
Anxiety and depression in patients with chronic urticaria

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Introduction

Urticaria is an allergic and dermatological disease caused by the degranulation of mast cells and clinically manifested by wheals and angioedema [1]. Acute urticaria lasts for six weeks, while chronic urticaria for more time [2]. Chronic Spontaneous Urticaria (CSU) deserves special attention from physicians and researchers as it impacts a person's quality of life and often lasts for several years [3]. This condition is accompanied by itching and psycho-neurological problems [4], which negatively affect a person's daily activities, mood and appearance. Recent studies have shown that 35-60% of patients with chronic urticaria have sleep disorders, anxiety, depression, and other psychiatric disorders [5-8].

This study aimed to assess the association between CSU and anxiety and CSU and depression while employing a data mining approach to match CSU patients to gender and age control participants. Were used the database of the Allergology and clinical immunology department clinics of TSMU (Tbilisi State Medical University). This assessment considered demographic and clinical factors (thyroid disease, diabetes, physical urticaria, obesity and smoking). Anxiety and depression rates were assessed using the GAD-7 (Generalized Anxiety Disorder) and PHQ-9 (Patient Health Questionnaire) questionnaires [25].

Methods

Study population

In chronic urticaria, the urticarial rash that lasted more than six weeks and recurred over months or years was assessed. Also, if this diagnosis has been made at least four times. Controls included individuals of randomly selected age and sex (including medical students) who did not have urticaria or any other allergic manifestations. Anxiety and depression were identified through appropriate questionnaires (GAD-7 and PHQ-9) by allergists, dermatologists, and general practitioners. The study

was conducted using a case-control protocol and included 690 individuals aged 18 to 70. The study and control groups had 330 people with chronic urticaria and 360 randomly selected healthy individuals. Demographic and clinical data of the subjects were obtained from the department database and included age, sex, diabetes, obesity, thyroid dysfunction, and smoking status.

Statistical analysis

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

Results

The homogeneity of the study and control groups according to demographic and clinical parameters was assessed first. This analysis confirmed that these groups did not differ in age (M = 47.4, SD = 16.7 and M = 46.2 SD=17.1) and sex (men -34% vs. 30%, OR= 0.80, 95% CI 0.58 -1.10; women - 65% vs. 70% OR = 1.25, 95% CI 0.91-1.72). The difference between the groups was observed only according to the coexisting clinical factors (74% CSU vs. 19.4% control; OR=0.26, 95% CI 0.13-0.52) such as physical urticaria ((OR = 0.09, 95% CI 0.05-0.15 95% CI), thyroid dysfunction ((OR = 0.23, 95% CI 0.12-0.43), diabetes (OR = 0.36, 95% CI 0.14-0.93), obesity (OR = 0.47, 95% CI 0.26-0.84), and tobacco use (OR = 0.42, 95% CI 0.22-0.79) (see in Table 1).

Table 1. Demographic and clinical characteristics of the study groups

Study or Subgroup	CSU		Control		Odds Ratio (Non-event)	Odds Ratio (Non-event)
	Events	Total	Events	Total	M-H, Random, 95% CI	M-H, Random, 95% CI
1.1.1 Demographic factors						
Anxiety (CSU vs Control)	330	690	360	690	1.19 [0.96, 1.47]	
Male	115	330	108	360	0.80 [0.58, 1.10]	
Female	215	330	252	360	1.25 [0.91, 1.72]	
1.1.2 Clinical factors						
Physical urticaria	118	330	17	360	0.09 [0.05, 0.15]	
Thyroid disease	47	330	13	360	0.23 [0.12, 0.43]	
Diabetes	15	330	6	360	0.36 [0.14, 0.93]	
Obesity	35	330	19	360	0.47 [0.26, 0.84]	
Smoking	31	330	15	360	0.42 [0.22, 0.79]	

Odds ratios for the association between CSU and anxiety, stratified by age and sex, are demonstrated in Table 2. Anxiety was almost 1.7 times more common in the CSU group than in controls (24% vs 14%, respectively; OR = 1.93, 95% CI 1.31- 2.84). More precisely in men with chronic urticaria anxiety was 1.9 times and in women 1.6 times more higher than in control groups respectively 30%

vs. 16% (OR = 2.19; 95% CI 1.15-4.16) and 21% vs. 13% (OR = 1.75; 95% CI 1.07-2.84). After age stratification, a higher rate of anxiety prevalence was observed only in the 50-69 age group with CSU than in the same age control group (OR = 0.36, 95% CI 0.18-0.75).

