

# The psychosocial burden of urticaria

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## OPEN ACCESS

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This article was submitted to RAD  
CASA - Medical Sciences  
as the original article

### Conflict of Interest Statement:

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Received:** 25 October 2021

**Accepted:** 15 November 2021

**Published:** 27 December 2021

### Citation:

Jerković H, Bešlić I, Ćesić D, Šitum M. The psychosocial burden of urticaria. RAD CASA - Medical Sciences. 548=56-57 (2021): 98-103. DOI: 10.21857/9xn31cogdy

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## ABSTRACT:

Urticaria is one of the most common dermatologic allergic diseases, but also holds a significant psychosocial burden due to possible long duration, frequent relapses, unknown cause or trigger and resistance to applied therapy. Many patients associate the onset and worsening of the disease with stressful experiences indicating it can be a psychosomatic disease within the psychoneuroimmunological approach. Apart from that, urticaria greatly affects the quality of life (QoL) of patients, disrupts their daily lives in all aspects, and is a dermatological disease with one of the highest prevalence of psychiatric comorbidities. Therefore, in this review article we discuss why a multidisciplinary approach, which includes both biological, psychological and social aspects of the disease, must be acknowledged for effective treatment. Finally, we provide suggestions for clinical management of patients suffering from urticaria.

**KEYWORDS:** Psychoneuroimmunology, psychosocial intervention, quality of life, urticaria

## SAŽETAK:

PSIHOSOCIJALNI TERET URTIKARIJE

Urtikarija je jedna od najčešćih dermatoloških alergijskih bolesti, ali nosi i značajan psihosocijalni teret zbog dugog trajanja, čestih recidiva, nepoznatog uzroka ili okidača bolesti te otpornosti na primijenjenu terapiju. Mnogi bolesnici nastanak i pogoršanje bolesti povezuju sa stresnim iskustvima što ukazuje da urtikarija može biti psihosomatska bolest unutar psihoneuroimunološkog pristupa. Osim toga, urtikarija uvelike utječe na kvalitetu života bolesnika, narušava njihov svakodnevni život u svim aspektima, te je dermatološka bolest s jednom od najviše prevalencije psihijatrijskih komorbiditeta. Stoga u ovom preglednom članku raspravljamo o tome zašto se za učinkovito liječenje mora prepoznati multidisciplinarni pristup, koji uključuje i biološke, psihološke i socijalne aspekte bolesti. Konačno, dajemo prijedloge za kliničko liječenje bolesnika koji pate od urtikarije.

**KLJUČNE RIJEČI:** psihoneuroimunologija, psihosocijalne intervencije, kvaliteta života, urtikarija

Urticaria is one of the most common dermatologic allergic diseases, but also holds a significant psychosocial burden. The aim of this study was to review why a multidisciplinary biopsychosocial approach is necessary in treatment. Firstly, we presented a short introduction on its clinical features, and then we discussed various psychosocial aspects of the disease, concluding with suggestions for clinical management of patients suffering from urticaria.

Urticaria occurs in about 1% of the global population, most often in adulthood<sup>1</sup>. Regarding duration, it can be acute or chronic. Chronic urticaria is defined by the appearance of urtica, accompanied by an intense subjective itching sensation, alone or together with angioedema, and lasting longer than 6 weeks<sup>2</sup>. With respect to the identification of its cause or trigger, chronic urticaria is most often classified as inducible or spontaneous (Figure 1). Among all chronic urticaria, the most common is chronic spontaneous urticaria (CSU) which denotes urticaria of unknown cause or trigger. The prevalence of CSU in the general population is about 1-2%, occurring more frequently in adults, especially in women, and between the ages of 30 and 50 years<sup>3</sup>.

