










NARRATIVE REVIEW OPEN ACCESS

Sleep Disturbance and Chronic Urticaria: A Narrative Review of Its Relationship, Treatment and Evolving Literature

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ABSTRACT

Background and Aims: Chronic Spontaneous Urticaria is characterized by the sudden onset of itchy wheals and angioedema and is primarily driven by mast cells. It can have a significant impact on the Quality of Life (QoL) of an individual. While the role of mast cells in urticaria is extensively described, the link between sleep disorders and inflammatory skin conditions such as urticaria is still being explored. The review aims to provide an overview of the current knowledge about chronic urticaria, elaborating on the impact of poor sleep quality on QoL of patients with urticaria, with a focus on their emotional well-being.

Methods: The review explores potential mechanisms linking chronic urticaria and sleep disturbances, such as persistent itching and discomfort, the release of inflammatory mediators, systemic inflammation, psychological factors, and effects of medication.

Results: The review finds that sleep disturbances have a significant impact on chronic urticaria. It identifies several potential mechanisms linking the two conditions, including persistent symptoms, inflammatory processes, psychological factors, and medication effects. Treatment approaches include a combination of pharmacological and nonpharmacological interventions.

Conclusion: The article emphasizes the significance of recognizing the impact of sleep disturbances on chronic urticaria. It lays the groundwork for future research to expand our understanding of this association, ultimately leading to improved management strategies and improved QoL for affected individuals.

1 | Introduction

Hives, or urticaria, are clinically described as the sudden emergence of itchy wheals and angioedema [1, 2]. Although there is a known association between irritating skin conditions and poor sleep in the general population, limited research has been conducted to investigate the relationship between oxidative stress, insomnia, and inflammatory skin conditions. The

aim of the recent enquiry was to investigate this particular connection.

Recurrent wheals and/or angioedema are hallmarks of chronic spontaneous urticaria (CSU), a debilitating condition primarily driven by mast cells. CSU is particularly relevant to sleep disorders due to the intense pruritus and discomfort it causes, which can significantly disrupt sleep patterns and contribute to

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insomnia [3, 4]. Type I autoimmune chronic spontaneous urticaria (CSU) is characterized by the presence of IgE antibodies against autoantigens like thyroid peroxidase and IL-24, whereas type IIb autoimmune CSU is driven by autoantibodies, including IgE and FcRI, that trigger mast cell activation. When strict criteria, such as triple positivity of the autologous serum skin test, immunoassays for IgG autoantibodies, and basophil activation tests, are applied, less than 10% of CSU patients exhibit type IIb autoimmune CSU. These two types of CSU represent distinct subpopulations among patients. Low levels of total IgE, elevated levels of IgG-anti-thyroid peroxidase, basopenia, eosinopenia, poor responsiveness to antihistamines, and concurrent autoimmune illnesses are all features of type IIb autoimmune CSU.

However, there is limited evidence in the scientific literature regarding the impact of poor sleep quality on the QoL of urticaria patients [5]. Studies have shown a correlation between poor sleep and reduced QoL but have not thoroughly examined the effects on emotional well-being or other aspects of QoL. Given the increasing evidence suggesting that poor sleep quality may contribute to the emergence of serious neuro-psychiatric [6, 7] and cardiovascular issues [8], more in-depth study on these topics is highly desirable.

2 | Methodology

The search strategy encompassed PubMed, EMBASE, Web of Science, and Cochrane Library databases, covering English-language publications from January 2000 to December 2023. Keywords included combinations of terms such as “chronic spontaneous urticaria,” “sleep disorders,” “quality of life,” “mast cells,” “pruritus,” “inflammation,” “psychological factors,” and “treatment.” The inclusion criteria comprised original research articles, systematic reviews, meta-analyses, clinical trials, and observational studies, while case reports, conference abstracts, and non-English publications were excluded. Data on study characteristics, patient demographics, CSU features, sleep quality assessments, quality of life measures, inflammatory markers, and treatment outcomes were assessed.

Due to the heterogeneity of study designs and outcomes, a narrative synthesis approach was employed to summarize and interpret the findings, organizing key themes to address the review's objectives: the impact of CSU on sleep quality, the relationship between sleep disturbances and quality of life in CSU patients, potential mechanisms linking CSU and sleep disorders, and treatment approaches addressing both issues. Limitations of this review, including potential publication bias, language restrictions, and inherent limitations of included studies, have been considered in the interpretation and discussion of results. This methodology ensures a rigorous and comprehensive analysis of the current literature, thereby providing a solid foundation for future research and improved management strategies.

3 | Sleep and Chronic Urticaria: An Overview of What Is Known

CSU has been associated with a potential decline in energy levels over time [9, 10]. Patients typically mention nocturnal

awakenings and trouble falling asleep as examples of sleep disturbances [10]. The intense pruritus associated with CSU is a primary driver of sleep disruption, particularly at night, though other physiological mechanisms, such as disruption of the skin's thermoregulatory function, may also contribute [4, 11, 12]. Despite the wide range of sleep-related respiratory problems, few studies have looked into the relationship between obstructive sleep apnea (OSA) and CSU [13, 14]. For instance, it was discovered that 40% of CSU patients had their OSA evaluated through polysomnography, a rate which appears higher than reported for the general population [15].