Patients with urticaria were more likely to suffer from depression than controls (36% vs 9.7%; OR = 5.45, 95% CI 3.60-8.24). However, it was more common in women with urticaria (37% vs 19%; OR = 2.46, 95% CI 1.62-3.72); It should be noted that this trend was not found in men. However, depression was particularly pronounced in patients of both sexes in the age group 30-49 years (CVD 36% vs 17%; OR = 2.73, 95% CI 1.05-7.08).

Table 2. Frequency of anxiety and depression in CSU stratified by demographic variables

Study or Subgroup	CSU		Control		Odds Ratio	
	Events	Total	Events	Total	M-H, Random, 95% CI	M-H, Random, 95% CI
1.2.1 Anxiety in CSU vs Control						
Anxiety CSU vs Control	81	330	52	360	1.93 [1.31, 2.84]	
Male	35	115	18	108	2.19 [1.15, 4.16]	
Female	46	215	34	252	1.75 [1.07, 2.84]	
age 18-29	20	81	5	52	3.08 [1.08, 8.82]	
age 30-49	28	81	9	52	2.52 [1.08, 5.92]	
age 50-69	33	81	34	52	0.36 [0.18, 0.75]	
1.2.2 Depression CSU vs Control						
Depression in CSU vs Control	122	330	35	360	5.45 [3.60, 8.24]	
Male	42	115	25	108	1.81 [1.06, 3.43]	
Female	80	215	49	252	2.46 [1.62, 3.72]	
age 18-29	32	122	13	35	0.60 [0.27, 1.33]	
age 30-49	44	122	6	35	2.73 [1.05, 7.08]	
age 50-69	46	122	16	35	0.72 [0.34, 1.54]	

Discussion

These results (anxiety (24.5%) and depression (36.9%)) support previous studies by other authors that have found a higher prevalence of anxiety and depression in patients with CSU [10] and confirm the hypothesis of an independent effect of this emotional distress on urticaria [9]. The study also found that anxiety and depression were more common in both sexes in the active group than in the control group. At the same time, anxiety is reliably elevated in individuals aged 50-69 with chronic urticaria and depression - in the 30-49 age group.

According to other authors association of CSU with anxiety was the strongest in the 18–29 and 30-49 age groups, and depression was highest in the 50-69 age group and not in the 18–29 and 30-49 age groups [10], in our study on the contrary - significant higher anxiety was in the 50–69 age group, and depression - in 30-49 age group. Our results support previous studies showing a higher prevalence of anxiety and depression in patients with CSU is often accompanied by physical urticaria, thyroid disorders, diabetes, obesity, and tobacco smoking [10].

Many studies indicate the influence of negative emotional factors on dermatological manifestations, including urticaria [11, 12], this association between chronic urticaria, on the one hand, and anxiety and depression, on the other hand, is still not well understood [13]. Some authors have

suggested that urticaria predominates in autoimmune diseases, predominantly in adult women [14] and that it is often associated with anxiety and depression (mainly in the 50-69 age group [15]). This is consistent with the data of our studies on the manifestation of anxiety in patients of both sexes. Most authors link depression and anxiety to the age factor. They believe that these emotional disorders are associated with feelings of loneliness, social exclusion, and isolation (especially at a later age). However, they also agree that they are pretty standard in the healthy population, which significantly complicates the study of the links between these two phenomena in different diseases [16, 17, 18, 19].

Some authors believe that urticaria predates the onset of autoimmune diseases, especially in adult women [20], and this trend is associated with an age factor. This disease is more common with anxiety in young people and depression in the elderly. Our research could not confirm such a clear connection, probably because different additives cause anxiety and depression at different ages. So, for example, young people experience dermatological problems more painfully than the elderly. In the elderly, this condition is associated with many unknown factors (ethnic, social, religious, geographical, etc.) [21].

The results of the current study have both scientific and practical significance. Most of the studies conducted in this direction differ in methodological terms. They were first selecting the subjects involved in the research, their distribution in the groups, and the agreed results' processing. The phenomenon of "P-hacking" is observed in most studies, which increases the likelihood of false-positive type I errors [22]. Current research provides additional information on the association between chronic urticaria, anxiety and depression. This study is also essential in the context of a total deficit of replication studies, which makes it significantly more difficult to conduct systematic reviews (highest level of evidence) [23]. Research confirms that concomitant psychiatric manifestations are quite common in skin diseases and that their consideration is essential in managing these conditions [24, 25].

