Chronic spontaneous urticaria – association with selected autoimmune diseases: a systematic review

Bartosz Bartosik, Dagmara Bartosik, Katarzyna Kapeluszna, Zenon Brzoza
Department of Internal Diseases, Allergology, Endocrinology and Gastroenterology, Institute of Medical Sciences, University of Opole

Abstract:
Urticaria is one of the most common diseases in allergological and dermatological practice. Depending on the duration of symptoms, urticaria is classified as acute or chronic. The etiology of urticaria often remains unknown, but in over 30% of cases, an association with autoimmune mechanisms is noted. This paper provides an overview of analyses examining the coexistence of chronic urticaria with selected autoimmune diseases.

Key words: chronic urticaria, autoimmune diseases, autoimmune thyroiditis, celiac syndrome, diabetes, systemic lupus erythematosus, rheumatoid arthritis, Sjoegren's syndrome, myasthenia gravis

Background

Chronic spontaneous urticaria (CSU) is characterized by spontaneous urticarial eruptions occurring at least 3 times a week for over 6 weeks, often accompanied by pruritus and angioedema. CSU affects individuals of all ages, races, and genders, with a higher prevalence in women, particularly in the fourth decade of life, which parallels the epidemiology of various autoimmune diseases such as celiac disease, type 1 diabetes, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and thyroid diseases. Studies indicate that CSU coexists with autoimmune diseases in approximately 30% of cases.

Aim of the study

To systematically review and evaluate studies examining the association between chronic spontaneous urticaria and selected autoimmune diseases.

Material and methods

This systematic review followed guidelines to identify and evaluate studies investigating the association between CSU and selected autoimmune diseases. Databases searched included PubMed, MEDLINE, and Scopus, using keywords such as "chronic urticaria", "autoimmune diseases", "thyroiditis", "celiac disease", "diabetes", "lupus" and "rheumatoid arthritis". Studies were included if they examined the coexistence of CSU with any autoimmune disease, provided statistical data, and were published in peer-reviewed journals in English. The exclusion criteria where studies not providing relevant statistical data, non-peer-reviewed studies or those published in languages other than English, studies that do not specifically address CSU. Study selection and data extraction were managed using Excel. Data extraction were done independently by two reviewers, focusing on the following: study characteristics (authors, year of publication, study design, sample size, and population), autoimmune diseases investigated, statistical data on the prevalence

Alergoprofil 2025, Vol. 21, Nr 4
DOI: 10.24292/01.AP.214200326

Received: 10.11.2025
Accepted: 28.02.2026
Published: 20.03.2026

of CSU in patients with autoimmune diseases, study results and conclusion. A qualitative synthesis were conducted for all included studies. Statistical heterogeneity were assessed using the I^2 statistic, and potential sources of heterogeneity were explored. Finally, 33 articles were chosen to be included as part of our investigation.

Risk of bias assessment

The risk of bias in included studies will be assessed using the Newcastle-Ottawa Scale for cohort studies and the Cochrane Risk of Bias Tool for randomized controlled trials.

Results

The association of CSU with autoimmune diseases has been well-documented across various studies. The findings for each condition are summarized below:

Autoimmune thyroiditis is the most common inflammatory disease of the thyroid gland. It is characterized by the presence of antithyroid antibodies and lymphocytic infiltration of the thyroid gland. Genetic, environmental and infectious factors are considered in the pathogenesis. It affects nearly 5% of the population. The association of chronic urticaria with autoimmune thyroiditis was first described in 1983 by Midelfart et al. and Leznoff et al. [1–3]. They showed a higher prevalence of antithyroid antibodies in patients with chronic urticaria compared to the general population. A number of subsequent studies confirmed the aforementioned study and proved a significant association between the two diseases [4–8]. In the Polish population, in a group of 148 subjects, Czarnecka-Operacz et al. [9] described the association of chronic urticaria with increased levels of antibodies to thyroglobulin and thyroid peroxidase, which are exponents of autoimmune thyroiditis. In the pathogenesis of this phenomenon, it has been suggested that the combination of thyroid autoantibodies with IgE receptors on mast cells may result in the release of mediators, including histamine [10]. The authors suggest that in all patients diagnosed with chronic urticaria, a diagnostic workup for thyroid disease should be performed. In the study performed in 2001 Kandeel et al. [11] showed that patients with chronic urticaria and autoimmune thyroiditis who showed perivascular fibrin deposits on skin biopsy and anti-FcεRI antibodies in serum may also have histamine release from mast cells. In contrast, another study showed that only 10% of patients with chronic urticaria and IgG class antibodies have IgE class antibodies, which could prove that these antibodies are not the cause of chronic urticaria [12].

