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Unraveling the Complex Nexus of Chronic Spontaneous Urticaria: Immunological, Infectious and Psychosomatic Dimensions

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Mini Review

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Abstract

Chronic Spontaneous Urticaria (CSU) is a complex dermatologic allergic condition characterized by unknown origins, frequent relapses, and resistance to therapy, contributing to a substantial psychosocial burden. Stressful experiences appear to coincide with CSU onset and exacerbation, suggesting a psychosomatic element within a psychoneuroimmunological framework. The condition significantly impairs patients' quality of life, disrupting daily activities and exhibiting a high prevalence of psychiatric comorbidities. Recent theories propose autoantibodies activating mast cells as a potential key factor in CSU development. Psychological stress is considered both a trigger for CSU onset and a factor influencing the disease course and therapy effectiveness. Although the skin's response mechanisms to psychological stress are not fully understood, inflammatory mediators, neuropeptides, and neurotransmitters are believed to play a role. Chronic Spontaneous Urticaria (CSU) is estimated to impact 0.5–1% of the global population at any given time, making up approximately two-thirds of all Chronic Urticaria (CU) cases. Among individuals with CSU/CIU, it is suggested that 33–67% experience both itchy welts and deeper skin swelling, while 29–65% solely have itchy welts, and 1–13% exclusively experience deeper skin swelling. Despite extensive research on the clinical aspects and origin of CSU/CIU in the last decade, the comprehensive understanding of the humanistic and economic implications of CSU/CIU remains unclear, especially for those with an inadequate response to initial treatment strategies. Research indicates that infections act as a facilitating factor for CSU initiation and perpetuation, with stress potentially necessary for the expression of the CSU phenotype. Detection and treatment of hidden infections have shown improvements in CSU patients, reinforcing the association between infections and CSU. A comprehensive, multidisciplinary approach that considers biological, psychological, and social aspects is emphasized for effective urticaria treatment. Current research underscores the significant psychological impact of CSU, particularly for individuals with more severe forms or those diagnosed with chronic autoimmune urticarial.

Keywords: Urticaria; Psychological Aspects; Immunology

Abbreviations: CSU: Chronic Spontaneous Urticarial; AST: Autologous Serum Tests; APT: Autologous Plasma Tests; TPO: Thyroperoxidase.

Introduction

Chronic spontaneous urticaria (CSU) is a severe skin condition marked by highly itchy welts, angioedema, or both. Symptoms reoccur spontaneously, almost daily, for more than 6 weeks. Many patients endure flare-ups for several years, leading to a diminished quality of life. It affects approximately 1–5% of the global population and significantly impacts the daily lives of patients. Symptoms of chronic spontaneous urticaria (CSU) emerge without dependence on external causes, although conditions such as infection or high levels of stress can worsen the disease. Many CSU patients undergo an extended disease course lasting for years. There are no curative treatments for CSU; approved therapies offer symptomatic control but do not seem to alter the natural progression of the disease. The primary treatment principle for CSU is to alleviate symptoms, including pruritus, wheals, and angioedema. Therefore, there has been an increased focus on identifying the underlying disease mechanisms and the development of novel therapeutics. Studies have highlighted the significant impact of CSU on patients' quality of life. Symptoms such as pruritus, urticaria, and angioedema contribute to the unpredictability of attacks, sleep disturbances, fatigue related to antihistamine use, and cosmetic dissatisfaction during episodes. Although the underlying pathophysiology is not fully understood, autoimmune mechanisms have been investigated since the 1960s.

Autoimmune mechanisms play a crucial role in the pathogenesis of Chronic Spontaneous Urticaria (CSU) and understanding these processes may lead to more targeted therapeutic strategies. There is added value in paying attention to potential connections between autoantibodies and infections, as this interaction can impact the overall immune response of the organism. It is significant to understand the complex nature of Chronic Spontaneous Urticaria (CSU) and its associations with autoimmune mechanisms. Positive results in autologous serum tests (AST) or plasma tests (APT) in a substantial percentage of patients (40% to 60%) suggest the presence of autoantibodies capable of stimulating mast cells.

There is a notable risk of acute cases of spontaneous urticaria transforming into the chronic form with positive AST results, along with reduced chances of symptom resolution within two years. Patients with CSU often coexist with various autoimmune diseases, especially those related to the thyroid, diabetes, rheumatoid arthritis, and Sjögren's syndrome. IgG anti-thyroid antibodies, particularly those directed against thyroperoxidase (TPO), are common in CSU patients, especially in females. Additionally, the presence of IgE antibodies to TPO suggests a potential mechanism of action for anti-IgE therapy in CSU treatment. An interesting revelation is the identification of a notable occurrence where elevated levels of overall IgE in individuals with CSU could be self-reactive, suggesting heightened lipophilicity. In a substantial proportion of CSU patients, there is the presence of IgG antibodies that directly bind to the FcεRI receptor, triggering the activation of mast cells. This underscores the pivotal involvement of self-reactive IgE and IgG antibodies in the activation of mast cells. Additionally, the functional capacity of IgE antibodies targeting IL24 to activate mast cells is observed, and this activity aligns with the level of disease activity.