Of course, several methodological factors were identified during and after the study that could not be ignored for various reasons. The study protocol we use (case-control) ranks third in the hierarchy of evidence (after cohort and experimental-control studies). Thus, the case-control study does not allow establishing a causal relationship between CHF and anxiety and CHF and depression. The study was limited to the evaluation of medical history and questionnaires, and the methods used in selecting and assigning subjects to groups also had certain shortcomings.

Conclusion

The study showed that: in patients suffering from chronic spontaneous urticaria, anxiety and depression are pretty common; this emotional distress probably has an independent effect on this state. Anxiety and depression occur in both sexes. In this disease, urticaria is more often observed at the age of 50-69 years and depression in the group of 30-49 years. The presence of anxiety and depression in CSU is often accompanied by physical urticaria, thyroid pathologies, diabetes, obesity and tobacco

smoking. The association of depression and anxiety with chronic urticaria is not well understood. Further study is required to elucidate the causal relationship between these conditions.

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Тревога и депрессия у больных хронической крапивницей

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Крапивница – аллергическо-дерматологическое заболевание, обусловленное дегрануляцией тучных клеток и клинически проявляющееся крапивницей и ангионевротическим отеком. Недавние исследования показали, что у 35-60% больных хронической крапивницей наблюдаются нарушения сна, тревога, депрессия и другие психические расстройства. Это исследование было направлено на оценку связи между хронической спонтанной крапивницей (ХСК - CSU) и тревогой и CSU и депрессией с использованием подхода интеллектуального анализа данных, чтобы сопоставить пациентов CSU с участниками контроля пола и возраста. Используются данные клинических баз департамента аллергологии и клинической иммунологии ТГМУ (Тбилисский Государственный Медицинский Университет). Уровень тревоги и депрессии оценивали с помощью опросников Генерализованного Тревожного Расстройства (ГТР - GAD-7) и Анкетой Здоровья Пациента (АЗП - PHQ-9). Исследование проводилось по протоколу случай-контроль и включало 690 человек в возрасте от 18 до 70 лет. В основную и контрольную группы соответственно вошли 330 человек с хронической крапивницей и 360 случайно выбранных здоровых лиц. Эти результаты (распространенность тревоги (24.5%) и депрессии (36.9%)) подтверждают предыдущие исследования, в которых была обнаружена высокая распространенность тревоги и депрессии у пациентов с CSU, и подтверждают гипотезу о независимом влиянии этого эмоционального расстройства на крапивницу. По данным других авторов, ассоциация CSU с тревожностью была наиболее сильной в возрастных группах 18–29 и 30–49 лет, а депрессия — в возрастной группе 50–69 лет, а не в возрастных группах 18–29 и 30–49 лет, в нашем исследовании, наоборот, достоверно более высокая тревожность была в возрастной группе 50-69 лет, а депрессия - в возрастной группе 30-49 лет. Наши результаты подтверждают предыдущие исследования, показывающие более высокую распространенность тревоги и депрессии у пациентов с CSU, которые часто сопровождаются физической крапивницей, нарушениями щитовидной железы, диабетом, ожирением и курением табака. Результаты настоящего исследования имеют как научное, так и практическое значение. Большинство исследований, проводимых в этом направлении, различаются в методологическом плане. Прежде всего, в части выбора испытуемых, участвующих в исследовании, их распределения по группам и обработки согласованных результатов. Феномен «P-hacking» наблюдается в большинстве исследований, что увеличивает вероятность ложноположительных ошибок типа-I. Это исследование также важно в условиях тотального дефицита репликационных исследований, что значительно затрудняет проведение систематических обзоров (высший уровень доказательности). Исследования подтверждают, что сопутствующие психические проявления довольно распространены при кожных заболеваниях и что их учет необходим для полноценного лечения этих состояний.