The association of chronic urticaria with autoimmune thyroiditis is indisputable, but the pathogenesis and molecular basis are still not fully explained.

Celiac syndrome is an immune-mediated disease caused by gluten (a fraction of proteins present in the seeds of wheat, rye, barley and cereal hybrids), occurring in people with a genetic predisposition (HLA-DQ2 or DQ8). When exposed to gluten, specific antibodies are produced and an autoimmune inflammatory reaction occurs, leading to villous atrophy of the small intestinal mucosa. Antibodies can be found in about 1% of the general population. The risk of celiac syndrome is increased in patients with type 1 diabetes, autoimmune liver disease, Down syndrome, Turner syndrome and Williams syndrome, with IgA nephropathy, IgA deficiency and in 1st degree relatives of patients with celiac syndrome. The disease picture is dominated by gastrointestinal symptoms – diarrhea, abdominal pain, weight loss, micro- and macronutrient deficiencies. The skin manifestation is Duhring's disease (*dermatitis herpetiformis*). Most of the literature to date on the relationship between celiac syndrome and urticaria is based on single reports. For the first time, in 1987 Hautekeete et al. [13] observed the association of chronic urticaria with visceral disease in a 47-year-old patient. In 2006 Haussmann et al. [14] described the case of a 24-year-old woman diagnosed with celiac syndrome with associated urticaria. Both papers described the resolution of symptoms of both urticaria and celiac syndrome following a gluten-free diet. In 1999 Scala et al. [15] described a case of a 24-year-old woman with chronic urticaria without symptoms suggestive of celiac syndrome. The patient had serum antibodies to gliadin, reticulin and endomysial antibodies and a positive duodenum biopsy for celiac syndrome. After following a gluten-free diet, resolution of skin symptoms was observed. In 2012 Confino-Cohen et al. [16] described a 27-fold increased risk of celiac syndrome in a patient with urticaria. In 2013 Ludvigsson et al. [17] conducted a large cohort study involving 453 patients with celiac syndrome and urticaria and described an approximately 1.5–2-fold increased risk of urticaria in a patient with celiac syndrome. The study found a similar risk regardless of the age and gender of the patients.

Type 1 diabetes is caused by the destruction of pancreatic β-cells by an autoimmune process initiated by triggers (environmental factors) in people with a genetic predisposition. Anti-islet antibodies are involved in the development of the disease, which

can appear months or even years before the occurrence of diabetic symptoms; during this period, there is a gradual loss of β-cell secretory capacity leading to overt diabetes, which is characterized by absolute insulin deficiency. It manifests in children and adolescents, as well as in people <30 years of age. A slow course of autoimmune β-cell destruction is possible, leading to manifestation of the disease in the 4th of 5th decade of life (LADA, latent autoimmune diabetes). Few studies emphasize the association of chronic urticaria with type 1 diabetes [18, 19]. Hyman et al. [20] described the case of a 12-year-old patient whose onset of diabetes was preceded by chronic urticaria. Mazzetti et al. [21] emphasize the validity of determining anti-GAD antibodies in children with long-standing chronic urticaria.

Systemic lupus erythematosus (SLE) is chronic inflammatory autoimmune disease with a multifactorial etiopathogenesis and a complex clinical picture. Most often, the disease manifests with symptoms from the musculoskeletal system, hematopoietic system, skin and kidneys, and results from the deposition of immune complexes in these organs. The disease is most common in women, with a peak incidence between 15–55 years of age. One of the uncommon skin manifestations seen in SLE is the co-occurrence of chronic urticaria, the prevalence of which is then estimated at 0–21.9% [22].