Isolated urticaria occurs in 50% of patients, while urticaria accompanied by angioedema occurs in 40% of patients, and isolated angioedema occurs in only 10% of patients. Diagnosis is based on the clinical representation, exclusion of other forms of urticaria and standard laboratory tests (DBC, CBC, ESR or CRP, TSH), but often possible causes are also identified by broader diagnostic processing. According to the latest guidelines, H1 antihistamines (mostly 2nd generation) are primarily used in the treatment of urticaria. The next therapeutic option is omalizumab, an anti-IgE antibody<sup>4</sup>. Chronic spontaneous urticaria lasts on average between 3 and 5 years and monitoring of patients has shown that in approximately 50% of patients spontaneous remission occurs in the first 3 months of the disease. However, in 10% of patients, the disease is expected to last longer than 5 years<sup>5</sup>. Due to possible long duration, frequent relapses, unknown cause or trigger and resistance to applied therapy, urticaria holds a significant psychosocial burden. Firstly, many patients associate the onset and worsening of the disease with stressful experiences indicating it can be a psychosomatic disease. Secondly, urticaria greatly affects the quality of life (QoL) of patients and disrupts

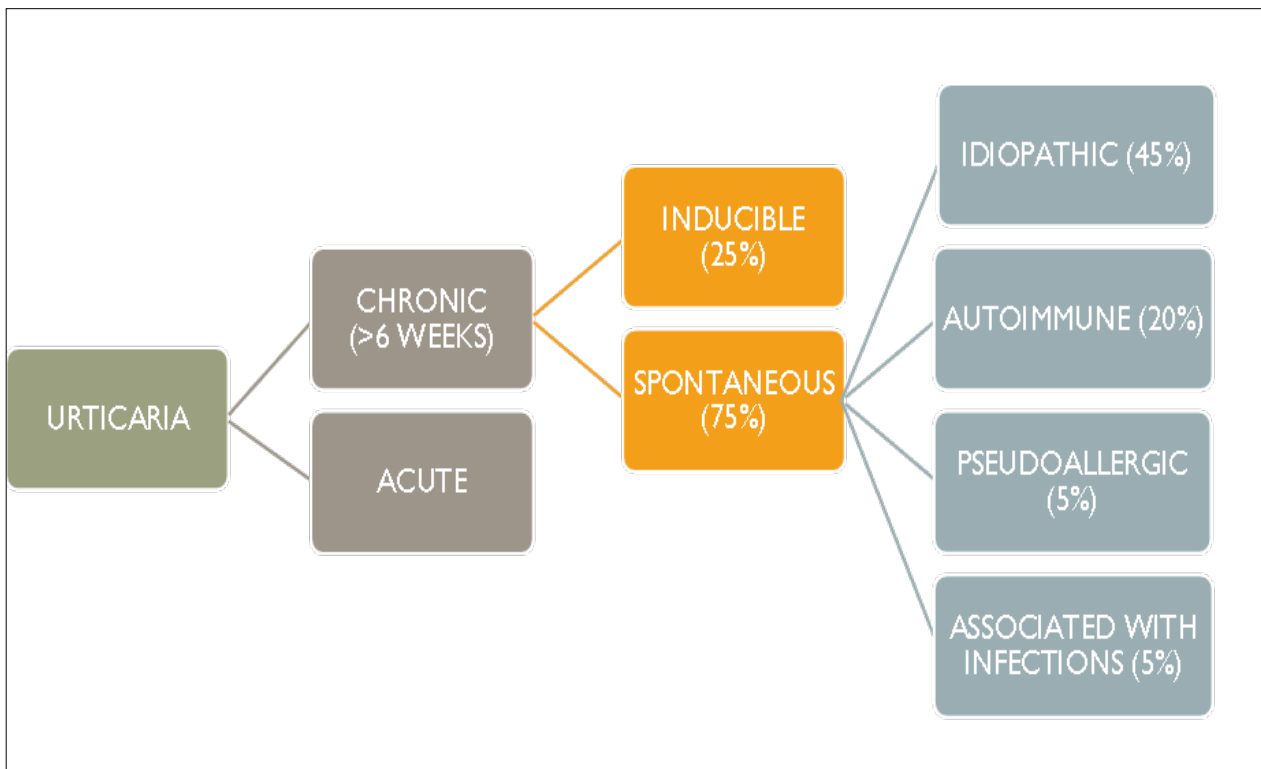


Figure 1. Classification of urticaria according to duration and causes

their daily lives in all aspects, which can, for example, lead to poorer educational and work achievement. Thirdly, urticaria is shown to be a dermatological disease with one of the highest prevalence of psychiatric comorbidities<sup>6</sup>. Therefore, we discuss why both biological, psychological and social aspects of the disease must be acknowledged for effective treatment<sup>7</sup>.

