAS) from 1 (no itching) to 10 (unbearable itching). An itch score  $\geq$  4 was considered significant [17].

### Statistical analysis

Statistical analysis was performed using software version 25 SPSS and Review Manager 5.4.1. Comparison between all the studied groups and subgroups was carried out by the graphical Forest plot method using Odds ratios (ORs), and Standard mean difference (SMD) utilized a 95% confidence interval, with a p-value lower than 0.05 considered significant. The analysis was carried out in 5 subgroups, which made up two main groups: In the first group (consisting of three subgroups), descriptive characteristics of the studied subjects, a comparative assessment of the manifestation of insomnia in different groups, as well as the use of medications affecting the sleep process by patients were evaluated. The second group (consisting of two subgroups) presents the demographic parameters of patients and the nature and severity of sleep disturbance.

#### **Results**

The study included 180 patients (men 56, women 124) suffering from Atopic Dermatitis (AD) – 74 and Chronic Spontaneous Urticaria (CSU) – 106; the patients were divided into two main groups: The first group (Table 1) was recruited from 3 subgroups in which data were compared using relative measurements (Odds ratio - OR); The second group (Table 2) included two subgroups in which data analysis was carried out using Standardized mean difference (SMD). All patients were asked to fill out the appropriate questionnaires.

Tab 1. Comparing the number of participants in demographic, insomnia and H1A users subgroups

	n/h	1	n/t	1	Odds Ratio (Non-event)	Odds Ratio (Non-event)	_
Study or Subgroup			Events		M-H, Random, 95% CI	M-H, Random, 95% CI	
3.1.1 Descriptive charact	eristics o	f group	os.				
Men (AD vs CSU)	29	74	27	106	0.53 [0.28, 1.01]	<b>→</b> -	
Women (AD vs CSU)	45	74	79	106	1.89 [0.99, 3.57]	<del> </del>	
Overweight (AD vs CSU)	29	74	31	106	0.64 [0.34, 1.20]	-+-	
Prurutus (AD vs CSU)	71	74	86	106	0.18 [0.05, 0.64]	<del></del>	
3.1.2 ISI (Clinical insomni	a)						
ISI_AD vs control	58	74	55	120	0.23 [0.12, 0.45]		
ISI_CSU vs control	79	108	71	120	0.50 [0.28, 0.87]	<del></del>	
ISI_AD vs CSU	58	74	65	106	0.44 [0.22, 0.86]		
3.1.3 Use of antihistamin	es						
H1A (AD vs control)	65	74	15	120	0.02 [0.01, 0.05]	<del></del>	
H1A (CSU vs control)	56	106	15	120	0.13 [0.07, 0.25]	<del></del>	
H1A (AD vs CSU)	70	74	80	106	0.18 [0.06, 0.53]	<del></del>	
						-1	-1-
						0.005 0.1 1 10	200

AD = Atopic Dermatitis; CSU = Chronic Spontaneous Urticaria; ISI = The Insomnia Severity Index; H1A = H1-Antihistamines; BMI = Body Mass Index

Tab 2. Comparing the SMD of age, BMI, ISI and pruritus severity in subgroups

	Atopic dermatitis			Chronic urticaria			Std. Mean Difference		Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI		IV, Random, 95% CI		
1.1.1 Demographic of	late	2000000		The Area	7,000	10000000					
Age, years,	43	16.4	74	47.2	12.4	106	-0.29 [-0.59, 0.00]				
BMI kg/m2	25.8	3.9	74	26.4	5.3	106	-0.13 [-0.42, 0.17]			-	
1.1.2 Descriptive cha	aracteris	tics of t	he inso	mnia se	verity						
ISI_clinical	15.2	3.6	74	18.4	3.2	106	-0.95 [-1.26, -0.63]				
Prurutus	5.8	1.6	74	6.5	2.3	106	-0.34 [-0.64, -0.04]				
								<del></del>		1	-1
								-2	-1 0 Atopic dermatitis	Chronic urticaria	2

BMI = Body Mass Index; ISI=The Insomnia Severity Index

Data comparison in groups and subgroups showed no significant difference in age, sex and body mass index (BMI). Patient age ranged from 18 to 77 years, with a mean of 43.0 years for patients with AD and 47.2 years for patients with CSU (SMD =-0.29, 95% CI -0.59, 0.00). BMI ranged from 17 to 42 kg/m2 with a mean of 25.8 kg/m2 in AD and 26.4 kg/m2 in CSU (SMD = -0.13, 95% CI -0.42, 0.17). The presence of insomnia and its severity were assessed in both main groups by binary and continuous variables (Table 2).