When obtaining a medical history from a patient in dermatology, inquiries concerning sleeplessness are common, despite this topic having received limited research focus. Clinically significant interactions between sleep disorders and skin conditions exist. Atopic dermatitis, eczema and psoriasis have been shown to be exacerbated by sleep problems and vice versa. The quality of sleep can have a beneficial or negative impact on how skin problems progress. However, further research is needed to fully understand the effects of the connection between dermatological conditions and sleep disorders, particularly with relation to chronicity and specific mechanisms involved. The Dermatology Life Quality Index (DLQI) and the Insomnia Severity Index (ISI) are scales used to assess the severity of insomnia in patients with chronic inflammatory dermatological disorders with pruritus.

Sleep disturbances have also been associated with an increased risk of cardiometabolic disease such as stroke, coronary artery disease, and myocardial infarction, as well as conditions like obesity, impotence and depression [16, 17]. Insomnia, which is particularly prevalent in the elderly, has a major negative influence on QoL (QoL) as well as daytime functioning. The sleep quality declines with chronic pain conditions and sleep impairments have been described as valuable predictors for new incidences and worsening of symptoms linked to chronic pain conditions.

4 | Relationship Between Sleep and Chronic Urticaria

Sleep disturbances are not unique to CSU but are also prevalent in other dermatological conditions. For instance, atopic dermatitis and psoriasis are commonly associated with nocturnal pruritus and sleep disruption [18, 19]. A study by Podder et al. highlighted the significant burden of sleep disturbances in patients with dermatological disorders, emphasizing the role of pruritus and inflammation in impairing sleep quality [20]. Other conditions, such as lichen planus and chronic prurigo, have also been linked to sleep disorders [21]. Understanding the shared mechanisms, such as the involvement of cytokines and neural pathways, can provide a broader perspective on the intersection of dermatology and sleep medicine [22].

There are several well-established connections between dermatological conditions and sleep disturbances. Firstly, the skin plays a crucial role in sleep physiology by regulating body temperature and facilitating sleep onset [23]. Secondly, circadian rhythms, or the body's internal biological clocks, can influence the severity of

skin symptoms. For example, the natural decline in cortisol levels during the evening may intensify pruritus in individuals with inflammatory skin disorders. Additionally, symptoms such as itching, excessive sweating, and skin dryness can significantly disrupt sleep quality for both patients and their families. The dermatological conditions may become worse by the presence of sleep-related issues such as insomnia, sleep apnea, sleep deprivation, and disrupted circadian rhythms. In CSU, heightened sympathetic neural activity, particularly the release of neurotrophin growth factor under stressful situations, can prime mast cells to activate in the skin, further exacerbating symptoms and sleep disturbances [12, 24].

Thirdly, some psychiatric illnesses, such as major depressive disorder and attention deficit hyperactivity disorder (ADHD), which are frequently linked to sleep complaints, often co-occur with dermatologic conditions. Sleep difficulties in atopic dermatitis (AD) may contribute to the development of ADHD-like symptoms, with scratching during various sleep stages potentially linked to increased sympathetic nervous system activity. Scratching throughout various stages of sleep may be related to the sympathetic nervous system's overall activity [11, 25]. Insomnia can be a predisposing factor, particularly in patients who have experienced significant life stressors within 6 months before symptom onset. Sleep deprivation is considered a stressor in itself, and stress has the potential to trigger sleep disturbances (SDs), creating a vicious cycle that exacerbates CSU symptoms [14, 26].

It is hypothesized that CSU brought on by stress affects how the body reacts to inflammation. The hypothalamic-pituitary-adrenocortical (HPA) axis is activated by stress. The hypothalamus releases corticotropin-releasing hormone (CRH) in reaction to acute stress, which causes the pituitary gland to release adrenocorticotropin which in turn releases cortisol which balances off the inflammatory cytokines. Prolonged stress in CSU may result in HPA axis fatigue, subsequently reducing cortisol production. Patients with CSU have been found to have higher levels of several indicators of systemic inflammation, including C-reactive protein, interleukins (IL)-17, IL-18, IL-23, IL-6, and tumor necrosis factor-alpha, and these levels are positively correlated with the severity of the illness [14, 27]. Table 1 shows chief insights of a few articles correlating sleep disturbances to CSU.

Stress can worsen CSU in addition to its psychological effects by interfering with the regularity of normal cortisol release, especially when sleep disorders are present. Pro-inflammatory cytokine levels are typically higher and cortisol levels are typically lower in patients with sleep problems [36, 37]. Additionally, sleep deprivation can affect regulatory T cells' (Treg) circadian cycle, which is crucial for maintaining tolerance in the body and preventing autoimmune disorders [38]. The presence of circulating Treg cells may noticeably decline in people with chronic urticaria [14].

