

# A clinical and epidemiological retrospective analysis of patients with urticaria

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## ABSTRACT

**Introduction:** Urticaria is a heterogeneous disease which affects nearly 1 in 5 individuals in their lifetime and significantly worsens the quality of life. The aim of this study is a five-year retrospective analysis of epidemiological and clinical aspects of patients hospitalized for urticarial.

**Material and methods:** Analysis of medical records of patients hospitalized for urticaria at the department of dermatology. The clinical and epidemiological data were analysed and compared to a control group composed of 137 healthy individuals' body mass index (BMI) and sex-matched. Statistical analysis was performed using the chi-square test, a statistically significant difference was at  $p < 0.05$ .

**Results:** In the analysed period 137 patients were hospitalized for urticaria, 93 females (68%) and 44 males (32%), with mean age 48.53. Thirty-eight per cent of patients have been previously diagnosed with an allergy. Over 60% of patients (60 women, 18 men) suffered from acute and 38% from chronic urticaria. A causal factor was identified in 62% of all cases, the most common were drugs (48%). Urticaria patients had significantly higher levels of C-reactive protein (CRP), neutrophils and glucose than controls (all  $p < 0.05$ ). The patients were treated with antihistamines (94%), glucocorticosteroids (81%), and one patient was classified for omalizumab treatment.

**Conclusions:** Urticaria still poses a challenge as the cause often remains unknown which highlights the need for novel diagnostic methods and interdisciplinary treatment. Recommended treatment includes antihistamines but among patients with chronic, treatment-resistant urticaria omalizumab should be considered.

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**Keywords:** urticaria, angioedema, antihistamines

## INTRODUCTION

Urticaria is a common disease with complex pathogenesis, characterized by wheals and/or angioedema accompanied by pruritus [1, 2]. The lifetime risk of urticaria is estimated at 20–25%, although it seems to be underestimated [3, 4]. In the pathogenesis of the disease, the key role is played by mast cells and pro-inflammatory mediators, mainly histamine, leukotrienes, prostaglandins, cytokines and chemokines, released during their degranulation, which results in increased vascular permeability [4, 5].

Urticaria is divided based on clinical criteria. Acute and chronic urticaria are distinguished [1]. Acute urticaria is common in all age groups and is usually idiopathic in 30–50% of cases [6]. In adults, it is more often caused by drugs (in 9.2–27% of patients), while in small children it often occurs in the course of infection [6]. Skin lesions usually last 1–24 hours [1]. Acute urticaria significantly reduces the quality of a patient's life, the key factor leading to the

deterioration is pruritus [1]. Acute urticaria may be accompanied by symptoms of anaphylaxis, which is a systemic reaction mediated primarily by immunoglobulin E (IgE), involving at least two organ systems [7–9]. The most common cause of anaphylaxis is food, other factors include drugs and insect venom [8, 10]. In one-fifth of patients, the cause of anaphylaxis remains unknown [10]. Due to the life-threatening risk during anaphylaxis, referral to a doctor to search for the possible causes of the episode and the provision of a pre-filled syringe with adrenaline solution are recommended [9]. Chronic urticaria, on the other hand, is diagnosed when symptoms persist for more than 6 weeks [11]. Its pathogenesis is associated with the activation of basophils and mast cells [12]. It is estimated that it occurs in 0.5–5% of the population, more often in women [2, 3, 12]. It most often appears between the third and fifth decades of life [2]. Chronic urticaria can be divided into spontaneous and induced [2, 4]. Chronic urticaria is idiopathic in

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80–90% of cases and often causes major diagnostic and therapeutic problems [3, 12]. Chronic-induced urticaria is less common than acute and is usually caused by drugs, stress and physical factors such as heat, cold, pressure, water or sunlight [2]. Both types of chronic urticaria may also coexist in one patient at the same time [2]. Chronic urticaria usually persists for two to five years [2]. In patients with this disease, the coexistence of autoimmune diseases, including celiac disease, systemic lupus erythematosus and Sjögren’s syndrome, is often observed [2].

Treatment depends on the type and severity of symptoms and includes second-generation antihistamines (LPII), systemic glucocorticosteroids (briefly, in case of exacerbation of symptoms), omalizumab, physical desensitization, and phototherapy [4, 13]. Recommendations suggest the use of non-sedative H-1 blockers for 2 to 4 weeks, and in the case of no improvement or intensified symptoms, increasing the dose 4 times [4]. If the pharmacotherapy is ineffective after another 2 to 4 weeks, it is recommended to include omalizumab in the treatment [4]. In the case of the ineffectiveness of biological treatment, the use of cyclosporine as a third-line treatment is suggested [11]. In addition to pharmacological treatment, it is necessary to identify and avoid factors provoking the symptoms of the disease and treat comorbidities that may be the cause of urticaria [4, 10]. In addition to pharmacotherapy, it is recommended to avoid the causative agent and to diagnose and treat comorbidities [4].