In the final years of the previous century, emerging data highlighted the substantial involvement of IgE autoantibodies in Chronic Spontaneous Urticaria (CSU). Autoimmunization is recognized as a prevalent contributor to CSU, encompassing both type I autoimmunization (linked to IgE targeting autoantigens) and type IIb autoimmunization (involving autoantibodies activating mast cells) as pivotal factors in its origin and development. An analysis of existing literature, applying Hill's causality criteria, suggests a level 3 association (indicating a causal link) for type I autoimmunization with CSU, while type IIb autoimmunization exhibits a level 2 association (indicating a highly likely causal link). Patients with CSU were found to harbor IgE against various antigens, including double-stranded DNA, IL-24, tissue factor, eosinophil cationic protein, FcεRI, and thyroglobulin. The functional significance of IgE in relation to some of these antigens, such as IL-24, double-stranded DNA, and TPO, was affirmed through in vitro studies. Collectively, individuals with CSU exhibit IgE directed against over 200 autoantigens, surpassing both the prevalence and diversity observed in healthy controls. It is crucial to note that these findings warrant validation through further investigations, given that some authors have reported the presence of IgE autoantibodies, including IgE-anti–IL-24, even in individuals without clinical symptoms [1].

Concerning antigens, type I CSU autoimmunization is associated with the existence of IgE antibodies targeting autoantigens like thyroid peroxidase and IL-24. Conversely, type IIb autoimmunization entails autoantibodies that activate mast cells, typically through IgE and the FcεRI receptor [1]. Significantly, both forms of autoimmunization may coexist within certain patients. Ongoing research into novel therapies for CSU, such as ligelizumab or Bruton's tyrosine kinase inhibitors, introduces new avenues for treatment [1].

This understanding, coupled with additional discoveries, prompted the initiation of the first randomized controlled trial involving omalizumab, an anti-IgE antibody, in CSU patients with IgE autoantibodies targeting thyroid peroxidase (TPO), a prevalent autoallergen in CSU (the Xolair in Chronic Urticaria induced by Serum IgE targeting Endoantigens [X-CUISITE] study) [2]. Treatment with omalizumab in these patients resulted in a rapid and highly effective response, achieving a complete response rate of 70%, surpassing subsequent studies with omalizumab in CSU. Subsequent investigations into the prevalence, role, significance, and targets of IgE autoantibodies in CSU patients further delineated the type I autoimmune CSU (type I aiCSU) or autoallergic CSU endotype [3].

Regarding the prevalence and pathogenesis of autoallergic CSU, the identification of IgE autoantibodies against TPO in a CSU patient in 1999 hinted at autoallergy as a significant mechanism. Follow-up analyses reported elevated IgE-anti-TPO levels in a substantial percentage of CSU patients, albeit with variations depending on the studies. Recent studies have also demonstrated heightened skin reactions to TPO in CSU patients compared to those with autoimmune thyroid disease and healthy controls [1].

The conclusions drawn from the conducted research suggest a complex relationship between infections and chronic spontaneous urticaria (CSU). Researchers, including Kay et al. , demonstrated that various elements of the immune response to infections may play a role in different stages of CSU. Increased cellular expression of Th2 cytokines, such as IL4 and IL5, as well as IL33, IL25, and thymic stromal lymphopoietin, was observed in the lesional but not non-lesional skin of CSU patients, indicating the activation of immune mechanisms. Important aspect to analyse is the link between Helicobacter infection and CSU. Protein of 23-35 kDa obtained from Helicobacter preparations was found to induce the release of substances such as histamine, TNF-a, IL-3, IFN-γ, and leukotriene B4 by mast cells. This suggests that infections may directly impact the activation of sensitized cells in CSU.

In other the studies, it was shown that anti-thyroid peroxidase (TPO) IgE antibodies are present in all three groups, with the highest percentage among patients with Chronic Spontaneous Urticaria (CSU) (34.0%), compared to patients with thyroid diseases (ATD) (16.6%) and healthy individuals (8.1%). Levels of anti-TPO IgE were higher in CSU patients, while anti-TPO IgG antibodies predominated in thyroid disease patients. In response to exposure to thyroid peroxidase (TPO), a significant increase in CD203c expression was observed in CSU patients with anti-TPO IgE antibodies compared to the other groups. In the CSU group, the percentage was 33.0%, in the ATD group 14.0%, and in the control group 9.0%. CSU patients also showed higher skin reactions to TPO in intradermal tests (CSU: 18.0%, ATD: 3.3%, control: 8.0%) and skin prick tests (12.0%, 0%, 0%, respectively). The passive transfer of anti-TPO IgE antibodies from a CSU patient to the skin of control subjects without anti-TPO IgE induced a positive skin reaction. This results confirm the presence of anti-TPO IgE antibodies in CSU patients, suggesting their potential pathogenic role. Additionally, these results emphasize significant differences in the levels and types of antibodies between the studied groups, which may have clinical significance in understanding the mechanisms of CSU and developing treatment strategies.