5 | Pathophysiology Behind the Association

Sleep disturbances in individuals with chronic urticaria arise from a complex interplay of underlying pathophysiological mechanisms (Figure 1). While the precise triggers may vary

from person to person, several factors have been consistently linked to sleep disruptions in chronic urticaria. These include the persistent itching and discomfort caused by the presence of hives, the release of inflammatory products such as histamine, the presence of systemic inflammation within the body, psychological factors such as anxiety or depression associated with the condition, and the potential effects of medications used for managing chronic urticaria symptoms [39–42]. These factors are particularly relevant as they directly contribute to sleep fragmentation, reduced sleep efficiency, and overall impaired sleep quality. Understanding these underlying mechanisms can aid healthcare professionals in developing comprehensive treatment strategies to address sleep disturbances in individuals living with chronic urticaria.

The pathophysiology underlying chronic urticaria involves the release of various mediators, with histamine playing a central role. Mast cells in the cutaneous tissues release histamine in response to triggers such as endogenous peptides, endorphins, enkephalins, and immunoglobulin E (IgE). Additionally, components of complement activation also contribute to this release [43–45]. Particularly during night-time, itching sensations can worsen due to elevated skin temperature and reduced external relief by reduced scratching, making it challenging to initiate sleep or maintain uninterrupted sleep throughout the night [44]. In addition to this, chronic urticaria has been observed to be linked with a chronic low-grade inflammatory state in certain individuals. This inflammatory state involves the release of pro-inflammatory cytokines and other mediators, including IL-17, IL-18, IL-23, and TNF- α . These substances contribute to systemic inflammation, which in turn can interfere with the natural rhythm of sleep. The resulting disturbances in sleep patterns may manifest as insomnia, frequent awakenings, or overall poor sleep quality [46]. Table 2 highlights the correlation between other dermatological disorders and sleep hinting at similar pathophysiological mechanisms at play.

Some studies have also suggested that the psychological effects of chronic urticaria can lead to depression and anxiety, which can affect the QoL, especially the sleep [41, 51]. The psychological burden of chronic urticaria can result in heightened levels of arousal, making it difficult to achieve the state of relaxation necessary for quality sleep. Sleep disruptions may manifest as increased awakenings during the night, difficulty returning to sleep after waking up, or overall reduced sleep duration [5]. The constant presence of itching, discomfort, and the unpredictable nature of urticarial outbreaks can lead to heightened levels of stress, anxiety, and frustration in individuals with the condition [52]. Additionally, the distress caused by the physical appearance of the hives can lead to body image concerns, self-consciousness, and decreased self-esteem, all of which can contribute to emotional distress and impaired sleep [53]. A common ectodermal origin of the skin and nervous system may also play a role in the embryological link of the association between sleep and urticaria and can be a subject of further exploration in future research.

The medications used to treat Chronic urticaria can also have a significant effect on the quality of sleep. For example, the use of antihistamines (specially first generation) may cause daytime drowsiness and sedation, eventually leading to poor nighttime

TABLE 1 | Chief insights of articles correlating sleep disturbances to CSU.

Author	Date	Name	Chief insights	Citation
Alicja Kasperska-Zajac et al.	01 Feb 2024	The UCARE Study on the Prevalence of Sleep Disorders and Nighttime Bruxism in People with Chronic Urticaria	Sleep disruptions are common among chronic urticaria patients, affecting their quality of life and potentially related with disease activity and control levels.	[28]
Azza M Abdel-Meguid et al.	01 Apr 2024	Does chronic urticaria affect quality of sleep and quality of life?	Chronic urticaria is related to considerably longer sleep latency, shorter total sleep duration, reduced sleep efficiency, and higher Pittsburgh Sleep Quality Index scores, all of which suggest poor sleep quality.	[29]
Manuel Sánchez-Díaz et al.	01 Feb 2023	Sleep Quality as a Predictor of Quality-of-Life and Emotional Status Impairment in Patients with Chronic Spontaneous Urticaria: A Cross-Sectional Study	Sleep disturbance in chronic urticaria patients is linked to poorer illness control, increased itching and swelling, and higher rates of anxiety and sadness.	[30]
Caroline Mann et al.	12 Mar 2020	Sleep Disturbance in Patients with Urticaria and Atopic Dermatitis: An Underestimated Burden.	Chronic urticaria is associated with increased sleeplessness, especially during disease flares, indicating that sleep problems may be caused by factors other than pruritus.	[4]
Ana Giménez-Arnet et al.	18 Aug 2016	Improvement of sleep in patients with chronic idiopathic/spontaneous urticaria treated with omalizumab: results of three randomized, double-blind, placebo-controlled studies	Sleep difficulties in chronic urticaria have a substantial impact on quality of life, with links found between disease activity and sleep concerns, indicating that itch and hives worsen sleep problems.	[12]
Ali Can et al	01 May 2023	Common but neglected problem in chronic spontaneous urticaria: Sleep disturbance.	Individuals with chronic spontaneous urticaria demonstrate diminished sleep quality, suboptimal sleep hygiene, and heightened daytime sleepiness, which are associated with disease activity and inflammatory markers.	[31]
Tuba Tülay Koca et al.	30 Jun 2019	The relation of chronic idiopathic urticaria with Fibromyalgia, sleep disturbance and anxiety	Sleep disturbance correlates positively with the severity of chronic idiopathic urticaria, indicating that greater urticarial activity is linked to heightened sleep issues, fatigue, and anxiety in affected individuals.	[32]
Hale Ates et al.	14 Feb 2022	Relationships between quality of life, sleep problems, and sleep quality in patients with chronic idiopathic urticaria	The study evaluates sleep quality in chronic urticaria patients, revealing significant relationships between sleep problems and quality of life, indicating that sleep disturbances are prevalent in this population.	[33]
Kiran Godse et al.	01 Apr 2022	Diagnosis and Management of Urticaria in Indian Settings: Skin Allergy Research Society's Guideline-2022	Chronic urticaria adversely affects sleep quality, leading to disturbances that diminish patients' overall performance and quality of life.	[34]
Jonathan A. Bernstein et al.	01 May 2023	Why a Complete Response Is the Treatment Aim in Chronic Spontaneous Urticaria	Chronic urticaria is significantly associated with sleep disturbances, as increased disease activity adversely affects sleep quality. Effective treatment results in enhanced sleep outcomes.	[35]