Kolkhir et al. [23], on the basis of their study, estimate the prevalence of autoimmune disease, including lupus in patients with chronic urticaria in about 1% of the general population. In the case of SLE, the cause of chronic urticaria may be the presence of specific antibodies (ANA, anti-dsDNA, anti-SM and others), exposure to UV radiation or the use of medications (including corticosteroids, nonsteroidal anti-inflammatory drugs, methotrexate, retinoids, antimalarials) [24, 25]. In paediatric patients, it was found that the onset of chronic urticaria symptoms proceeded the later onset of systemic lupus erythematosus in about 0.7% of cases, with these patients having elevated antinuclear antibody titers from the onset of skin lesion manifestation [26]. It should be noted, however, that antinuclear antibodies are frequently detected in the healthy population, with a low titer of 1:40 in up to 31.7%, as well as in the course of pregnancy, infections, malignancies, organ-specific autoimmune diseases (such as autoimmune thyroiditis or hepatitis) [27].

Rheumatoid arthritis (RA) is systemic connective tissue disease characterized by non-specific, symmetrical arthritis (affecting mainly small and medium-sized joints), extra-articular lesions and systemic complications. It follows with periods of remission and exacerbation. It leads to joint destruction, deformity, contractures and impaired function.

It is one of the most common rheumatic diseases. It is estimated that 0.5–2% of the population over the age of 15 in Europe and the US suffers from it. The disease affects women 3 times more often than men. The peak incidence is in the 4th and 5th decades of life, and the incidence of RA increases with age. T and B lymphocytes, as well as autoantibodies to cyclic citrullinated peptide and rheumatoid factor are involved in the pathogenesis of RA. Kolkhir et al. [22] similarly to SLE, estimate the risk of RA comorbidity in patients with chronic urticaria at 1% of the general population. Lai et al. [28] in the study of 106 patients of the Taiwanese population with severe chronic urticaria described concomitant RA in 3 patients. Positive ANA antibodies were found in 10.4% of patients, which is about 3 times lower than in the general population. The authors of the aforementioned paper emphasize that in patients with chronic urticaria with concomitant rheumatic disease, in addition to antihistamines drugs, disease-modifying drug therapy is important.

Sjögren's syndrome (Mikulicz–Radecki disease) is the second most common autoimmune disease. The incidence ranges from 0.5–5%. More than 90% of patients are women. The peak incidence is at the age of 50. Sjögren's syndrome is an inflammatory autoimmune disease of unknown etiology, with lymphocytic infiltrates in the exocrine glands leading to their progressive dysfunction. It is associated with the presence of anti-Ro/SS-A and anti-La/SS-B antibodies. The incidence of urticaria comorbidity is estimated at 6.2%. The study confirmed that if anti-RO/SS-A and anti-LA/SS-B antibodies were absent and the first symptom was the seeding of urticarial wheals, the diagnosis of Sjögren's syndrome was made at a later age. Lai and Su [28] in the study of 106 patients of the Taiwanese population with severe chronic urticaria described Sjörgen syndrome in 5 patients.

Myasthenia gravis and Lambert–Eaton myasthenic syndrome are chronic diseases [29] of the neuromuscular junction whose symptoms include weakness and fatigue of selected skeletal muscles. Myasthenia gravis is an acquired, chronic disease of the neuromuscular junction with an autoimmune basis, while Lambert–Eaton syndrome is 60% paraneoplastic and 40% autoimmune. About 10% of myasthenia gravis patients are diagnosed with a thymic tumor (*thymoma*). Myasthenia gravis affects people of all ages, but two peaks of incidence are observed: in young women and in men over 60. The pathogenesis

of the disease involves antibodies against acetylcholine receptors, T and B lymphocytes, epithelial cells. It is debated whether particles similar to acetylcholine receptors can be presented on the surface of other cells (except thymus cells), which could trigger an autoinflammatory response. Rymarczyk et al. [30] described the cases of 2 patients in whom an association between chronic urticaria and myasthenia gravis was observed. The first involved a 67-year-old man with recurrent episodes of severe urticaria accompanied by angioedema of the tongue. The skin lesions were mainly localized to the feet, hands and face. Several years earlier, the patient had been diagnosed with myasthenia gravis, asymptomatic and untreated. Immunologic studies showed no significant abnormalities.

On the other hand, a 54-year-old patient with recurrent, severe angioedema and urticaria was diagnosed with myasthenia gravis. The patient underwent a thymectomy, then was treated with mestinone with good clinical results. No abnormalities in laboratory tests were observed. Darley et al. [31] in 1977 described the case of a patient whose chronic urticaria was accompanied by myasthenia gravis and systemic lupus erythematosus.