Both research studies and clinical experience show that various dermatological diseases are psychosomatic, urticaria being one of them. Research suggests that the relation between stress and urticaria is due to complex interrelations of the neurological and immune systems with the skin, involving numerous neuropeptides, neurokinins, inflammatory mediators, and HPA axis cells and hormones<sup>8</sup>. The results of a recently published systematic review clearly show that many patients experience elevated levels of psychological stress before the onset of urticaria and link the onset and worsening of the disease to unpleasant and stressful experiences<sup>8</sup>. For example, one study investigated the relationship between disease activity and stress levels in patients with spontaneous and inducible urticaria. Patients with spontaneous urticaria, compared to those with inducible urticaria, are shown to have significantly higher urticarial activity and a stronger perception of stress<sup>9</sup>. Also, another study showed a significant association between stress levels, systemic inflammation, elevations (IL) -18, and C-reactive protein (CRP) levels, and this relationship was even more pronounced in patients with a more severe clinical representation and other autoimmune diseases<sup>8</sup>. In addition, several studies have shown that abnormalities in the functioning of the hypothalamic-pituitary-adrenal axis (HPA axis) are present in patients suffering from urticaria<sup>8</sup>. New studies shed light to the psychosomatic nature of urticaria and other diseases. Namely, it was for long believed that immune system functions are primarily regulated by factors such as pathogen exposure, injury, and internal physiological processes. However, modern research clearly shows that immune activity also changes under the influence of other factors, especially psychosocial<sup>10</sup>, which include various psychological, social, neurocognitive and behavioural factors such as social exclusion, life stress and unpleasant emotions. Psychological research has clearly shown that life stress can have a detrimental effect on health, both mental and physical<sup>11</sup>. Thereby, inflammatory processes are considered a key link between stressful events and physical health, and chronic stress has been shown to suppress cellular and humoral immunity<sup>10</sup>. One study found that exposure to multiple and cumulative stress by the age of eight years was associated with higher levels of inflammatory cytokines between the ages of ten and fifteen years<sup>12</sup>. Another study found that people who were socially isolated had twice as high levels of CRP as people who were adequately socially integrated<sup>13</sup>. Changes in the functioning of the HPA axis were also found in individuals who have been exposed to stressful experiences in early life. Experiences of such stress alter the functioning of the HPA axis, which

then continues into adulthood and disrupts normal responses to stress<sup>14</sup>. Altered functioning and neurological sensitivity to stress persist even when stressful experiences cease.

Contrary to the effects of adverse life events, resilience factors such as social support, mitigate the negative effects that such stress has on immune functions and health. In this context, the results of a meta-analysis by Shields et al. showed that the application of psychosocial interventions (counselling, psychoeducation, psychotherapy) improve the functions of the immune system<sup>15</sup>. A total of 56 randomized controlled experiments with more than 4,000 participants were included in this meta-analysis. Participants included in the experimental group showed an improvement of 14.7% in protective immune functions, and a decrease of 18% in harmful immune functions. This effect lasted for six months after the intervention and proved to be robust regardless of age, gender and duration of psychosocial intervention. Cognitive-behavioural therapy and multiple or combined interventions proved to be more effective than other interventions. The results were clearest in studies evaluating inflammatory cytokines and markers. Therefore, psychosocial interventions may be important and sustainable strategies for maintaining not only our mental health, but also immunity related health, which may be especially important in the context of psychosomatic diseases.

