

Research Paper

Investigating Anxiety and Depression in Chronic Urticaria: Cause or Effect?



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ABSTRACT

Background: Chronic urticaria is a complex multifactorial dermatological disease characterized by wheals lasting more than 6 consecutive weeks. The resultant physical discomfort from chronic urticaria may worsen the patient's quality of life. Emotional manifestations are shown to occur in these patients, among which, depression and anxiety are the two most common conditions. Accordingly, this study evaluates the role of anxiety and depression in the course of chronic urticaria.

Materials and Methods: A total of 170 adult patients with chronic urticaria and 50 healthy adults were asked to complete the questionnaires to be evaluated for the presence of any stigma regarding anxiety and depression. The inclusion criteria were individuals 18 years of age and above, and suffering from chronic urticaria.

Results: The mean age of healthy individuals (control group) was 38.255±13.44 years. Most of the patients (74%) were female. Anxiety was found in 59.5% of the patients with chronic urticaria and 42% of healthy control individuals (P=0.029). Depression was found in 17.6% of patients with chronic urticaria and 6% of healthy individuals (P=0.022).

Conclusion: A strong relationship exists between chronic urticaria and emotional conditions, including anxiety and depression exists.

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Introduction

Chronic urticaria (CU) is a complex multifactorial dermatological disease characterized by wheals lasting >6 consecutive weeks [1-3]. CU is a highly prevalent disorder affecting 0.5% to 1% of the general population [4]. The resultant physical discomfort from CU may worsen the patient's quality of life [5]. Meanwhile, CU and cardiovascular diseases are estimated to have similar effects on quality of life [6]. Although CU does not usually have an identifiable external cause, emotional manifestations are shown to occur in patients with CU, among which, depression and anxiety are the two most common conditions [4]. Findings from recent studies indicate that these two emotional factors are more prevalent in patients with CU than in healthy people and any increase in their intensity may intensify the urticaria and its course [7]. Another study estimates the risk of anxiety and depression in CU patients as 1.79 and 1.61 times compared to the general population, respectively [4]. However, there is no potential pathophysiological pathway, which could explain the coexistence or sequels from one entity to another [8]. The itching caused by CU may strongly affect mental health because of the existing inflammation with the capacity to induce serotonin networks in the brain leading to anxiety and depression later. Sleep disruption due to itching may become a mediator of anxiety and depression in these patients [9]. However, it is unknown whether CU and itching may cause emotional problems through sleep disturbances, such as sleep disruption, or anxiety and depression play a major role in creating a vicious cycle in the development of CU and in worsening the condition. In addition, classic antihistaminic medications with their increased daytime sleepiness may adversely affect the mood of these patients without having a beneficial effect on their sleep quality scores [10]. Furthermore, natural sleep and improved sleep quality are important factors in better control of anxiety and depression in patients with CU. Accordingly, this study evaluates the presence of depression and anxiety concomitant with CU, which may worsen disease control in patients.

Materials and Methods

Study design

This was a case-control study on patients diagnosed with CU at the allergy clinics of [Azad University Hospitals](#) in Tehran from January 2021 to January 2022. CU was defined as adult patients with recurrent wheals persisting for more than 6 weeks according to the international EAACI/GA2LEN/EuroGuiDerm/APAAACI

guideline [11]. Although CU is classified into subtypes, in this study we considered CU as spontaneous urticaria with no specific eliciting factor and the patients participating in this study were individuals with refractory lesions despite receiving full-dose antihistaminic therapy.

The inclusion criteria were individuals with 18 years of age and above and suffering from CU. Meanwhile, the exclusion criteria were patients younger than 18 years old, suffering from systemic illnesses, or unwilling to participate in the study. Two different questionnaires were implemented to evaluate the state of emotional conditions of the participants in terms of anxiety and depression as well as their demographic information including age and gender. All patients with CU were asked to complete both questionnaires. An informed consent was taken from all eligible participants who met the inclusion criteria. The obtained data were compared with a healthy control group.