**MATERIAL AND METHODS**

A group of patients hospitalized in the department of dermatology due to urticaria between 2015–2020 was subjected to a retrospective analysis. The patients’ medical records, sex, age, comorbidities, potential causative agent, clinical picture, laboratory tests and administered treatment were analysed. The control group consisted of 137 patients hospitalized in the Department of Dermatology due to scabies, matched for sex and age. The obtained results were statistically analysed and compared with a control group using the chi-square test.

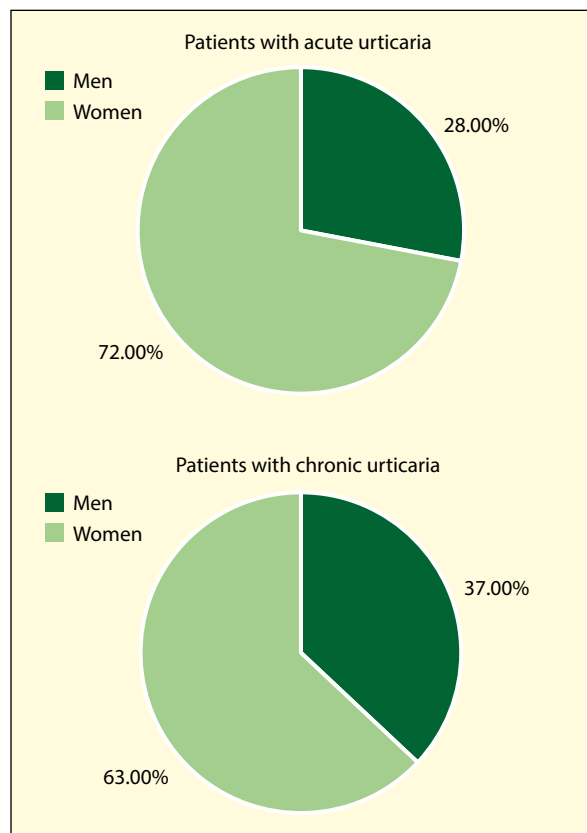
**RESULTS**

In the analysed period, 137 patients were hospitalized in the clinic due to urticaria, which constituted 2.16% of all patients, including 93 females (67.88%) and 44 males (32.12%), aged 13 to 91, with a median age of 49 years. Most patients were in the group of people over 56 years old (39.42%) (Tab. 1).

Most of the respondents lived in urban areas (77.37%), the rest in rural areas (22.63%). Acute urticaria was diagnosed in 78 patients (56.93%), and chronic urticaria in 59 hospitalized patients (43.06%), in both groups more

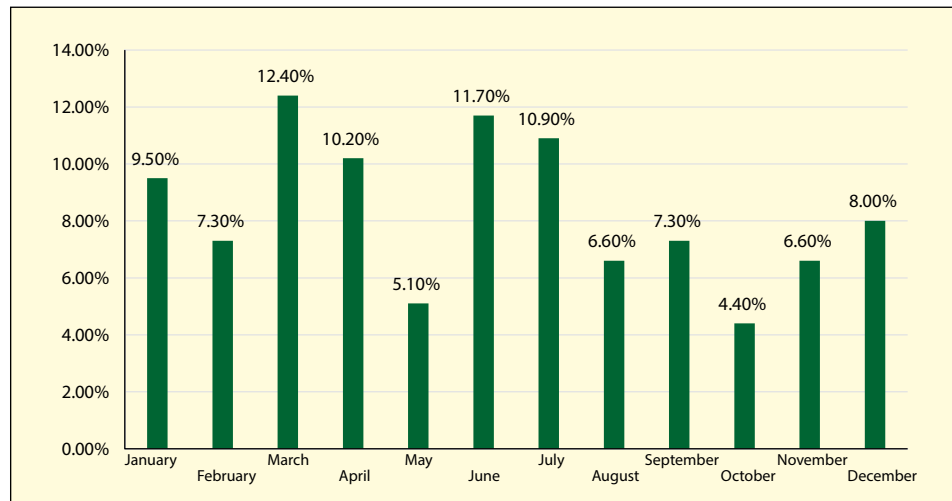
**Table 1.** Age and sex of patients hospitalized for urticaria and the control group

Parameter	Patients with urticaria		Control group	
	N	%	N	%
Sex				
Females	93	67.88	93	67.88
Males	44	32.12	44	32.12
Age [years]				
13–35	39	28.47	41	29.83
36–55	44	32.11	20	14.92
> 56	54	39.42	76	55.25



**Figure 1.** Gender differences in hospitalized patients with acute and chronic urticaria

women than men were diagnosed. (Fig. 1). Most patients were admitted to the department in March and June (Fig. 2). An increased incidence of hospitalization due to urticaria was noted in the spring. In more than half of the patients (77 persons, 56.20%), urticarial wheals were localized on a limited area of the body, in the remaining 55 patients (40.15%) they covered the whole body, in 5 patients (3.64%) skin lesions were not present during the admission to the department. In the group of patients with lesions limited to a specific area of the body, localization within the