Kageyama-Yahara et al. [32] proved that nicotinic acetylcholine receptors presented on mast cells show an inhibitory effect on their degranulation. Therefore, it is speculated that nicotinic acetylcholine receptor agonists may find application in the treatment of food allergies [33].

There are single reports in the literature of the co-occurrence of chronic urticaria with myasthenia gravis. This topic requires further research.

Discussion

The review underscores the significant association between CSU and various autoimmune diseases, though the exact mechanisms remain elusive. Symptoms such as fever, lymphadenopathy, abdominal pain, joint pain, ocular symptoms, and mucosal changes in CSU patients warrant further autoimmune diagnostics. Morphologically, urticarial lesions in autoimmune diseases tend to be more intense, less pruritic, and longer-lasting, often with perivascular infiltrates on histopathology.

Conclusion

In patients with CSU, an increased risk of autoimmune diseases should be considered. Expanded diagnostic workups are recommended for patients unresponsive to standard antihistamine treatment, particularly those with a family history of autoimmune conditions. Further research is needed to elucidate the pathogenesis and improve management strategies for CSU with concomitant autoimmune diseases.

References

1. *Midelfart K, Moseng D, Kavli G et al. A case of chronic urticaria and vitiligo, associated with thyroiditis, treated with PUVA. Dermatologica. 1983; 167: 39-41.*
2. *Leznoff A, Josse RG, Denburg J et al. Association of chronic urticaria and angioedema with thyroid autoimmunity. Arch-Dermatol. 1983; 119: 636-40.*
3. *Leznoff A, Sussman GL. Syndrome of idiopathic chronic urticaria and angioedema with thyroid autoimmunity: a study of 90 patients. J Allergy Clin Immunol. 1989; 84: 66-71.*
4. *Turktas I, Gokcora N, Demirsoy S et al. The association of chronic urticaria and angioedema with autoimmune thyroiditis. Int J Dermatol. 1997; 36: 187-90.*
5. *Ryhal B, DeMera RS, Shoenfeld Y et al. Are autoantibodies present in patients with subacute and chronic urticaria. J Investig Allergol Clin Immunol. 2001; 11: 16-20.*
6. *Verneuil L, Leconte C, Ballet JJ et al. Association between chronic urticaria and thyroid autoimmunity: a prospective study involving 99 patients. Dermatology. 2004; 208: 98-103.*
7. *Palma-Carlos AG, Palma-Carlos ML. Chronic urticaria and thyroid auto-immunity. Eur Ann Allergy Clin Immunol. 2005; 37: 143-6.*
8. *Aamir IS, Tauheed S, Majeed F et al. Serum antithyroid antibodies in female patients with chronic urticaria; J Coll Physicians Surg Pak. 2008; 18(8): 498-501.*
9. *Czarnecka-Operacz M, Sadowska-Przytocka A, Jenerowicz D et al. Thyroid function and thyroid autoantibodies in patients with chronic spontaneous urticaria. Adv Dermatol Allergol. 2017; XXXIV(6): 566-72.*
10. *Delèvaux I, André M, Tridon A et al. Chronic urticaria and Hashimoto-Hashimoto's thyroiditis: report of 6 cases. Rev-Med Intern. 2001; 22: 232-7.*
11. *Kandeel AA, Zeid M, Helm T et al. Evaluation of chronic urticaria in patients with Hashimoto thyroiditis. J Clin Immunol. 2001; 21: 335-47.*
12. *Concha LB, Chang CC, Szema AM et al. IgE antithyroid antibodies in patients with Hashimoto's disease and chronic urticaria. Allergy Asthma Proc. 2004; 25: 293-6.*
13. *Hautekeete ML, DeClerck LS, Stevens WJ. Chronic urticaria associated with coeliac disease. Lancet. 1987; 1(8525): 157.*
14. *Haussmann J, Sekar A. Chronic urticaria: A cutaneous manifestation of celiac disease. Can J Gastroenterol. 2006; 20(4): 291-3.*
15. *Scala E, Giani M, Pirrotta L et al. Urticaria and adult celiac disease. Allergy. 1999; 54: 1008-9.*

