Ghazanfar et al. World Allergy Organization Journal (2023) 16:100835
http://doi.org/10.1016/j.waojou.2023.100835

WORLD ALLERGY ORGANIZATION JOURNAL

Open Access

Occurrence and risk factors of mental disorders in patients with chronic urticaria

Misbah Noshela Ghazanfar, MD, PhD[a]*, Jennifer Astrup Sørensen, MD[a], Ditte Zhang, MD[a], Nikolaj Kondrup Holgersen, MD[a], Christian Vestergaard, MD, PhD[b] and Simon Francis Thomsen, MD, PhD[a,c]

ABSTRACT

This study aimed to evaluate the prevalence and risk factors of mental disorders in patients with chronic urticaria (CU) in a cohort of adult outpatients. Mental disorders occurred in almost one-sixth of the patients with CU, depression (9.7%), and anxiety (5.0%) being the most prevalent conditions. Furthermore, a significant difference in impairment of quality of life was seen between patients with mental disorders compared to patients without. Although, the prevalence of mental disorders in patients with CU is high, larger clinical studies are needed to investigate and understand the association and risk factors of mental disorders in patients with CU.

Keywords: Chronic urticaria, Mental disorders, Comorbidities, Quality of life, Prevalence

DEAR EDITOR,

Chronic urticaria (CU) has a negative impact on patients' quality of life (QoL) and is associated with several comorbidities.[1] Particularly, there is a high prevalence of mental disorders in patients with CU, and there is a greater impairment of QoL in patients with CU, who exhibit mental disorders;[2,3] still little is known about the relationship to clinical characteristics. Therefore, we aimed to investigate the prevalence and risk factors of mental disorders in patients with CU in a well-characterized cohort of adult outpatients.

All adult patients with CU, who were referred to the outpatient clinic at a dermatological university department between January 2016 and November 2022, were included in the study. A complete medical history and blood samples were obtained, and for each patient the following data were recorded: sex, age, age at urticaria onset, smoking habits, family history of urticaria, presence of concomitant chronic inducible urticaria (CIndU), comorbidities, including history of current mental disorders diagnosed from either their general practitioner or psychiatrist, presence of angioedema, urticaria basophil histamine release assay (BHRA), serum total IgE, leukocytes, neutrophil count, basophils, eosinophils, C-reactive protein (CRP), and thyroid stimulating hormone (TSH). Urticaria activity was evaluated with weekly Urticaria Activity Score (UAS7), disease control was evaluated with Urticaria Control Test (UCT), overall disease bother score was evaluated with a visual analogue scale (VAS), while QoL was assessed with Dermatology Life Quality Index (DLQI).

A total of 741 patients were included, 506 women (68.3%) and 235 men (31.7%). The mean age was 42.0 years (range: 18–94 years). Age at urticaria

[a]Department of Dermatology, Bispebjerg Hospital, Copenhagen, Denmark
*Corresponding author. Department of Dermatology, Bispebjerg Hospital, Bispebjerg Bakke 23, DK-2400 Copenhagen NV, Denmark,. E-mail: misbah.noshela.ghazanfar.02@regionh.dk
Full list of author information is available at the end of the article
http://doi.org/10.1016/j.waojou.2023.100835

Received 25 April 2023; Received in revised from 29 September 2023; Accepted 12 October 2023

onset was 33.7 years (SD = 16.8) and disease duration was 4.2 years (SD = 7.6). Concomitant CIndU, angioedema and positive BHRA were present in 38.1%, 41.6% and 10.5% of the patients, respectively. A total of 195 patients (26.3%) were current smokers. At least 1 comorbidity was reported by 59.4% of the patients and 124 (16.7%) had at least 1 current mental disorder. Of these, a total of 97 patients (78.2%) had one mental disorder, while 21 patients (16.9%) and 6 patients (4.8%) were diagnosed with 2 and 3 mental disorders, respectively. Overall, the most prevalent mental disorder was depression, being present in 58.1% of the CU patients with at least 1 known mental disorder followed by anxiety (29.8%), ADHD (attention deficit hyperactivity disorder) (11.3%), PTSD (post-traumatic stress disorder) (8.9%), personality disorders (6.4%), and OCD (obsessive compulsive disorder) (5.6%) (Fig. 1).