Moreover the study's outcomes highlight significant insights into the relationship between Helicobacter pylori (HP) infection and Chronic Spontaneous Urticaria (CSU). Notably, HP-negative patients exhibited a substantially higher rate of spontaneous remission of urticarial symptoms (Risk Ratio: 0.39; 95% CI: 0.19-0.81). In the context of HP-positive CSU patients, the findings indicate that the remission of CSU was more likely in those undergoing HP eradication therapy compared to the untreated group, irrespective of achieving HP elimination (Risk Ratio: 2.10; 95% CI: 1.20-3.68). When assessing the impact of antibiotic therapy on CSU remission in the context of HP eradication, the study revealed no significant difference in CSU remission based on the success or failure of antibiotic therapy in eradicating HP (Risk Ratio: 1.00; 95% CI: 0.65-1.54). These nuanced insights underscore the complexity of the relationship between HP, antibiotic therapy, and CSU remission, necessitating further exploration for comprehensive treatment strategies.

Additionally, mast cells can be activated by inflammatory cytokines, such as IL6, and elevated levels of IL6, IL1β, and TNFα have been reported in patients with infection and CSU, indicating a connection between inflammation and the occurrence of urticaria. The conclusions from the text emphasize the significant role of autoantibodies in chronic spontaneous urticaria (CSU) and suggest the need for investigations in patients unresponsive to high doses of antihistamines. Targeted examinations for autoimmunity, vitamin D deficiency, gastrointestinal dysbiosis, and potential Helicobacter infection are recommended. Further research into the connections between autoimmunity and infections, along with the exploration of more effective therapies, is crucial for improving the treatment of patients with CSU. First and foremost, efforts are directed towards finding medications that could influence the mechanisms described above. However, both the practical use of psychiatric medications and numerous data indicating the psychosomatic nature of this disease prompt consideration of the potential impact of psychological factors, including psychosocial interactions, as an important aspect of treatment.

CSU as a Psychosomatic Illness

The first half of the 20th century was a time of simultaneous development in psychoanalysis and allergology, coupled with significant interest in the psychological basis of dermatological diseases. This interest was heightened by the well-known bidirectional relationships between the skin and the central nervous system, as both originate from ectoderm in the fetus, develop in close proximity, and remain interconnected throughout life.

Based on the psychoanalytic model, attempts were made to create a psychological profile leading to the development of diseases, and similar efforts were made regarding urticaria. However, over time, disillusionment with psychoanalysis, increasing knowledge of immunology, and the availability of medications (mainly antihistamines) that assisted patients led to the dominance of the biomedical model of the disease. Thinking about the psychological aspects of CSU in clinical research was pushed to the sideliners. Although knowledge about the involvement of psychological factors in the pathogenesis of CSU is quite widespread among allergists - as believed by 80% of Canadian allergists.

However, in the era of methodologically superior research, with the dominance of questionnaire methods, the psychological correlates of CSU become less clear. An example of such a process was provided by Broom, who observed that while in a standard study using a screening questionnaire, only 16% of CSU participants reported the occurrence of a stressful life event within the year before the onset of the illness, a multidimensional study using several questionnaires and analysing a wide range of patient functioning revealed significantly more stressful life events, psychosomatic symptoms, reduced social support, and coping abilities in CSU patients (compared to patients with foot fungus). But fundamentally, newer studies, for methodological reasons, formulate more cautious conclusions than early reports. Moreover, their correlational nature prevents drawing methodologically sound conclusions regarding the directions of dependencies between CSU and psychological phenomena.

It is however very clear that stress contributes to the development of skin diseases by delaying wound healing through a direct impact on interleukins and by directly disrupting the balance of the epidermal permeability barrier. The experience of CSU can be perceived as a stressor, triggering a stress response in individuals. This stress response follows a universal mechanism observed in various stressful situations.

The study showed that patients with Chronic Spontaneous Urticaria (CSU) more frequently experience anxiety and depression compared to the control group. The frequency of anxiety was 9.6% compared to 5.7% in the control group ($p < 0.001$), and the frequency of depression was 11% compared to 7.9% ($p < 0.001$), even after adjusting for demographic and clinical factors. The association of CSU with anxiety was particularly strong in the 18–29 age group and in the high socio-economic status (SES) group, while the association of CSU with depression was highest in the 50–69 age group and in the low SES group.