When comparing groups according to binary variables, it was established that compared to the control group, patients with AD (OR=0.23, 95% CI 0.12, 0.45) and CSU (OR=0.50, 95% CI 0.28, 0.87) had more frequent sleep disturbances. A similar trend was observed between groups of AD and CSU (OR=0.44, 95% CI 0.22, 0.86), see Table 1. The second subgroup of the second group presents a comparative characteristic (according to the SMD index) of the severity of insomnia in patients with atopic dermatitis and chronic spontaneous urticarial. These data show a significant difference in the presence of insomnia and pruritus in the compared groups in favor of AD compared with CSU (SMD = -0.95, 95% CI -1.26, -0.63), (SMD = -0.34, 95% CI -0.64, -0.04), and thus coincide with the results obtained using the binary outcomes, see Table 2.

Since patients with AD and CSU most commonly use antihistamines, which can interfere with sleep, we analyzed the use of these drugs in our study patients. The analysis confirmed that individuals with atopic dermatitis and chronic urticaria used mentioned medications more frequently (OR=0.02, 95% CI 0.01, 0.05) than those in control (OR=0.13, 95% CI 0.07, 0.25) groups (OR=0.18, 95% CI 0.06, 0.53). At the same time, patients with AD are prone to use antihistamines compared to those with CSU (OR=0.18, 95% CI 0.06, 0.53), see Table 2.

#### Discussion

It is well known that many people worldwide have insomnia, which often accompanies many conditions, including chronic skin diseases. In the present study, we attempted to determine the association of insomnia with common chronic skin diseases (atopic dermatitis and chronic spontaneous urticaria), which, according to many studies, are associated with various mental disorders. Our results indicate that AD and CSU may influence the onset and severity of insomnia. However, it should always be taken into account that these diseases last for many years, and, as a rule, patients self-medicate as they are not satisfied with the results of the proposed treatment [1, 13].

Our study confirmed the existence of such a phenomenon. It turned out that patients included in the study groups constantly took various drugs (antihistamines, sedatives and antidepressants) to suppress itching and improve sleep. Therefore, we compared these groups with each other and with the control group.

Unlike other authors [1, 5, 8, 9, 14], this study did not find any correlation between gender, age, and BMI. Differences between the two diseases were observed regarding pruritus and sleep quality. However, it is impossible to objectively interpret these results against the background of the use of these drugs (affecting itching and sleep). Our data are consistent with the data of other authors, which confirm the presence of pruritus and sleep disturbances in individuals with AD and CSU [6, 10, 11].

### Conclusion

In our study, we rejected the null hypothesis and confirmed the presence of sleep disorders and pruritus in patients with AD and CVS, which may influence the course of these disorders. This trend is especially pronounced in patients with atopic dermatitis. We were unable to confirm the usefulness of using this risk factor for predicting (logistic regression) these diseases because the studied patients usually used drugs that affect the sleep process. Based on the foregoing, it is advisable to conduct additional repeated studies.

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#### **SUMMARY**

Insomnia affects a considerable number (10-20%) of people worldwide. Many primary clinical diseases may underlie the occurrence of these symptoms. Among them may be atopic dermatitis (AD) and chronic spontaneous urticarial (CSU). A causal relationship between these two pathological conditions has not yet been established. We were tasked with studying the relationship between sleep disorders, AD and CSU, and determining the feasibility of adding this risk factor to the previous two (anxiety and depression) to increase their combined predictive power. The study was conducted in 2020-2021 years. at the clinics of TSMU. The study included 180 patients (men 56, women 124) suffering from AD (74) and CSU (106); we could reject the null hypothesis of an association between sleep disturbances and AD and CSU. It was found that individuals with atopic dermatitis and chronic urticaria had significant sleep disturbances compared with the control group. Therefore, we consider it reasonable to conduct additional repeated studies on more homogeneous scientific groups.

**Keywords:** Insomnia, urticaria, atopic dermatitis