Compared to urticaria patients without mental disorders, the patients with a current mental disorder were more often female (75.8 vs. 66.8%, $p < 0.05$), more often had a first degree relative with CU (27.4 vs 14.6%, $p < 0.01$), had a higher prevalence of atopic disease comorbidities (29 vs 24%, $p < 0.05$), had higher levels of leukocytes ($p = 0.01$), neutrophils ($p = 0.02$), and basophils ($p = 0.02$). Furthermore, a significant difference in impairment of QoL was seen between patients with mental disorders compared to patients without (DLQI: 10.7 vs 8.8 points) ($p < 0.05$). The following factors did not show a statistically significant difference between the groups; age, age at disease onset, duration of symptoms, presence of CIndU, smoking, presence of angioedema, positive BHRA, serum total IgE level, eosinophils, CRP, TSH, UAS7, UCT and VAS (Table 1).

Mental disorders were present in 19.3% of the patients with early onset of CU (<18 years of age), as opposed to 16.4% in patients with late onset of CU (>18 years of age). This could indicate that patients who develop CU at a young age are more likely to develop mental disorders *after* onset of CU. However, this difference was not statistically significant ($p = 0.278$). Furthermore, in a subgroup analyses no statistically significant associations were found between age at onset of CU and depression or anxiety, selectively.

In patients with CU, we found that mental disorders were present in almost 17% of the CU patients. These findings are lower than those previously seen in a systematic review and meta-analysis,[4] which reported a *pooled prevalence* of mental disorders in patients with CU of 26.3% in studies without control-groups and 31.6% in studies with a control group. The *pooled prevalence* of mental disorders in the healthy control groups was 24.4%. The estimated prevalence of mental disorders in the general population is 8.5–16%.[5] Other studies have reported a prevalence of mental disorders in CU ranging from 11 to 70%.[3,4] In patients with CU, the reported prevalence of depression and anxiety ranges from 13.5 to 40% and 7–30%, respectively.[6] The most commonly occurring mental disorders in our study group were depression and anxiety. Depression

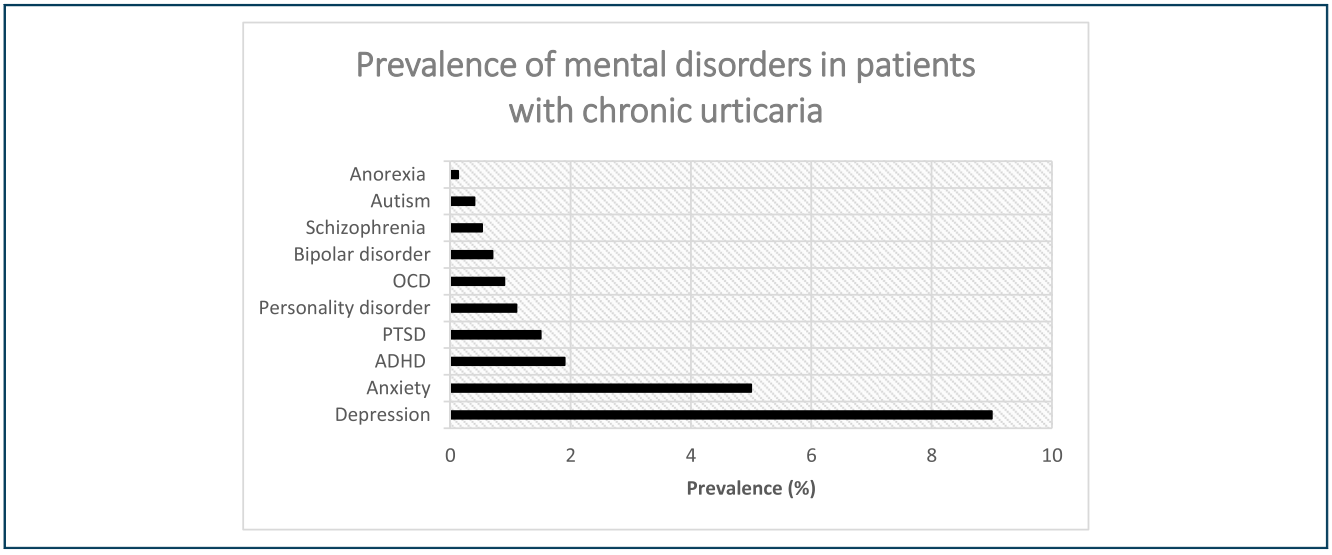

Fig. 1 Prevalence of mental disorders in patients with chronic urticaria (CU)