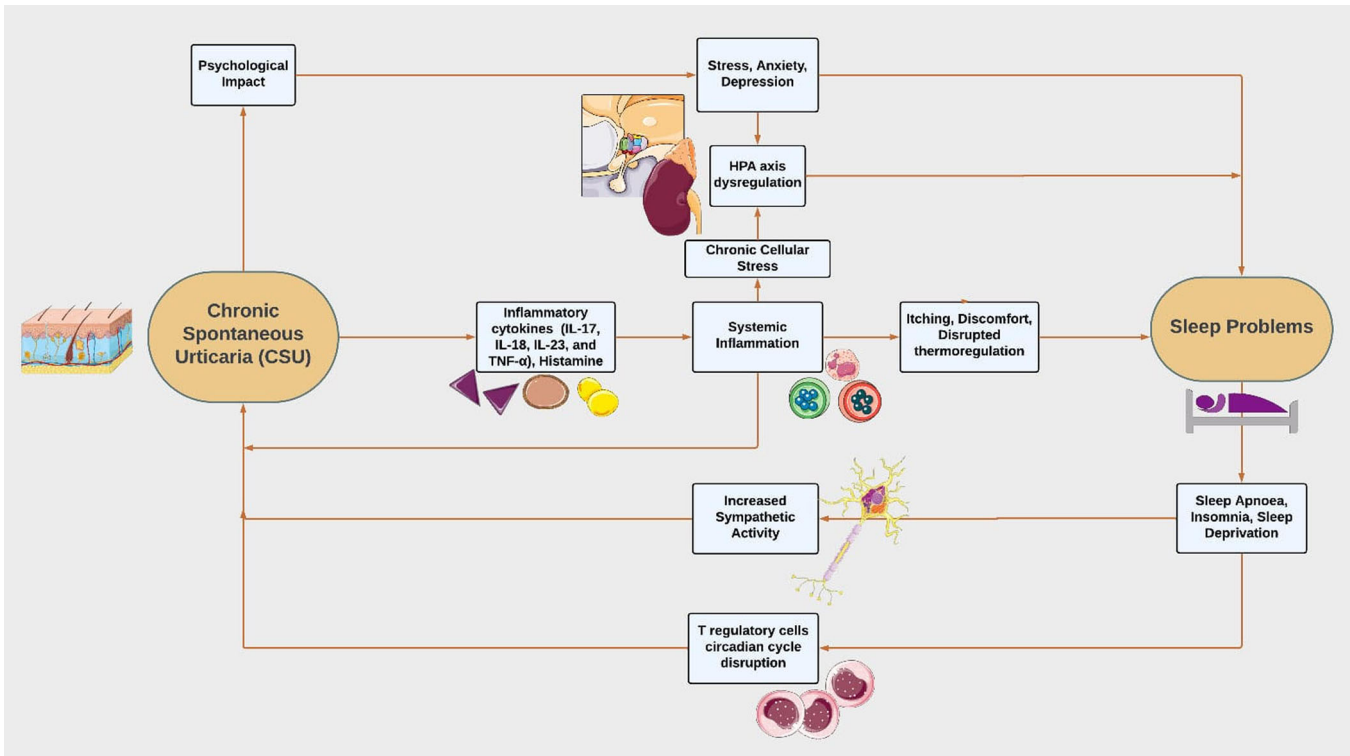


FIGURE 1 | Bidirectional relationship between sleep and chronic spontaneous urticaria.

sleep [54]. Corticosteroids, such as prednisone or prednisolone, can cause increased alertness, restlessness, and difficulty falling asleep, particularly when taken at higher doses or for an extended period [55]. Glucocorticoids can alter sleep architecture by reducing REM sleep, and lead to nocturia ultimately leading to sleep interruptions thus interfering with the natural circadian rhythm by suppressing the production of cortisol and sleep-regulating hormones like melatonin [56–58].