Dermatological inflammatory conditions, such as urticaria, atopic dermatitis, psoriasis, and acne, make the skin particularly susceptible to the influences of stress. The skin's reactivity threshold is lowered, likely due to the continuous accumulation and activation of immune cells, pro-inflammatory cytokines, and chemokines both in the affected and unaffected skin. Additionally, it has been shown that chronic stress, especially traumatic experiences in early childhood, may lead to the development of dermatological diseases similar to psychiatric and physical disorders by causing changes in a wide range of areas, from deterioration of brain plasticity to disturbing hypothalamic-pituitary-adrenal axis activity, immunological response, and development of emotion. A recent study has been published on the co-occurrence of CSU and childhood trauma, indicating that higher scores on the Childhood Trauma Questionnaire (CTQ-28) are associated with the early onset and severity of the disease in CSU patients, along with accompanying depression and anxiety. While prospective findings support the causal relationship between chronic stress and its long-term adverse health effects, little is known about the exact pathways through which it translates into health risk. However, there is more evidence for the psychosomatic nature of CSU. For example, the increasingly frequent occurrence of urticaria during the COVID-19 pandemic also confirms that urticaria is closely associated with anxiety states.

CSU and Stress

The relationship between CSU and psychological stress is bidirectional. On one hand, acute and chronic stressors are recognized as etiological factors. In empirical studies, individuals suffering from CSU exhibit higher levels of stress related to perceived events or actual life experiences. On the other hand, skin changes and the associated discomfort constitute a serious, chronic, and challenging-to-control stressor that impacts not only the patient's mental state and well-being but also the condition of their skin. It seems that itching and the related sleep disturbances are of utmost significance among the symptoms. In a recent study conducted in the youth population. The analysis included 2358 students without systemic diseases and itch-related conditions (except CSU), 393 CSU patients, and 1965 healthy individuals from the control group matched for age and gender. CSU showed a significant association with anxiety

and depression, and the mediation model suggested that CSU influences anxiety and depression through itching and sleep disturbances. Itching and sleep quality accounted for 65.4% and 77.6% of the impact of CSU on anxiety and depression, respectively, with no significant direct influence of CSU on anxiety or depression observed in the mediation models.

The experience of CSU can be perceived as a stress-inducing factor, triggering a stress response in individuals. Its intensity may vary depending on objective factors (severity of symptoms, course, and effectiveness of treatment) but also subjective experiences. The subjective nature of this process means that individuals may evaluate the same situation differently depending on their stress transactions. Patients dealing with uncertainty about when symptoms will appear find themselves in a challenging cycle. The disease itself negatively affects their mental well-being, while psychological factors such as emotions and stress additionally exacerbate the severity of the disease. It's worth noting that studies consistently reveal a correlation between the intensity of the disease and psychological factors, although the cause remains unclear. This suggests that actions aimed at reducing stress may potentially alleviate CSU symptoms.

Broad clinical observations highlight a significant association between the initiation and exacerbation of skin inflammation and increased exposure to psychological stress. Increased psychological stress is closely associated with worsening conditions and more frequent relapses. A promising intervention pathway is the implementation of therapeutic support and care from a collaborative medical team. This comprehensive approach can not only alleviate the severity of the skin condition but also improve the mental well-being of patients. By breaking the cycle of mutual influence between CSU and psychological stress, this integrated strategy offers hope for better outcomes and a higher quality of life for individuals affected by the disease.

Psychological and Psychopathological Correlates of CSU

Clinicians have long recognized the connection between psychological factors and CSU. However, research is scarce (the latest systematic review of studies from 1995 to 2022 analysed only 18 studies) and methodologically weak. Most of them assessed the impact of psychosocial factors by estimating the frequency of occurrence, and the studies typically have a cross-sectional (rather than longitudinal) design. A general paucity of research, combined with limitations in study design, variability in the operationalization of constructs, and heterogeneity in the measurement of outcomes, makes it difficult to draw firm conclusions in this area. They do not allow for a clear answer as to whether observed psychological problems and the frequently co-occurring psychopathology with CSU are a consequence of CSU or a predisposing factor probably both. There are many credible biological mechanisms by which interactions between the nervous and immune systems can induce skin symptoms.

Chronic urticaria poses a significant challenge to the well-being of individuals, impacting their quality of life. Conclusions drawn from the obtained results unequivocally indicate that chronic urticaria (CU) significantly affects the quality of life of almost half of the patients (50.3%). However, only a limited number of studies have examined its associations with mental health. A study involving 100 patients with chronic spontaneous urticaria (CSU) found that 48 of them (24 males and 24 females) had at least one psychiatric disorder. Among these disorders, anxiety disorders were most common (30%), followed by depressive and somatic disorders (17% each) [4]. Agoraphobia was the most prevalent anxiety disorder (15%). Patients with CSU and depression often experienced recurrent depressive disorders or dysthymia, while the most common somatic disorders included somatization disorders, autonomic dysfunction in somatic form, and undifferentiated somatic disorders. Another study, predominantly comprising women (85.72%), reported similar findings. Agoraphobia remained the most prevalent anxiety disorder (15%). Patients with CSU and depression often had recurrent depressive disorders or dysthymia, while the most common somatic disorders included somatization disorders, autonomic dysfunction in somatic form, and undifferentiated somatic disorders [5-12].