16. *Confino-Cohen R, Chodick G, Shalev V et al. Chronic urticaria and autoimmunity: associations found in a large population study. J. Allergy Clin. Immunol. 2012; 129(5): 1307-13.*
17. *Ludvigsson JF, Lindelöf B, Rashtak S et al. Does urticaria risk increase in patients with celiac disease. A large population-based cohort study. Eur J Dermatol. 2013; 23(5): 681-7.*
18. *Kolkhir P, Borzova E, Grattan C et al. Autoimmune comorbidity in chronic spontaneous urticaria: A systematic review. Autoimmun Rev. 2017; 16(12): 1196-1208.*
19. *Fraser K, Robertson L. Chronic urticaria and autoimmunity. Skin Therapy Lett. 2013; 18(7): 5-9.*
20. *Hyman SJ, Shreffler WG, Rapaport R. Type 1 diabetes, autoimmune thyroid disease, and chronic urticaria. Pediatr Diabetes. 2008; 9(5): 508-11.*
21. *Mazzetti A, Borici-Mazi R. Childhood chronic urticaria and type 1 diabetes. Allergy Asthma Clin Immunol. 2011; 7(Suppl 2): A18.*
22. *Kolkhir P, Pogorelov D, Olisova O et al. Comorbidity and pathogenic links of chronic spontaneous urticaria and systemic lupus erythematosus – a systematic review. Clin Exp Allergy. 2016; 46(2): 275-87.*
23. *Kolkhir P, Borzova E, Grattan C et al. Autoimmune comorbidity in chronic spontaneous urticaria: A systematic review .Clin Exp Allergy. 2016; 46(2): 275-87.*
24. *Sánchez J, Sánchez A, Cardona R. Prevalence of Drugs as Triggers of Exacerbations in Chronic Urticaria. J Investig Allergol Clin Immunol. 2019; 29(2): 112-7.*
25. *Balamurugesan K, Davis P, Ponprabha R et al. Chloroquine induced urticaria: A newer adverse effect. J Family Med Prim Care. 2019; 8(7): 2545-7.*
26. *Spadoni M, Jacob C, Aikawa N et al. Chronic autoimmune urticaria as the first manifestation of juvenile systemic lupus erythematosus. Lupus. 2011; 20(7): 763-6.*
27. *Kavanaugh A, Tomar R, Reveille J et al. Guidelines for clinical use of the antinuclear antibody test and tests for specific autoantibodies to nuclear antigens. American College of Pathologists. Arch Pathol Lab Med. 2000; 124: 71-81.*
28. *Lai KL, Su CC. Association of chronic urticaria with rheumatic diseases and thyroid autoimmunity. J Intern Med Taiwan. 2010; 21: 277-284.*
29. *Kostera-Pruszczyk A. Miastenia i zespół miasteniczny Lamberta-Eatona https://podyplomie.pl/wiedza/neurologia/210,miastenia-i-zespol-miasteniczny.*
30. *Rymarczyk B, Glück J, Rogala B et al. Chronic urticaria in myasthenia gravis patients – more than occasional coexistence? Allergol Immunopathol (Madr). 2014; 42(6): 626-7.*
31. *Darley CR, Munro DD, Borrie PF. Myasthenia gravis, systemic lupus erythematosus and urticaria. (Case 1). Myasthenia gravis and herpetiform acantholysis. (Case 2). Proc R Soc Med. 1977; 70(10): 734-7.*
32. *Kageyama-Yahara N, Suehiro Y, Yamamoto T et al. IgE induced degranulation of mucosal mast cells is negatively regulated via nicotinic acetylcholine receptors. Biochem Biophys Res Commun. 2008; 377: 321-5.*
33. *Utsunomiya N, Yamamoto T, Kodama T et al. Pathophysiological role of the cholinergic antiinflammatory and immune pathway in a murine model of food allergy. Gastroenterology. 2006; 130: A557.*

Author's contributions:
All authors contributed equally to the article.
Sources of funding
The research was funded by the authors.
Conflicts of interests
The authors report that there were no conflicts of interest.

ORCID
Bartosz Bartosik – ID – https://orcid.org/0000-0002-8785-509X

Corresponding author
Bartosz Bartosik, MD
Department of Internal Diseases, Allergology, Endocrinology and Gastroenterology, Institute of Medical Sciences, University of Opole
45-040 Opole, ul. Oleska 48
e-mail: bartosz.bartosik@uni.opole.pl