6 | Sleep Assessment in Chronic Urticaria

Due to its disruptive symptoms, chronic urticaria can greatly affect sleep quality. Healthcare providers frequently use a variety of sleep assessment instruments and methodologies to gauge the severity of sleep disturbances and their effects on general wellbeing to provide complete therapy for people with chronic urticaria.

6.1 | Objective Measures

Objective measures of sleep quality and quantity could play an important role in urticaria-related sleep disturbances. Tests such as Polysomnography assess sleep disorders by monitoring various physiological parameters during sleep and can show fragmented sleep or reduced sleep efficiency. They measure the individual's duration of sleep at different stages and thus help associate sleep disorders with urticaria [15]. The primary limitation of polysomnography is that it requires the examination to be carried out at a specialized sleep facility. Actigraphy is simply a digital wrist watch-like device that records the time of falling asleep, awakening time, duration taken to fall asleep,

and total sleep duration, as well as any naps taken during the day [59]. Actigraphy is able to quantify the nocturnal wrist movements associated with itching, which can be indicative of sleep disruptions caused by urticaria [60].

6.2 | Subjective Measures

Subjective assessment can also provide valuable information and should not be disregarded in the evaluation of sleep disturbances in chronic urticaria. Scales such as the Stanford Sleepiness Scale might not be useful for assessing sleep disturbances in urticaria as the scale is not sensitive to partial sleep deprivation but only for complete sleep-deprived patients [61]. Further, the Glasgow sleep effort scale is used to assess the difficulty of falling asleep [62]. It can be used to assess the difficulty of falling asleep in urticaria patients. The Epworth Sleepiness Scale measures daytime sleepiness due to sleep disorders and can be used in conjunction with objective measures to provide a comprehensive evaluation of sleep quality in chronic urticaria patients [63]. The Pittsburgh Sleep Quality Index (PSQI) has been employed to monitor sleep disturbances over a period of 1 month, providing insights into the relationship between urticaria and sleep problems [64]. The Athens Insomnia Scale is a tool that can be used to evaluate the severity of insomnia symptoms [65]. The scale ranges from the ability to fall asleep to sleepiness during the day. The Regensburg insomnia scale (RIS) was developed to assess the impact on daily functioning and allows for the differentiation between three subtypes of insomnia: sleep onset insomnia (difficulty falling asleep), sleep maintenance insomnia (difficulty staying asleep), and early morning awakening insomnia (waking up too early and unable to fall back asleep) [66]. RIS is commonly used

TABLE 2 | Correlation of other dermatological disorders with sleep.

Author	Date	Name	Chief insights	Citation
Caroline Mann et al.	26 May 2023	Sleep disorders in dermatology – a comprehensive review	Sleep issues exacerbate atopic dermatitis, eczema, and psoriasis, with bidirectional effects implying that sleep disruptions can worsen these dermatological disorders and vice versa.	[47]
Charbel Skayem et al.	05 Feb 2024	Global study reveals almost half of patients with skin disease suffer from sleep disturbances and identifies predictive factors.	Sleep disturbances are common in patients with cutaneous disorders and have a substantial impact on fatigue, attention, and professional life, emphasizing the importance of assessing and managing sleep concerns in these individuals.	[48]
Harneet K Walia et al.	30 Apr 2016	Overview of Common Sleep Disorders and Intersection with Dermatologic Conditions	Sleep disorders are associated with many dermatologic illnesses, impacting skin inflammation, aging, and possibly raising the risk of skin cancer through underlying mechanisms related to sleep dysfunction.	[49]
Minjie Zhang et al.	02 May 2023	The association between pruritic dermatoses and inflammatory factors on sleep disorders: a cross-sectional study of the National Health and Nutrition Examination Survey (NHANES).	Pruritic dermatoses are highly related with sleep disturbances, which are impacted by inflammatory markers such as lymphocyte count and prognostic nutritional index, emphasizing the importance of prompt therapeutic care.	[50]

in clinical practice and research to assess insomnia symptoms, monitor treatment progress, and evaluate the effectiveness of interventions for insomnia. These scales and measurements can be used to create effective treatment plans for urticaria patients and provide vital information on the relationship between sleep disorders and chronic urticaria. Table 3 highlights various assessment tools used for measuring sleep disturbances.

6.3 | Challenges in Sleep Assessment of the Patient Cohort

There is a need for the above assessments to be used extensively in clinical practice for a thorough evaluation of sleep in CSU patients. Subjective tools, such as the Pittsburgh Sleep Quality Index and the Regensburg Insomnia Scale, can provide valuable insights into insomnia when used together. On the other hand, objective assessments such as actigraphy are very practical and can be performed in situations when polysomnography is not possible. In contrast to polysomnography, however, actigraphy is unable to provide particular information regarding different stages of sleep (such as REM sleep or deep sleep) or the architecture of sleep, which can be very helpful in analyzing sleep disturbances with chronic urticaria [67]. However, to conduct a thorough analysis of a person's sleep pattern, it may be necessary to combine actigraphy with other techniques, such as sleep diaries or polysomnography, to acquire a more complete picture of the person's sleep profile.