შფოთვა და დეპრესია ქრონიკული ჭინჭრის ციების მქონე პაციენტებში

ზ. თელია

თბილისის სახელმწიფო სამედიცინო უნივერსიტეტის ალერგოლოგიისა და კლინიკური იმუნოლოგიის დეპარტამენტის დოქტორანტი

ჭინჭრის ციება არის ალერგიულ-დერმატოლოგიური დაავადება, რომელიც გამოწვეულია პოხიერი უჯრედების დეგრანულაციით და კლინიკურად ვლინდება ურტიკარიული გამონაყრით და ანგიონევროზული შეშუპებით. ბოლო კვლევებმა აჩვენა, რომ ქრონიკული ჭინჭრის ციებით დაავადებულთა 35-60%-ს აღენიშნება ძილის პრობლემები, შფოთვა, დეპრესია და სხვა ფსიქიკური ხასიათის დარღვევები. ეს კვლევა მიზნად ისახავდა ქრონიკულ სპონტანურ ურტიკარიას (ქსუ - CSU) და შფოთვას და CSU-სა და დეპრესიას შორის კავშირის შეფასებას მაქსიმალურად ჰომოგენურ საკვლევ ჯგუფებში. გამოყენებულ იქნა თსუ-ის (თბილისის სახელმწიფო სამედიცინო უნივერსიტეტის) ალერგოლოგიისა და კლინიკური იმუნოლოგიის დეპარტამენტის კლინიკურ ბაზათა მონაცემები. შფოთვისა და დეპრესიის დონე შეფასდა გენერალიზებული შფოთვითი აშლილობის (გშა - GAD-7) და პაციენტის ჯანმრთელობის კითხვარის (ჰკკ - PHQ-9) გამოყენებით. კვლევა ჩატარდა საცდელ-საკონტროლო პროტოკოლის მიხედვით და მოიცავდა 18-დან 70 წლამდე ასაკის 690 საკვლევ სუბიექტს. ძირითად და საკონტროლო ჯგუფებში შევიდა 330 ქრონიკული ჭინჭრის ციებით და 360 შემთხვევით შერჩეული ჯანმრთელი ინდივიდი. კვლევამ გამოავლინა, რომ ქრონიკული ურტიკარიის მქონე პირების 24.5%-ს ასევე აღენიშნებოდა შფოთვითი, ხოლო 36.9%-ს კი - დეპრესიული აშლილობები. სხვა ავტორების აზრით, CSU-ს კავშირი შფოთვასთან ყველაზე ძლიერი იყო 18-29 და 30-49 ასაკობრივ ჯგუფებში, ხოლო დეპრესია - 50-69 ასაკობრივ ჯგუფში და არა 18-29 და 30-49 ასაკობრივ ჯგუფებში; ჩვენს კვლევაში, პირიქით, - შფოთვა მნიშვნელოვნად მაღალი იყო 50-69 ასაკობრივ ჯგუფში, ხოლო დეპრესია - 30-49 ასაკობრივ ჯგუფში. ჩვენი შედეგები ადასტურებს წინა კვლევებს, რომლებიც აჩვენებენ შფოთვისა და დეპრესიის უფრო მაღალ პრევალენტობას CSU-ის მქონე პაციენტებში, რომელსაც ხშირად თან ახლავს ფიზიკური ჭინჭრის ციება, ფარისებრი ჯირკვლის დარღვევები, დიაბეტი, სიმსუქნე და თამბაქოს მოწვევა. ამ კვლევის შედეგებს აქვს როგორც სამეცნიერო, ასევე პრაქტიკული მნიშვნელობა, ვინაიდან ამ მიმართულებით ჩატარებული კვლევების დიდი წილი განსხვავებულია მეთოდოლოგიური თვალსაზრისით, უპირველეს ყოვლისა, კვლევაში მონაწილე სუბიექტების შერჩევის, ჯგუფებად განაწილებისა და მიღებული მონაცემების დამუშავების კუთხით. კვლევათა უმრავლესობაში შეინიშნება ე. წ. „P-ჰაკინგ“ ფენომენი, რომელიც მნიშვნელოვნად ზრდის ცრუ დადებითი მიზეზ-შედეგობრივი რეზულტატების მიღების (I-ტიპის შეცდომა) ალბათობას. კვლევა მნიშვნელოვანია რეპლიკაციური კვლევების ტოტალური დეფიციტის კონტექსტშიც, რაც მნიშვნელოვნად ართულებს სისტემატური მიმოხილვების ჩატარებას (მტკიცებულების უმაღლესი დონე). კვლევა ადასტურებს, რომ თანმხლები ფსიქიატრიული გამოვლინებები საკმაოდ ხშირია კანის დაავადებებში და რომ მათი გათვალისწინება აუცილებელია ამ მდგომარეობების ოპტიმალური მართვის თვალსაზრისით.