It is important to highlight that exacerbation of urticaria is not associated with stressful experiences for all patients. Nevertheless, even such patients who do not react psychosomatically, may need psychological treatments as well due to their impaired quality of life. Namely, chronic urticaria is one of the dermatological diseases that has the greatest impact on quality of life, both physically, socially and emotionally, and in about 30% of patients the impact of the disease on everyday life is significant or extreme<sup>16</sup>. Different instruments assess the impact of the disease on the patient's emotional status, pain perception, or specific subjective disturbances that occur with the disease symptoms. One of the most commonly used instruments for assessing health quality of life in patients with chronic urticaria is *Chronic urticaria quality of life questionnaire* (CU-Q2oL) by Baiardini et al<sup>17</sup>. The instrument covers six categories that include subjective itching sensation, swelling, appearance, impact on daily activities, sleep problems, and other limitations related to the disease. For example, if urticaria is accompanied by an intense subjective itching sensation, even in a small part of the body, it can strongly affect the disease symptom component and consequently interfere with other areas of functioning, such as sleep and daily activities. A study showed that urticaria, in relation to other skin diseases, has the greatest impact on the domain of symptoms, followed by emotions and functioning<sup>18</sup>. Moreover, the international AWARE 2020 study followed patients with urticaria for two years and identified the main reasons why chronic urticaria has such a strong impact on quality of life<sup>19</sup>. These include the

appearance of sudden urticaria that constantly occurs on the skin with or without swelling of the lips or periorbital area, intense subjective sensation of itching, then the appearance of fatigue, disturbed sleep, lack of concentration, while the appearance of urticaria can cause discomfort and shame and consequently lead to social difficulties. Patients also often experience a lack of concentration, difficulty falling asleep, waking up prematurely and feeling confused, which impairs functioning during the day and leads to limitations in social and even sexual functioning, and much less often engage in leisure activities such as sports or hobbies. Some also experience a reduced personal well-being, disturbed relationships with relatives and disturbances in family functioning, have a disturbed self-image and are in a worse mood, are less successful at work or school. Problems in work functioning occur in about 27% of patients, with presentism present in about 25% of patients and absenteeism in about 6%<sup>6</sup>. Although these difficulties in the literature are most often associated with chronic spontaneous urticaria, one study conducted in Croatia specifically focused on chronic inducible cold-induced urticaria and showed similar results<sup>20</sup>. In-depth interviews were conducted with patients, which made it possible to capture the complexity of their experiences related to the disease itself. The results showed that patients have difficulty with a number of psychosocial aspects of the disease, including those related to physical symptoms, urticaria and swelling, then the psychological and social aspect, work-related aspect, general quality of life, and adjustment to illness. They reported, for example, that due to illness they had to change jobs and careers, as well as avoided leaving their home for fear of sudden onset of symptoms, and felt stigmatized because of the look of their skin. It has been suggested that this type of urticaria also carries a significant psychosocial burden, pointing to the need for a holistic approach to care that includes assessing and managing psychosocial aspects and quality of life.

Apart from disrupting daily life, impaired quality of life can in the long term pose a risk for developing psychiatric comorbidities. One study showed that long-term urticaria, difficulty in identifying causes and / or triggers, and unsatisfactory response to therapy contribute to the development of disorders such as anxiety, depression, irritability or stress<sup>19</sup>. Furthermore, another study showed that impaired quality of life and the development of psychological disorders in patients with chronic spontaneous urticaria are particularly affected by reduced sleep quality, most often due to an intense itching sensation<sup>21</sup>. Within the biopsychosocial model of chronic pruritus, it is clear that psychological factors may contribute to exacerbation or improvement of pruritus, so psychological interventions are necessary in the treatment as well<sup>22</sup>.