7 | Treatment Approaches for Sleep Disturbances in Chronic Urticaria

The treatment approaches for sleep disturbances in chronic urticaria involve a comprehensive strategy targeting the underlying causes and providing relief. This includes managing urticaria symptoms with antihistamines, addressing inflammation through appropriate medications, seeking psychological support to manage emotional factors, practicing good sleep hygiene, evaluating medication regimens, and considering a multidisciplinary approach involving various healthcare professionals [68]. By implementing these strategies, individuals with chronic urticaria can work towards improving sleep quality and overall well-being.

7.1 | Pharmacological Interventions

Medical management of urticarial symptoms mainly involves proper use of sedating and non-sedating antihistamines to synchronize their use with the circadian rhythm of the body [69]. Sedating antihistamines, such as diphenhydramine, Hydroxyzine and Belastine have a stronger sedative effect and are more likely to cause drowsiness. They can be useful for individuals experiencing severe itching or needing immediate relief, especially at nighttime when the sedating effect can aid in promoting sleep. However, their use during the day may impair alertness and productivity [54]. On the other hand, nonsedating antihistamines, such as loratadine and cetirizine, have a reduced sedative effect. They are generally preferred for

TABLE 3 | Assessment tools for sleep disturbances and their clinical utility.

Assessment tool	Self-administered	Clinically administered	Clinical utility
Stanford Sleepiness Scale	No	Yes	Assessing subjective sleepiness levels for clinical evaluation and research purposes.
Glasgow Sleep Effort Scale	No	Yes	Evaluating the perception of effort in sleep, useful in clinical settings for sleep disorder assessment
Epworth Sleepiness Scale	Yes	Yes	Assessing daytime sleepiness and potential sleep disorders.
Pittsburgh Sleep Quality Index	Yes	Yes	Evaluating sleep quality and disturbances in clinical and research settings.
Athens Insomnia Scale	Yes	Yes	Assessing the severity of insomnia symptoms and its impact on daily functioning.
Regensburg Insomnia Scale	Yes	Yes	Measuring the various aspects of insomnia and also aiding in diagnosis and treatment planning.

daytime use as they are less likely to cause drowsiness and allow individuals to maintain normal daily activities without significant impairment [70].

Corticosteroids, such as prednisolone, are considered an effective treatment option for managing urticarial symptoms, particularly in severe or refractory cases of chronic urticaria [71]. These medications function by impeding the release of inflammatory substances, including histamine, from immune cells. By suppressing the activation and function of mast cells and basophils, which play a role in the allergic response and contribute to hives and itching, corticosteroids can alleviate symptoms effectively [72]. Moreover, corticosteroids have the ability to diminish the production of pro-inflammatory cytokines like interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor- α (TNF- α), thus mitigating the inflammatory response associated with urticarial symptoms [73]. However, the potential side effects and the risk of rebound symptoms upon discontinuation make corticosteroids less suitable for long-term treatment of chronic urticaria.

Montelukast, sulfasalazine, and methotrexate are some of the other medications that have shown potential in reducing symptoms of chronic urticaria, which can consequently contribute to improved sleep for patients [69]. These medications have distinct individual mechanisms to modulate, suppress and block specific components of the immune response system. These medications may be considered when standard treatments are ineffective or for specific cases [74, 75]. However, their use should be carefully monitored, and the decision to prescribe them should be based on individual patient factors and potential risks and benefits. Regular follow-up with a healthcare professional is crucial to evaluate their effectiveness and ensure patient safety.

Omalizumab, a humanized anti-immunoglobulin E (IgE) antibody, has emerged as an effective treatment option for chronic idiopathic urticaria in adults who continue to experience symptoms despite H1-antihistamine treatment [76]. Omalizumab works by binding to IgE antibodies, thereby preventing their interaction with mast cells and basophils. This inhibits the release of inflammatory mediators, such as histamine, and

reduces the hypersensitivity response associated with chronic urticaria. By targeting the underlying immune system dysregulation, omalizumab provides significant relief from symptoms, improves QoL, and therefore, may contribute to better sleep outcomes for patients [77]. A study investigating the impact of omalizumab on sleep-related outcomes in patients with chronic idiopathic urticaria demonstrated a notable decrease in sleep problems with omalizumab treatment compared to placebo. Patients receiving a dosage of 300 mg of omalizumab exhibited the most substantial improvement in sleep quality compared to other treatment groups. The study observed the greatest reduction in sleep problems during the initial 4 weeks of therapy. However, sleep quality deteriorated upon discontinuation of treatment. The findings also indicated a strong correlation between sleep scores and changes in itch and hives, suggesting a relationship between improved sleep and alleviation of urticaria symptoms [12]. Table 4 shows the recommended dosages of the medications used with their effect on sleep and urticaria.

7.2 | Nonpharmacological Interventions

Patients with chronic urticaria often experience psychological distress, including anxiety and depression, due to the unpredictable nature of the disease and its impact on daily life. Addressing these psychological factors is essential for managing sleep difficulties in chronic urticaria [41]. Psychological support interventions, such as cognitive-behavioral therapy (CBT) and relaxation techniques, can help individuals develop coping strategies and reduce anxiety related to their symptoms. CBT focuses on identifying and challenging negative thought patterns and behaviors that contribute to stress and sleep disturbances. It can also provide patients with skills to manage anxiety and improve sleep hygiene [84]. Additionally, mindfulness-based interventions, such as meditation, have shown promise in reducing stress levels and improving sleep quality in individuals with chronic conditions [85].