Study population

A total of 170 adult patients with CU refractory to conventional treatments who were referred to allergy clinics of [Azad University Hospitals](#) agreed to participate and completed the survey. Meanwhile, 50 healthy adults with similar demographics to the patients in the study participated in acting as the control group. After confirming the diagnosis of CU by an allergist, the participants were asked to complete the questionnaires to be evaluated for the presence of any stigma regarding anxiety and depression. The questionnaire also included their demographic information. The questionnaires took 15 min to complete on average. The patients were screened for the probability of the existence of anxiety using a 7-item questionnaire (general anxiety disorder-7) translated into Farsi with a sensitivity and specificity of 89% and 82%, respectively. An 8-item questionnaire (patient health questionnaire-8) translated into Farsi was used for screening depression with sensitivity and specificity of 86% and 81%, respectively. The collected data was evaluated by a psychiatrist.

Statistical analysis

The data analysis was performed using the SPSS software, version 25. Continuous data were presented as Mean±SD. Categorical data was presented as numbers (%) and between-group difference was tested using the chi-square and the Fisher exact tests. The statistical level of $P < 0.05$ was considered significant.

Results

After careful screening, a total of 170 patients with CU refractory to antihistaminic therapy were identified. Meanwhile, a matched healthy control group consisting of 50 individuals was selected based on age and gender. The evaluated patients were between 18 and 80 years with a mean age of 40.54 ± 13.77 years. The mean age of healthy individuals (control group) was 38.255 ± 13.44 . Most of the patients ($n=126[74\%]$) were female. The same female predominance was considered in the control group (69.8%).

To limit the rate of biased diagnoses after evaluating the general anxiety disorder-7 and patient health questionnaire-8, we considered moderate to severe cases (with scores >10) as defined cases of anxiety and depression. Anxiety was found in 101 patients with CU and 21 individuals in the healthy control group (Tables 1, 2 and 3).

Depression was found in 30 patients with CU and 3 individuals in the healthy control group.

Discussion

This study investigated the association of anxiety and depression with CU and compared their occurrence with a healthy control group. The results of the research, which were statistically significant, showed that patients with CU showed higher levels of anxiety and depression when compared with the healthy group.

Emotional distress and psychosocial disorders are reported in at least 30% of patients with skin diseases, including CU [4, 12]. CU seems to adversely affect activities of daily living, mood, and appearance; therefore, it also impacts the quality of life [12].

Depression and anxiety are the most common psychiatric disorders found in CU patients, which can significantly influence both control of the urticaria and quality of life [13, 14]. The role of psychological factors in the development or aggravation of CU is a puzzle, as far as determining which comes first. However, many experts consider the pathogenic role of psychological factors in the development or exacerbation of CU [15].

In a study recently performed seeking the cause of CU in young patients, anxiety or depression was associated with CU [16]. There are reports of CU patients with high rates of anxiety, more depressive symptoms and an overall activity impairment compared to patients with psoriasis [17].

While evaluating the link between depression and CU in literature, we found substance P (SP). SP is a peptide with neuronal origin and wide expression in different parts of the brain, which is involved in response to emotional stimuli and has a powerful vasodilator effect causing plasma leakage and increased vascular permeability with specific mast cell stimulation and subsequent histamine release [18]. SP mediates acute stress response and

Table 1. Comparing the occurrence of anxiety in patients and healthy control subjects

| variable | No. (%) | | P |
|----------|-----------|------------|-------|
| | Patients* | Controls** | |
| Anxiety | 101(59.4) | 21(42) | 0.029 |

IMMUNOREGULATION

*Patients with chronic urticaria, **Controls without chronic urticaria.