In the Chronic Urticaria Quality of Life Questionnaire, the overall score was 36 (0-100), with the most significant impact on the quality of life observed in Dimension I (sleep/psychological state/eating). Among individual items, nervousness and shame related to skin changes received the highest average scores, while lip swelling and limitations in sports activities received the lowest scores. Furthermore, the level of emotional distress is higher and more frequently elevated in patients with CSU who also have psychiatric disorders. Studies consistently revealed a high percentage of psychiatric disorders among CSU patients, ranging from 35% to 60% . Anxiety, depression, and somatic disorders were identified as the most common psychiatric disorders in CSU patients. It is worth examining individual personality traits and psychological predispositions in the case of CSU. Various studies speak to the correlation of CSU with anger, affect regulation, particularly alexithymia with worst condition.

The coherence may be poorer in patients with CSU, especially those with angioedema . Results from a study conducted between 2016-2018, analysing personality traits in patients with chronic spontaneous urticaria (CSU) compared to healthy individuals, suggest several important

observations. The Temperament and Character Inventory (TCI) and a demographic questionnaire were used for the assessment. The results indicate that patients with chronic spontaneous urticaria tend to seek novelty and avoid harm. These patients seem to be more open to new experiences while simultaneously avoiding situations that may lead to potential threats. Patients with chronic spontaneous urticaria scored higher in novelty seeking (P = 0.041) and harm avoidance (P = 0.015) compared to healthy individuals. These findings suggest that these patients tend to seek new experiences while avoiding potential threats. Healthy individuals scored higher in self-directedness (P = 0.003) and cooperation (P = 0.001) compared to patients with chronic spontaneous urticaria. This suggests that healthy individuals exhibit greater autonomy and willingness to cooperate [12-18].

Among male patients, higher scores were obtained in novelty seeking (P = 0.006) and reward dependence (P = 0.013), while female patients scored higher in self-transcendence (P = 0.001) and cooperation (P = 0.019). These results suggest that there are certain gender differences in personality traits among patients with chronic spontaneous urticaria. Correlations were observed between the duration of the disease and reward dependence, self-directedness, and self-transcendence. This suggests that the duration of the disease may influence certain aspects of personality traits in patients with chronic spontaneous urticaria.

It is worth to mention results of other study that shed light on significant differences in temperament and character traits between patients with Chronic Urticaria (Urticaria) and the control group. Individuals with Urticaria scored lower in dimensions such as novelty-seeking, extravagance, fear of uncertainty, cooperativeness, social acceptance, empathy, helpfulness, compassion, virtuousness-scrupulousness, and self-directedness according to the Temperament and Character Inventory (TCI) compared to healthy individuals [18-24].

Previous research has already indicated a connection between psychological factors and Urticaria. This condition is often associated with psychiatric symptoms such as depression and anxiety, as well as stress, which may play a role in the genesis and progression of the disease. High prevalence rates of mental disorders have been observed in patients with Urticaria, with anxiety disorders being the most common. Additionally, studies have identified personality disorders in individuals with Urticaria, especially obsessive-compulsive personality disorder.

While previous studies used the NEO-Five Factor Inventory to assess personality traits in Urticaria patients, the uniqueness of this study lies in the use of the TCI. The results indicated that patients with Urticaria scored higher in the areas of novelty-seeking and extravagance, traits associated with impulsive and exploratory behavior. Importantly, they also scored lower in the fear of uncertainty dimension, suggesting a potential deficit in social interactions.

The study emphasizes the role of personality traits in the development and progression of health problems, focusing on Cloninger's model of personality, which connects brain systems responsible for behavioral activation, inhibition, and maintenance. The study found weak correlations between the duration of the disease, the intensity of Urticaria and itching symptoms, and certain personality traits, suggesting that psychological factors influence the exacerbation of Urticaria symptoms. The authors suggest that the assessment and treatment of Urticaria should incorporate psychosomatic approaches in clinical practice. No conflicts of interest were reported by the authors [24-29].

Data on sociodemographic variables, disease activity, quality of life, sleep, sexual dysfunction, anxiety, depression, and Type D personality (TDp) were collected using validated questionnaires. The presence of TDp was identified in 28% (21/75) of the patients. Although TDp was not associated with poorer disease control, patients with TDp had a higher prevalence of anxiety and depression. Based on the presented text, it can be observed that Type D personality (TDp) may have a significant impact on patients with Chronic Spontaneous Urticaria (CSU). Individuals with Type D personality, characterized by stable traits, more frequently experience emotional difficulties, such as increased feelings of anxiety and depression, which may be linked to a higher risk of developing CSU. Data from the study indicate that while TDp does not directly correlate with poorer disease control in CSU, patients with this personality type more frequently experience anxiety and depression [30-35].

Regarding therapy, especially psychological support, it may play a crucial role in improving the condition of CSU patients, particularly those with Type D personality. Data from the study suggest that TDp is associated with poorer quality of life and more frequent sleep disturbances, indicating that interventions focused on improving mental and emotional well-being may be beneficial. The study suggests that behavioral therapies, psychotherapy, or psychological support can be effective forms of treatment, especially for CSU patients experiencing emotional difficulties associated with Type D personality. Therefore, a coordinated approach, encompassing both medical treatment and psychological support, may contribute to improving the quality of life and the effectiveness of therapy for patients with Chronic Spontaneous Urticaria.