As explained by the Cummins' theory of homeostasis and subjective quality of life<sup>23</sup>, chronic physical discomfort, such as pain and itching, breaks the natural homeostasis of the organism. People who suffer from severe physical discomfort often isolate

themselves from others, which contributes to the disturbance of general mental status, feelings of helplessness, lower self-confidence, and loss of control, which impairs the quality of life. Ultimately, these disorders overall pose a risk for the development of anxiety and depressive disorders, especially if they last for a long time. Various studies have clearly confirmed this and shown that anxiety and depressive disorders are negatively associated with quality of life<sup>24</sup>. Therefore, this theory may explain the association of quality of life with psychological characteristics and psychiatric comorbidities in patients with chronic urticaria. In line with that, a meta-analysis published in 2019 showed that psychiatric disorders and diseases are present in about 32% of patients<sup>25</sup>. The most common are sleep and wakefulness disorders (36%), depression and mood disorders (39%), anxiety disorders (30%), trauma and stressor disorders (17%), somatic symptoms disorders and related disorders (17%), obsessive-compulsive and related disorders (9%) and disorders related to psychoactive substances and addictions (4%). Chu et al. calculated the relative risk of developing psychiatric illness in patients with spontaneous urticaria, and the results showed that these patients had a significantly higher risk of developing anxiety disorders, depression, sleep disorders, drug addiction, and dissociative and somatoform disorders<sup>26</sup>. Some authors argue that psychiatric comorbidities in urticaria patients are even more common and numerous than in patients with psoriasis or atopic dermatitis<sup>27</sup>, which are considered as the most common psychosomatic dermatological diseases. Such high prevalence of psychiatric comorbidities may be also due to some specific personality traits found in urticaria patients. Research has shown that these patients are more often of a submissive nature, with a pronounced need to seek guilt in external circumstances and in themselves, with anxiety and depressive features<sup>28</sup>. Another study found that patients with spontaneous urticaria were significantly depressed, anxious, had difficulty forming relationships, focused on somatic symptoms, and had obsessive-compulsive traits, compared with the control group<sup>29</sup>. In other words, patients were more often in conflict with their environment, perfectionists, and sought confirmation, control and love. All these traits could make them more vulnerable and susceptible for developing further psychopathological issues. Although based on the available findings, it is not possible to say with certainty whether psychiatric disorders pose a risk for the development of chronic urticaria or are a consequence of urticaria, the need for interdisciplinary treatment is clear. Based on the reported literature, we also suggest some practical guidelines for clinical management of patients in everyday practice. Firstly, it is necessary to accomplish cooperation between dermatologists and mental health professionals that will certainly contribute to improving the health and quality of life of patients. Next, it is important to include the topic of the impact of stress on the disease itself and impaired quality of life, because just raising awareness and recognizing the unpleasant mood associated

with the disease can make it easier for patients to cope with it<sup>30</sup>. Short educations on the association between stress and worsening of the disease are very useful, and it is especially important to examine the subjective experience and perception of the disease of the patients themselves (for example, how the disease affects their daily lives, and what are their experiences with symptoms). Such conversations also encourage patient cooperation and adherence. In addition, several techniques are available that have been shown to be useful in reducing the experience of itching: *Habit reversal training* and *Arousal reduction*<sup>31</sup>. It is useful to empower patients to take an active role in managing their health, engage in activities that have a relaxing effect on them, as well as motivate them to generally beneficial health behaviours, such as healthy eating, exercise and maintaining good sleep hygiene. If a dermatologist suspects that a particular individual has more serious psychopathological disorders or notices severely impaired functioning due to illness, it is important to refer him for additional assessment by mental health professionals - psychiatrists and clinical and health psychologists. Given that the prevalence

of psychiatric disorders, as well as the risk of their development, in patients with urticaria is significantly increased, a multidisciplinary approach to treatment is necessary. Depending on intensity of the psychosocial impairment, the patient may then be referred to various psychological interventions. These may include counselling, education, various treatments and techniques, psychotherapy or psychiatric and pharmacological treatment. These interventions have been shown to be useful for people in whom stress leads to worsening of symptoms, but also for other patients for whom the onset and experience of the disease is stressful, for example due to itching, discomfort, treatment uncertainty and sleep disorders. Furthermore, cognitive-behavioural and group therapy and mindfulness techniques have proven to be interventions that contribute to symptom relief and faster remission, stress reduction and more successful ability to control and adapt to dermatological diseases<sup>32</sup>. In selecting the most appropriate intervention, an individualistic approach is crucial, in which a mental health professional conducts an assessment and indicates further treatment.

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