Practicing good sleep hygiene habits can also promote better sleep quality. Establishing a consistent sleep schedule,

TABLE 4 | Recommended dosages of the medications used with their effect on sleep and urticaria.

Medication class	Medication [47, 68]	Recommended dosage	Effect on urticaria and sleep
Second-generation antihistamines	Cetirizine	Adults and children ≥ 6 years: cetirizine 5–10 mg PO once daily; children 6 months–5 years: cetirizine 2.5 mg PO once or twice daily	Second-generation antihistamines efficiently treat urticaria with less sedation, resulting in better sleep quality than first-generation antihistamines, which are linked to poor sleep and next-day impairment [78, 79].
	Loratidine	Adults and children ≥ 6 years: loratadine 10 mg PO once daily; children 2–5 years: loratadine 5 mg PO once daily	
	Fexofenadine	Adults and children ≥ 12 years: fexofenadine 60 mg PO twice daily; children 6–11 years: fexofenadine 30 mg PO twice daily	
	Bilastine	Adults and children ≥ 12 years: 20 mg once daily children 6–11 years: 10 mg once daily	
H2-antihistamine	Famotidine	Adults: 20 mg twice daily	H2-receptor antagonists may relieve urticaria symptoms, but their effects on sleep are not well established in the literature, necessitating additional research into their cognitive influence [80].
	Cimetidine	400 mg twice daily	
Leukotriene-receptor antagonist	Montelukast	Adult: 10 mg once daily	Montelukast significantly reduced sleep interference and improved urticaria symptoms, resulting in more symptom-free days than cetirizine and placebo, demonstrating its efficacy in treating chronic urticaria [74].
First-generation H1 antihistamine	Hydroxyzine	Adults: 10 to 25 mg single dose before bed; children up to 12 years: 0.5 mg/kg; children < 12 years: 10 mg	First-generation antihistamines are helpful for treating urticaria, but their sedative effects and limited receptor selectivity can interfere with sleep quality [81]
	Doxepin	Adult: 10 to 25 mg	
	Cyproheptadine	Children < 6 years: 2 mg before bedtime; 6 years or older: 4 to 8 mg before bedtime	
Steroids	Prednisolone	40 mg daily (in the morning, with food) for two to three days. Tapering down to 10 mg daily or less	Steroids can reduce inflammation in urticaria, perhaps increasing sleep quality by reducing symptoms; however, prolonged treatment may have negative consequences on sleep patterns [82, 83].

including going to bed and waking up at the same time each day, helps regulate the body's internal clock. Creating a sleep-friendly environment by ensuring the bedroom is cool, dark, and quiet can enhance comfort and promote better sleep [86]. Avoiding stimulating activities and substances close to bedtime, such as caffeine, nicotine, and heavy meals, can minimize sleep disruptions. Wearing loose clothes during sleep can avoid delayed pressure urticaria and thus promote non itchy sound sleep. Engaging in regular physical activity during the day can help regulate sleep patterns. By incorporating these additional sleep hygiene practices, individuals with chronic urticaria can optimize their sleep environment, reduce itching sensations, and improve overall sleep quality [87].

7.3 | Treatment Recommendations

The treatment of sleep disturbances in chronic urticaria should follow a patient-centered, stepwise approach that addresses both the dermatological and sleep-related aspects of the condition. First-line therapy should include non-sedating antihistamines during the day and sedating antihistamines at night to manage pruritus and promote sleep. For refractory cases, omalizumab should be considered due to its dual benefit in reducing urticaria symptoms and improving sleep quality. Nonpharmacological interventions, such as cognitive-behavioral therapy (CBT) and sleep hygiene practices, should be integrated into the treatment plan to address psychological distress and optimize sleep

patterns. A multidisciplinary approach involving dermatologists, sleep specialists, and mental health professionals is essential for comprehensive care. Regular follow-up and patient education on the importance of adherence to treatment and lifestyle modifications are critical for long-term success.

8 | Evolving Literature and Future Directions

Recent research examining the relationship between sleep and urticaria has focused on the possibility of a correlation between poor sleep quality and the intensity of urticaria symptoms [4, 5]. According to a number of studies, the incidence of urticaria is much higher in individuals who suffer from insomnia compared to those who do not suffer from insomnia [88]. Both, a disturbed sleep pattern and an increase in the frequency or severity of urticaria breakouts can be attributed, at least in part, to the negative effects of stress [89]. Individuals who suffer from both poor sleep quality and urticaria symptoms should give careful consideration to treatments that aim at improving both the quality of sleep and the management of urticaria. Examples of these are cognitive behavioral methods and specialized drugs that target histamine receptors [90]. It is essential to address both concerns to enhance one's general QoL and lessen the effect that urticaria has on one's ability to carry out daily activities. A discussion with a trained medical practitioner can assist in determining optimal and individualized treatment strategies. Changes in one's lifestyle, such as establishing a regular sleeping pattern or reducing one's stress levels, can reduce the frequency and severity of urticaria flare-ups and improve one's sleep quality [23].