In summary, it seems that personality traits are significantly associated with chronic spontaneous urticaria. This understanding may help tailor treatment strategies and more effective psychological interventions for patients with this skin condition . These findings underscore the multi-faceted impact of CSU on the mental well-being of patients, emphasizing potential significant implications for the effective treatment of the disease. Further research may be crucial for a better understanding of the relationships between these factors and the development of more personalized therapeutic strategies. Therefore, the development of effective treatment strategies considering both physical and psychological aspects becomes crucial for improving the quality of life for individuals affected by chronic urticaria. Additionally, these results highlight the need for further research and interventions aimed at understanding the deeper mechanisms influencing the experience of the disease and developing more personalized therapeutic strategies [18].

Conclusion

These findings highlight a high prevalence of anxiety, depression, and somatic disorders among CSU patients, with every other patient suffering from at least one of these conditions. CSU patients experiencing mental disorders exhibit significantly elevated levels of emotional distress and reduced quality of life. Most current research emphasizes the importance of routine assessments of the mental health status of CSU patients, so questionnaires such as HADS and SCL90R should be considered for their potential use as screening tools [26]. Moreover, CSU patients should be evaluated for improvement in emotional stress levels and quality of life after psychosomatic therapy, if indicated, through controlled clinical trials.

Review

Review on chronic spontaneous urticaria (CSU) presented here delves into the intricate connections between various factors influencing the onset, progression, and treatment of the condition. A notable risk discussed is the transformation of acute cases of spontaneous urticaria into the chronic form, often associated with positive AST results and reduced chances of symptom resolution within two years. The coexistence of CSU with autoimmune diseases, particularly those related to the thyroid, diabetes, rheumatoid arthritis. The presence of IgG anti-thyroid antibodies, especially those against thyroperoxidase (TPO), and the potential role of IgE antibodies to TPO in the mechanism of anti-IgE therapy in CSU treatment are highlighted.

CSU has very multi-faced nature, encompassing autoimmune, infectious, and psychosomatic components. It calls for a holistic approach in understanding and treating the condition, recognizing the intricate interplay of immunological, psychological, and personality factors. Future research in Chronic Spontaneous Urticaria (CSU) should prioritize advancements in diagnostic tools, aiming for more accurate and standardized methods to identify CSU endotypes. The exploration of underlying mechanisms of pseudoallergic reactions, particularly in relation to food intolerance, is crucial. Long-term effects and sustainability of pseudoallergen-free elimination diets, considering patient responses and adherence, need in-depth analysis.

Comprehensive studies on infections in CSU patients, accounting for factors like age and geography, are essential. Specific diagnostic measures for infections associated with CSU require exploration to understand the diagnostic workup needed for effective detection and treatment. Further investigation into the role of autoantibodies in auto-reactive CSU and the exploration of alternative or improved methods for diagnosing delayed pressure urticaria are warranted. Personalized therapeutic approaches tailored to individual biomarkers, psychological stressors, and personality traits should be a focal point. The insights provided pave the way for further research and the development of more targeted therapeutic interventions to improve the quality of life for individuals affected by chronic urticaria. Personality traits are examined, indicating that patients with CSU tend to seek novelty and avoid harm, with gender differences observed. The duration of the disease is suggested to influence certain aspects of personality traits. The findings stress the need for personalized therapeutic strategies considering both physical and psychological aspects. The comprehensive review on Chronic Spontaneous Urticaria (CSU) yields actionable insights for clinicians and researchers. Key findings underscore the pivotal role of autoimmunization, specifically the presence of IgE and IgG antibodies, in the activation of mast cells. Two distinct autoimmunization types, type I and type IIb, contribute to the origin and progression of CSU. Noteworthy is the association of IgE antibodies targeting various autoantigens, such as thyroid peroxidase and IL-24. Targeted therapies, including omalizumab, show promise, especially in patients with IgE autoantibodies. The complex relationship between infections and CSU is highlighted, with immune responses playing a crucial role. Helicobacter infection is implicated, inducing substances that activate mast cells. Studies emphasize the potential impact of antibiotic therapy on CSU remission in the context of Helicobacter eradication.

Psychosomatic aspects of CSU are explored, revealing bidirectional links between psychological stress, anxiety, depression, and disease exacerbation. Itch-related disturbances play a central role, influencing the mental well-being of patients. The subjective nature of stress

transactions emphasizes the need for holistic approaches targeting both physical and psychological aspects for optimal outcomes. Personality traits in CSU patients, including novelty-seeking and fear of uncertainty, provide insights into the psychosocial dimensions of the disease. The study also highlights significant associations between personality traits and the exacerbation of Urticaria symptoms, emphasizing the importance of psychosomatic approaches in clinical practice. Clinicians are encouraged to adopt holistic approaches, considering the intricate interplay of immunological, psychological, and personality factors. Further research avenues include standardizing diagnostic methods for CSU endotypes, exploring economic impacts, and developing interventions for stress reduction. The findings aim to deepen understanding and enhance treatment outcomes for individuals affected by CSU.