Table 2. Comparing the occurrence of depression in the patients and healthy control subjects

| variable | No. (%) | | P |
|------------|-----------|------------|-------|
| | Patients* | Controls** | |
| Depression | 30(17.6) | 3(6) | 0.022 |

IMMUNOREGULATION

*Patients with chronic urticaria, **Controls without chronic urticaria.

Table 3. Comparing the concurrent occurrence of depression and anxiety in the patients and healthy control subjects

| variable | No. (%) | | P |
|----------------------------------|-----------|------------|-------|
| | Patients* | Controls** | |
| ConcurrentAnxiety and Depression | 24(14.1) | 2(4) | 0.036 |

IMMUNOREGULATION

*Patients with chronic urticaria, **Controls without chronic urticaria.

is also produced by macrophages, eosinophils, lymphocytes, mast cells and dendritic cells [18]. SP increases lymphocyte proliferation, immunoglobulin production, and release of histamine and serotonin from mast cells [18], with the latter playing a major role in the pathogenesis of both urticaria and depression [18]. Therefore, it is rational for serum levels of SP to be increased in patients with CU [19, 20]. Skin mast cells are near sensory nerve endings and can be activated by SP, neurotensin and pituitary adenylate cyclase-activating polypeptides, which are released from dermal neurons [18].

The symptom most associated with urticaria is pruritus. Itching is a complex subjective sensory phenomenon with discriminative, cognitive, motivational and affective components [21]. Compared to skin disorders without itching, the mental health and depression of patients with CU are strongly correlated with this symptom [22, 23]. The reason for this correlation is attributed to skin inflammation, which induces serotonin networks in the brain, resulting in depression and anxiety [4]. Chronic itch itself is associated with increased stress, anxiety, and mood disorders [21]. In turn stress and anxiety exacerbate itching, resulting in a vicious cycle with potential effects on the patient's quality of life [21]. Some of these patients experience social anxiety due to visible skin damage [24].

Stress plays a major role in the activation of the immune system inducing the T cell function. It may also cause abnormal tension in the autonomic nervous system, which affects the level of histamine in plasma and skin. In acute stress, activation of adrenocortical and medullary systems may lead to enhanced release of cortisone and catechol-amines, while chronic stress may induce hypo-responsiveness of the hypothalamic-pituitary-adrenal axis and increased secretion of inflammatory cytokines [8]. Therefore, in stressful situations, some inflammatory disorders, such as CU with degranulation and mediator release from mast cells and basophils may ensue [8].

Another study revealed that the greatest burdens on quality of life were sleep disturbances, irritability, and tiredness due to itching, collectively leading to anxiety and depression in the long term [4].

Overall, several studies in addition to the aforementioned articles were in line with our study, all of them indicating the bidirectional role of CU and emotional conditions [25-27]. Although the background mechanism of psychological stress is not fully elucidated, the emerging role of neuro-immune interactions in the shadow of a

variety of inflammatory mediators, neuropeptides, and neurotransmitters is suggested. Surprisingly, there were no credible studies against these findings in recent years.

Conclusion

A strong relationship exists between CU and emotional conditions, including anxiety and depression. Itching is the major factor in inducing these complications. Itching is associated with higher levels of anxiety and, stress exacerbates itch and scratching. Breaking this vicious cycle may improve the quality of life in patients with CU.

Study limitations

There were some limitations to this study. The major limitation was the small study sample. Secondly, the urticaria activity score was not included in the evaluation of the patients.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of [Islamic Azad University of Medical Sciences](#), Tehran (Code: IR.IAU.TMU.REC.1400.11). A written informed consent was taken from all participants.

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Authors' contributions

Conceptualization and study design: Sepideh Darougar and Amir Hashemitari; Data collection: Zahra Farshidfar and Sepideh Darougar; Data analysis and interpretation: Zahra Farshidfar and Amir Hashemitari; Writing—original draft: Sepideh Darougar and Seyedeh Paniz Hashemitari; Final approval: All authors.

Conflicts of interest

The authors declared no conflict of interest.

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