	Patients without mental disorders (N = 617)	Patients with mental disorders (N = 124)	p-value
Sex, n (%)			
Female	412 (66.8)	94 (75.8)	
Male	205 (33.2)	30 (24.2)	0.05*
Age, years, mean (SD)	42.3 (16.2)	41.2 (15.8)	0.180
Age at disease onset, years, mean (SD)	34.0 (17.0)	32.9 (16.3)	0.165
Duration of symptoms, mean (SD)	4.2 (7.8)	4.4 (6.9)	0.678
First degree relative with urticaria, n (%)	90 (14.6)	34 (27.4)	<0.01*
Current smoking, n (SD)	110 (17.8)	24 (19.4)	0.693
Positive basophil HR assay, n (%)	68 (11.0)	10 (8.1)	0.334
Angioedema, n (%)	250 (40.5)	58 (46.8)	0.197
Concomitant CIndU[a], n (%)	123 (19.9)	26 (21.0)	0.07
Serum IgE [x 10^3 IU/L], mean (SD)	215.1 (627.1)	169.0 (264.0)	0.199
CRP [mg/L], mean (SD)	4.6 (11.8)	4.1 (9.7)	0.632
Leukocytes [x 10^9 L], mean (SD)	6.8 (2.0)	7.4 (2.3)	0.01*
Neutrophils [x 10^9 L], mean (SD)	4.1 (1.8)	4.6 (1.9)	0.02*
Eosinophils [x 10^9 L], mean (SD)	0.17 (0.13)	0.17 (0.13)	0.877
Basophils [x 10^9 L], mean (SD)	0.03 (0.02)	0.04 (0.03)	0.02*
Thyrotropin (TSH) [mIU/L], mean (SD)	1.67 (1.22)	1.80 (1.2)	0.284
Comorbidities, n (%)			
Atopic disease**	148 (24.0)	36 (29.0)	0.04*
Thyroid disease	57 (9.2)	10 (8.1)	0.678
Patient reported outcomes (PROs)[b], mean (SD)			
UAS7	21.6 (13.8)	22.3 (14.7)	0.649
UCT	6.1 (4.0)	5.4 (4.2)	0.178
VAS	6.1 (2.9)	6.3 (3.0)	0.438
DLQI	8.8 (6.8)	10.7 (7.5)	0.012*

Table 1. Patient characteristics in chronic urticaria patients with and without mental disorders **Significant. **Including allergic rhinitis, atopic dermatitis and asthma.* [a]Chronic inducible urticaria (CIndU). [b]Patient reported outcomes: Urticaria activity score (UAS7); Urticaria control test (UCT); Dermatology quality of life index (DLQI); Visual analogue scale (VAS).

was present in almost 10% of the patients with CU. Similar observations were reported in a Turkish study, where depression and anxiety were more common in patients with CU compared to a control group.[7] In a nationwide register based Danish study, depression was reported as the most frequently occurring comorbidity in the CU group with a prevalence of 4%.[8] This could indicate that the prevalence of mental disorders is higher in patients with higher disease activity. Furthermore, this could also be the reason for a higher impairment of QoL observed in patients with mental disorders, which is also seen in our results. Our findings were congruent with previously reported impairment of QoL in CU patients with mental disorders.[2,3,9]

Patient characteristics such as female gender, family history of urticaria, presence of atopic diseases and elevated leukocytes, neutrophil and

basophil count were significantly more prevalent in patients with mental disorders compared to patients without mental disorders. One explanation may be that disease activity, which is linked to some of these patient characteristics,[10] may be related to development of mental disorders such as depression and anxiety in some patients with CU.