Emerging treatments that are aimed at lowering sleep disturbances in people who suffer from chronic urticaria are currently the focus of research into a number of novel treatments that are being evaluated for their capacity to enhance the QoL of these persons. Antihistamines and omalizumab are successful in bringing urticaria under control. However, there are patients who do not respond to these treatments and may require more modern medications. Because Ligelizumab has a stronger affinity than Omalizumab, it has the potential to replace Omalizumab as the treatment given before immunosuppressants. The CRTH2 Antagonist inhibits the activity of prostaglandin D2 as well as the erythropoietin receptor EPOR, both of which are found on basophils and eosinophils [91]. Further research is needed to determine the optimal dosage and duration of treatment for CRTH2 antagonists. Additionally, Anti-Siglec-8 is another effective drug that suppresses mast cells and reduces the number of eosinophils in the body. It has been demonstrated to be effective in treating omalizumab-resistant patients who suffer from urticaria. Topical Syk Inhibitor, which has been used for the treatment of skin diseases, may also be a potential choice for people who suffer from chronic urticaria. This is due to the fact that it has demonstrated efficacy in early clinical trials of urticaria [91]. Tyrosine kinase inhibitors like Remibrutinib highlighted effectiveness in the treatment of chronic urticaria; however, additional study is required to confirm both their efficacy and safety [92]. However, additional research is required to get a complete understanding of the efficacy, possible benefits and side effects of these drugs. It is essential for patients to maintain open communication with their providers of medical care to arrive at the

treatment strategy that is most suited to their specific requirements. The application of cognitive-behavioral therapy to the study of techniques to reduce sleep disturbances in those who suffer from urticaria is now being researched [93]. The importance of nutrition in the treatment of symptoms investigating how particular foods can either set off or exacerbate symptoms. Finding healthy dietary adjustments that could help relieve discomfort is important [94]. It is essential to conduct a patient-centered history and physical examination to determine the underlying reasons for urticaria and sleep disturbances [95].

Moreover, it is imperative that urticaria and restless leg syndrome (RLS) be subjected to in-depth research, as the two illnesses may have a common etiology [96]. In addition, investigating the use of alternative therapies such as acupuncture, herbal medicine, and ways to reduce stress may also be helpful in the management of urticaria [97]. Urticaria can only be adequately managed and patients' overall health can only be improved by using a holistic strategy that takes into account both medical and lifestyle aspects.

9 | Limitations

Despite an extensive review of the existing literature, the article carries a few limitations. There is a lack of literature on the evidence of a converse relationship between sleep and urticaria. We need further research into whether treating sleep influences urticaria and to what extent. Additionally, further large sample studies need to be conducted and reviewed involving newer drugs thereby providing an efficient treatment by the understanding of this correlation.

10 | Conclusion

In conclusion, this article highlights the significant impact of chronic urticaria on sleep and vice versa. The evidence presented shows that poor sleep quality can aggravate urticaria symptoms and have a detrimental effect on the overall QoL of the patients. By incorporating comprehensive treatment plans that target both the underlying causes of urticaria and the improvement of sleep quality, healthcare professionals can provide patients with holistic care and support. Future research should look into the links between poor sleep quality and the severity of urticaria symptoms, as well as the efficacy of tailored interventions for improving sleep and overall well-being in people who have urticaria.

Author Contributions

Asad Ullah Wasim: investigation, writing – original draft, methodology, visualization, writing – review and editing, supervision. **Sri Anugna Miriyala:** writing – original draft, methodology, writing – review and editing, visualization, supervision. **Raymond Haward:** investigation, writing – original draft, methodology, validation, writing – review and editing, visualization, supervision. **Zeinab Hammoud:** investigation, writing – original draft, supervision, writing – review and editing, visualization. **Pratik Agarwal:** investigation, writing – original draft, visualization, validation, writing – review and editing, supervision, project administration, resources. **Nirja Kaka:** resources, supervision,

project administration, writing – review and editing, visualization, validation, writing – original draft, investigation. **Neil Patel:** investigation, writing – original draft, writing – review and editing, supervision, formal analysis, validation, visualization. **Yashendra Sethi:** investigation, writing – original draft, methodology, supervision, writing – review and editing. **Poonam Gupta:** investigation, writing – original draft, supervision, visualization, writing – review and editing.

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Figure 1 was partly generated using Servier Medical Art, provided by Servier, licensed under a Creative Commons Attribution 3.0 unported license. The flow chart was created using Lucid (lucid.co).

Disclosure

All authors have read and approved the final version of the manuscript and the Corresponding author had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

This study is based on data extracted from publicly accessible research articles in various databases, including PubMed, EMBASE, Web of Science and Cochrane. All data sources are available through these databases, and citations are provided in the manuscript references. No new primary data were created or collected for this study.

Transparency Statement

The lead author Zeinab Hammoud affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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