The insights provided pave the way for further research and the development of more targeted therapeutic interventions to improve the quality of life for individuals affected by chronic urticaria. Personality traits are examined, indicating that patients with CSU tend to seek novelty and avoid harm, with gender differences observed. The duration of the disease is suggested to influence certain aspects of personality traits. The findings stress the need for personalized therapeutic strategies considering both physical and psychological aspects. Evaluating the economic impact of CSU, including diagnosis, treatment, and long-term management costs, is necessary. Assessing the quality of life under different therapeutic interventions will identify areas for improvement in overall patient well-being.

Summary

Future research endeavors should concentrate on refining diagnostics, deepening the understanding of underlying mechanisms, and exploring personalized therapeutic strategies. Investigating the economic impact and patient quality of life will contribute to a more holistic approach to managing this challenging disease. There are several key areas for future research in Chronic Spontaneous Urticaria (CSU). It calls for advancements in diagnostic tools, emphasizing the need for more accurate and standardized methods to identify CSU endotypes. The exploration of pseudoallergic reactions, particularly in relation to food intolerance, is deemed crucial, along with an in-depth analysis of the long-term effects of elimination diets. Comprehensive studies on infections in CSU patients are highlighted, urging researchers to consider factors like age and geography. Specific diagnostic measures for infections associated with CSU need exploration for effective detection and treatment. Further investigation into the role of autoantibodies in auto-reactive CSU and improved methods for diagnosing delayed pressure urticaria are warranted. It is worth to explore the research on personalized therapeutic approaches, tailored to individual biomarkers, psychological stressors, and personality traits. It stresses the importance of evaluating the economic impact of CSU, covering diagnosis, treatment, and long-term management costs, and emphasizes the assessment of quality of life under different therapeutic interventions. These research directions aim to deepen the understanding of CSU's multi-faceted nature and contribute to the development of more targeted therapeutic interventions, ultimately enhancing the quality of life for individuals affected by chronic urticaria.

References

1. Kay AB, Clark P, Maurer M, Ying S (2015) Elevations in T-helper-2-initiating cytokines (interleukin-33, interleukin-25 and thymic stromal lymphopoietin) in lesional skin from chronic spontaneous ('idiopathic') urticaria. Br J Dermatol 172(5): 1294-302.

2. Tan RJ, Sun HQ, Zhang W, Yuan HM, Li B, et al. (2016) Mixed protein component from helicobacter pylori activates mast cells effectively in chronic spontaneous urticaria. Helicobacter 21(6): 565-574.

3. Desai A, Jung MY, Olivera A, Gilfillan AM, Prussin C, et al. (2016) L-6 promotes an increase in human mast cell numbers and reactivity through suppression of suppressor of cytokine signaling 3. J Allerg 137(6): 1863-1867.

4. Staubach P, Dechne M, Metz M, Mager M, Siebenhaar F (2011) High Prevalence of Mental Disorders and Emotional Distress in Patients with Chronic Spontaneous Urticaria. Acta Derm Venereol 91(5): 557-561.

5. Maurer M, Weller K, Bindslev-Jensen C, Giménez-Arnau A, Bousquet PJ, et al. (2011) Unmet clinical needs in chronic spontaneous urticaria. Allergy 66(3): 317-330.

6. Weller K, Maurer M, Grattan (2015) SSURE-CSU: a real-world study of burden of disease in patients with symptomatic chronic spontaneous urticarial. Clin Transl Allergy 5: 29.

7. Kaplan A, Lebwohl M, Giménez-Arnau AM, Hide M, Armstrong AW, et al. (2023) Chronic spontaneous urticaria: Focus on pathophysiology to unlock treatment. Allergy 78(2): 389-401.

8. Johal KJ, Saini SS (2020) Current and emerging treatments for chronic spontaneous. Ann Allergy Asthma Immunol 125(4): 380-387.

9. Rorsman (1962) Basophilic leucopenia in different forms of urticaria. Allergy 17(2): 168-184.

10. Caffarelli C, Cuomo B, Cardinale F, Barberi S, Dascola CP, et al. (2013) Aetiological factors associated with chronic urticaria in children: a systematic review. Acta Derm Venereol 93(3): 268-272.

11. Kumaran MS, Mangal S, Narang T, Parsad D (2017) Autologous serum and plasma skin tests in chronic spontaneous urticaria: a reappraisal. Indian Dermatology 8(2): 94-99.

12. Confino-Cohen R, Chodick G, Shalev V, Leshno M, Kimhi O, et al. (2012) Chronic urticaria and autoimmunity: associations found in a large population study. J Allergy Clin Immunol 129(5): 1307-1313.

13. Bansal CJ, Bansal AS (2019) Stress, pseudoallergens, autoimmunity, infection and inflammation in chronic spontaneous urticaria. Allergy Asthma Clin Immunol 15: 56.