Limitations of this study are the single center design, the lack of a control group and that mental disorders were not assessed with validated patient reported outcomes. Furthermore, the temporal relationship between CU and mental disorders could not be explored fully as data on duration and onset of mental disorders were missing.

According to the results of our study, mental disorders occur in almost one-sixth of patients with CU, with the most prevalent mental disorder being depression. However larger clinical studies are needed to investigate and understand the association and risk factors of mental disorders in patients with CU.

Abbreviations
CU, Chronic Urticaria; QoL, Quality of life; CIndU, Chronic inducible urticaria; BHRA, basophil histamine release assay; CRP, C-reactive protein; TSH, Thyrotropin; UAS, Urticaria activity score; UCT, Urticaria control test; DLQI, Dermatology quality of life index; VAS, Visual analogue scale; ADHD, Attention deficit hyperactivity disorder; PTSD, Post-traumatic stress syndrome; OCD, Obsessive compulsory disorder

Author contribution statement
MNG, CV and SFT conceived and planned the experiments. MNG, JAS, DGZ, NKH, and SFT collected the data. All authors discussed the analysis, results and contributed to the final manuscript.

Funding
No funding var received.

Availability of data and material
Data is available upon request.

Ethics approval
The study is approved by the Ethical committee and Data protection agency.

Author consent for publication
All authors have given their consent for publication.

Acknowledgements
No acknowledgements.

Declaration of competing interest
The other authors have no conflicts of interest in relation to this study.

Author details
[a]Department of Dermatology, Bispebjerg Hospital, Copenhagen, Denmark [b]Department of Dermatology, Aarhus University Hospital, Aarhus, Denmark [c]Department of Biomedical Sciences, University of Copenhagen, Copenhagen, Denmark.

REFERENCES

1. Thomsen SF, Pritzier EC, Anderson CD, et al. Chronic urticaria in the real-life clinical practice setting in Sweden, Norway and Denmark: baseline results from the non-interventional multicentre AWARE study. *J Eur Acad Dermatol Venereol*. 2017;31(6):1048–1055.
2. Staubach P, Eckhardt-Henn A, Dechene M, et al. Quality of life in patients with chronic urticaria is differentially impaired and determined by psychiatric comorbidity. *Br J Dermatol*. 2006;154(2):294–298.
3. Staubach P, Dechene M, Metz M, et al. High prevalence of mental disorders and emotional distress in patients with chronic spontaneous urticaria. *Acta Derm Venereol*. 2011;91(5):557–561.
4. Konstantinou GN, Konstantinou GN. Psychiatric comorbidity in chronic urticaria patients: a systematic review and meta-analysis. *Clin Transl Allergy [Internet]*. 2019;9(1):1–12. https://doi.org/10.1186/s13601-019-0278-3.
5. Uguz F, Engin B, Yilmaz E. Axis I and Axis II diagnoses in patients with chronic idiopathic urticaria. *J Psychosom Res*. 2008;64(2):225–229.
6. Rafique MR, Masood S, Tanzil S, Tabassum S, Naveed S. Frequency of depression and anxiety among patients with chronic spontaneous urticaria visiting a tertiary care hospital in Karachi, Pakistan. *J Pakistan Med Assoc*. 2020;70(3):511–514.
7. Tat TS. Higher levels of depression and anxiety in patients with chronic urticaria. *Med Sci Mon Int Med J Exp Clin Res*. 2019;25:115–120.
8. Ghazanfar MN, Kibsgaard L, Thomsen SF, Vestergaard C. Risk of comorbidities in patients diagnosed with chronic urticaria: a nationwide registry-study. *World Allergy Organ J [Internet*. 2020;13(1), 100097. https://doi.org/10.1016/j.waojou.2019.100097.
9. Choi GS, Nam YH, Park CS, et al. Anxiety, depression, and stress in Korean patients with chronic urticaria. *Korean J Intern Med*. 2020;35(6):1507–1516.
10. Folci M, Heffler E, Canonica GW, Furlan R, Brunetta E. Cutting edge: biomarkers for chronic spontaneous urticaria. *J Immunol Res*. 2018;2018.