Alexithymia prevalence in individuals with chronic urticaria and its association with illness severity and therapeutic profile

Dear Editor, there is increasing evidence suggesting that the skin and brain are functionally linked[1]. Psychiatric comorbidity in chronic urticaria (CU) patients is estimated at 32%[2]. Alexithymia, anxiety, and depression are hypothesized as triggering factors for CU, though mechanisms remain unclear [2–4]. A few studies with small samples have examined the relationship between alexithymia and CU[5,6], showing a prevalence of as much as 50% of alexithymia in patients with CU.

We performed a cross sectional multicenter study in Europe, Asia, and Latin America to assess the prevalence of alexithymia among individuals with CU. Moreover, the study evaluated the relationship between alexithymia and various factors related to CU, such as disease activity, severity, disease control, quality of life, pharmacological profile, and comorbidities. Participants completed the TAS20 (Toronto Alexithymia Scale). Urticaria patient reported outcomes and demographic information were collected.

Four hundred twenty-three patients (54.4% females) were included with a mean age of 42.4 years, 37.1% had noncontrolled CU (examined by Urticaria Control Test, UCT). Chronic Urticaria Quality of Life assessment (CU-Q2oL) showed most affected domains were itching embarrassment, mental status, and limits-looks and 37% had moderate or severe CU activity (measured by Urticaria Activity Score, UAS7). Based on the TAS 20, a total of 42.1% of the participants were found to have alexithymia, 21.5% had possible alexithymia, whereas 36.4% did not have alexithymia. The differences among these groups based on the presence of alexithymia were found to be statistically significant ($p<0.001$).

Ordinal adjusted logistic regression models with UCT, CU-Q2oL, and UAS7 as predictors, and TAS-20 categories as the primary ordinal outcome variable were performed (Table 1). According to UCT categories, over half of the individuals with alexithymia had uncontrolled urticaria and had a 58% greater likelihood of having alexithymia. One of the models reveal that with every one-unit increase in the CU-Q2oL mental status domain score, the odds of having alexithymia increased by 2.4%. Comparing patients who are urticaria free, those with mild, moderate, or severe CU activity using UAS7, the odds of being more likely to have alexithymia doubled.

Additionally, across the three models, female patients exhibited approximately 40% higher odds of being more likely to have alexithymia. As age increased by one unit, the likelihood of

alexithymia decreased by about 1%. Patients with cardiovascular comorbidities were 2.5 times more likely to have alexithymia, while those using first-generation antihistamines had twice the odds of being more prone to alexithymia.

It is estimated that 10-13% of the general population is affected by alexithymia. Studies have reported a high prevalence of alexithymia in various skin conditions, including alopecia areata, vitiligo, psoriasis, and acne[7]. The authors suggest that managing alexithymia can improve treatment outcomes and quality of life[7]. Our findings reveal that 4 out of 10 CU patients have alexithymia, with an additional 2 out of 10 possibly affected. It is important to consider alexithymia as a possible contributing factor in the evaluation and management of CU.

The evidence presented suggests a potential association between alexithymia and CU, which prompts the question of whether identifying and addressing alexithymia could lead to improved management of CU. Considering that physicians who manage patients expect alexithymia in severe disease, our findings have practical implications because the clinical suspicion should now include mild disease. A larger study is necessary to identify the correlation between these variables, and to confirm our results.

A multimodal therapeutic strategy that includes prompt recognition and management of suspected psychological issues is needed. Unexpectedly, our findings revealed OFG-ATH1 (older first-generation Antihistamine-1-receptor), use doubles the likelihood of alexithymia. Patients with mental disease comorbidities have a higher rate of OFG-ATH1 use (20.83%), with a positive association between mental disease comorbidities and antihistamine use.

This novel finding suggests that there may be a correlation between this class of drugs and the presence of alexithymia, which should be thoroughly investigated in future research, even though the TAS-20 has not been validated in CU, which is one of our study's limitations. We recommend patients with CU should undergo routine mental health evaluations. A coordinated effort between allergists, dermatologists, and psychiatrists should be made to identify and treat any mental conditions to improve their health and quality of life.

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Table 1: Ordinal logistic regression predicting TAS20 categories of alexithymia.

VARIABLES	MODEL 1: MAIN PREDICTOR UCT CATEGORY	MODEL 2: MAIN PREDICTOR UAS7	MODEL 3: MAIN PREDICTOR CUQ2OL
UCT CATEGORY (REF=CONTROLLED)			
NON-CONTROLLED	1.583* (1.065-2.353)		
UAS7 INTERPRETATION (REF=URTICARIA FREE)			
Well controlled		1.680+ (0.912-3.093)	
Mild activity of CU		2.042* (1.124-3.711)	
Moderate activity of CU		2.225* (1.155-4.283)	
Severe activity of CU		2.124* (1.161-3.886)	
CUQ2OL DOMAIN (0-100)			
MENTAL STATUS DOMAIN			1.024*** (1.013-1.035)
FEMALE	1.400+ (0.961-2.040)	1.391+ (0.953-2.030)	1.482* (1.003-2.189)
AGE IN YEARS	0.985* (0.970-0.999)	0.984* (0.970-0.999)	0.987+ (0.972-1.002)
CARDIOVASCULAR COMORBIDITY	2.533*** (1.461-4.392)	2.626*** (1.508-4.574)	2.428** (1.385-4.259)
MENTAL DISEASE COMORBIDITY	2.021* (1.066-3.832)	2.148* (1.130-4.084)	1.723 (0.883-3.362)
OFG-ATH1 USE	2.192* (1.123-4.278)	1.973* (1.007-3.864)	2.497* (1.237-5.039)
SG-ATH1 USE	1.454 (0.000-0.000)	1.431 (0.802-2.552)	1.286 (0.715-2.314)

Note: Confidence intervals in parentheses. *** p<0.001, ** p<0.01, * p<0.05, + p<0.1. Statistical model was performed in all cased based on a sample of 423 participants.

OFG-ATH1: Older first-generation antihistamine-1-receptor

SG-ATH1: Second-generation antihistamine-1-receptor