14. Sánchez J, Sánchez A, Cardona R (2019) Causal Relationship Between Anti-TPO IgE and Chronic Urticaria by In Vitro and In Vivo Tests. Allergy Asthma Immunol Res 11(1): 29-42.

15. Jung Kim H, Kim YJ, Lee HJ, Hong JY, Park AY, et al. (2019) Systematic review and meta-analysis: Effect of Helicobacter pylori eradication on chronic spontaneous urticaria. Helicobacter 24(6): e12661.

16. Rodriguez-Cerdeira C, Telmo Pera-Grasa J, Molares A, Isa-Isa R, Arenas-Guzman R (2011) Psychodermatology: past, present and future. The Open Dermatology Journal 5(1): 21-27.

17. Ben-Shoshan M, Clarke A, Raz A (2012) Psychosocial factors and the pathogenesis of chronic hives: a survey. Allergy Therapy BMC Psychol 11: 239.

18. Yang HY, Sun CC, Wu YC (2005) Stress, insomnia, and chronic idiopathic urticariaa case control study. Formos Med Assoc 104(4): 254-263.

19. Garg A, Chren MM, Sands LP, Matsui MS, Marenus KD (2001) Psychological stress perturbs epidermal permeability barrier homeostasis: implications for the pathogenesis of stress-associated skin disorders. Arch Dermatol 137(1): 53-59.

20. Tzur Bitan D, Berzin, D, Cohen (2021) The association of chronic spontaneous urticaria (CSU) with anxiety and depression: a nationwide cohort study. Arch Dermatol Res 313(1): 33-39.

21. Agorastos A, Pervanidou P, Chrousos GP, Baker DG (2019) Developmental trajectories of early life stress and trauma: a narrative review on neurobiological aspects beyond stress system dysregulation. Front Psychiatry 10: 118.

22. Cansel N, Turkmen D, Altunisik N (2010) The role of childhood trauma in patients with chronic urticaria. North Clin Istanb 10(1): 79-86.

23. Metin N, Turan Ç, Utlu Z (2020) Changes in dermatological complaints among healthcare professionals during the COVID 19 outbreak in Turkey. Acta Dermatovenerol Alp Pannonica Adriat 29(3): 115-125.

24. Huang H, Xiao Y, Jing D, Jie L, Zhang J (2021) Association of Chronic Spontaneous Urticaria With Anxiety and Depression in Adolescents: A Mediation Analysis. Frontires in Psychiatry 12: 655802.

25. Ben-Shoshan M, Blinderman I, Raz A (2013) Psychosocial factors and chronic spontaneous urticaria: A systematic review. Allergy 68(2): 131-141.

26. Malhotra SK, Mehta V (2008) Role of stressful life events in induction or exacerbation of psoriasis and chronic urticaria. Indian J Dermatol Venereol Leprol 74(6): 594-599.

27. Dalgard FJ, GielerU, Aragones LT, Lars L, Francoise P, et al. (2015) The psychological burden of skin diseases: A cross-sectional multicenter study among dermatological out-patients in 13 European countries. Dermatol 135(4): 984-991.

28. Donnelly J, Ridge K, O'Donovan R (2023) Psychosocial factors and chronic spontaneous urticaria: a systematic review. BMC Psychol 11: 239.

29. Tawil S, Irani C, Kfoury R, Abramian S, Salameh P, et al. (2023) Association of Chronic Urticaria with Psychological Distress: A Multicentre Cross-sectional Study. Acta Derm Venereol 14: 103.

30. Dias GA, Pires GV, Valle SO, Dortas SD Júnior, Levy S, et al. (2016) Impact of chronic urticaria on the quality of life of patients followed up at a university hospital. An Bras Dermatol 91(6): 754-759.

31. Ozkan M, Oflaz SB, Kocaman N (2007) Psychiatric morbidity and quality of life in patients with chronic idiopathic urticaria. Ann Allergy Asthma Immunol 99(1): 29-33.

32. Maniaci G, Epifanio M, Marino S, Amoroso S (2006) The presence of alexithymia investigated by the TAS-20 in chronic urticaria patients a preliminary report. Eur Ann Allergy Clin Immunol 38(1): 15-19.

33. Khoshkhui M, Kamrani M, Emadzadeh M, Jafari Z (2022)

Temperament and Personality Traits in Patients with Chronic Spontaneous Urticaria: A Cross-Sectional Study. Psychiatry Behav Sci 16(1).

34. Alan S, Canan F, Karakaş A, Geçici N (2015) Temperament and character profiles of patients with chronic idiopathic urticaria. Advances in Dermatology and Allergolog 32(3): 167-172.

35. Sánchez-Díaz M, Salazar-Nievas MC, Molina-Leyva A, Arias-Santiago S (2022) Type D Personality Is Associated with Poorer Quality of Life in Patients with Chronic Spontaneous Urticaria: A Cross-sectional Study. Acta Dermato-Venereologica 102: adv00734.