**Figure 2.** The month of admission to the clinic

lower limbs was present in 48.61% of cases, followed by the chest (27.78%), upper limbs (20.83%), and the area of head and neck (2.78%). Furthermore, 29 patients (21.17%) had angioedema and 10 patients (7.29%) suffered from red dermographism. Fourteen patients (10.22%) had coexisting dermatoses: psoriasis (4 people), acne (4 people), vitiligo (3 people) and atopic dermatitis (3 people). In 85 patients (62.04%) (46 women, 39 men) a potential factor causing urticaria was identified. The most common causative factor was drugs (48%) — mainly non-steroidal anti-inflammatory drugs (NSAIDs) and beta-lactam antibiotics, followed by food (40%) — mainly tomatoes, strawberries, bananas and seafood. One person suffered from contact urticaria. Fifty-two subjects (37.95%) were previously diagnosed with allergies. Half of the patients in this group were allergic to drugs (mainly analgesics and antibiotics, including beta-lactams), the rest had inhalant allergies to grasses and cereals (20%), animal hair (13%) and dust mite (10%). Out of the 137 patients included in the analysis, 70 had comorbidities (51.09%). The most common were hypertension (22.62%), type 2 diabetes (10.21%), urinary tract infections (5.10%), hypothyroidism (5.10%) and dyslipidaemia (5.10%). In laboratory tests, elevated CRP (26.27%), leucocytosis (16.05%), elevated glycaemia (13.86%), neutrophilia (13.86%) and leukocyturia (8.76%) were noted. Second-generation antihistamines were used in 129 patients (94.16%), glucocorticosteroids in 111 patients (80.29%) — in 74 cases by intravenously (66.67%), 1 patient was qualified for biological treatment with omalizumab.

The potential link between urticaria, other comorbidities and laboratory parameters was investigated using the chi-square test. Among patients with both acute and chronic urticaria, elevated levels of CRP and leukocytes were observed significantly more often than in the control group

(all  $p < 0.05$ ). Increased glucose and neutrophil levels were significantly more common among patients with chronic urticaria than in the control group (all  $p < 0.05$ ). These patients were more likely to be diagnosed with hypothyroidism, urinary tract infections, and dyslipidaemia compared to those without urticaria (all  $p < 0.05$ ). No statistical significance was found for the incidence of urticaria in specific seasons or age groups ( $p > 0.05$ ).

## DISCUSSION

Urticaria is characterized by the presence of wheals, oedema, or both, which affects up to 40% of the patients [6]. They occur through the release of histamine from mast cells, which causes an increase in capillary permeability [1]. The total incidence of urticaria in the department of dermatology in the analysed period of five years was 2.16% (acute urticaria — 1.23% of all patients, chronic urticaria 0.93%). In a similar seven-year retrospective study involving 267 people, the incidence of urticaria was 1.71% [14]. Balp et al. [15] in a multi-centre study on a large group of 36,000 patients reported the frequency of chronic urticaria at 0.41%. In another study, it was 1.9% during one year [14]. In literature, urticaria is considered to be a relatively common disease, 20% of the population experienced acute urticaria and 5% chronic urticaria [1]. Hives can occur at any age. The first episode most often appears in the third and fourth decades of life [1]. In the present analysis, patients were between 13–91 years old, with a median age of 49 years. Most patients were in the group between 40 and 50 years of age, which is consistent with the data from the literature [1]. Patients living in the city were more often affected, which is also confirmed in the literature [16]. When analysing the time of patients' admission to the department, more frequent occurrences of urticaria in January, March, April, June and

July were noted. The observed connection may be related to the most common factors causing urticaria. Inhalant allergens reach the highest concentration in spring and summer, and other causative factors of urticaria include bacterial infections, which are usually observed in winter and often require the use of medications that may cause an allergic reaction [3].

Urticaria affects women more often than men [14, 17]. In the present analysis, women accounted for as much as 68%, which is more than twice as many as men, with an average age of 49. Criado et al. [14] also noted a higher incidence of urticaria among women (80.15%), their average age was 43 years. Furthermore, in the study by Dias et al. [18], there were 85.72% of women with chronic urticaria, with an average age of 46 years [14, 18]. Criado et al. [14] reported similar values among a group of patients with chronic urticaria and angioedema — women accounted for 79.5% [14, 19]. The results found in the literature, together with those obtained in this analysis, confirm that urticaria is much more common in women than in men, and this applies not only to chronic urticaria but to this entire heterogeneous group [17]. So far, it has not been possible to clearly explain these differences, as it seems that neither the criteria for selecting patients for the study nor the period of analysis or the country matter [17]. Eun et al. [20] suggested the influence of oestrogen, which stimulates the humoral response and synthesis of antibodies [14, 20]. The social aspect should be taken into consideration, as it seems that women seek medical help more often than men [14]. In 40% of hospitalized patients, urticarial wheals were located on all body areas. Data from the literature are consistent, Sabroe et al. [7] made similar observations — 48% of patients had lesions in similar localization. In the remaining group of patients, urticarial wheals are most often located on the lower limbs, chest and upper limbs. Angioedema occurred in 21.17% of the analysed patients. In the literature, in one of the studies conducted among patients with chronic urticaria, angioedema was reported in 55.7% of the patients [21].

Acute urticaria most often occurs after contact with an initiating factor that exacerbates the disease. Unfortunately, many patients are unable to identify it. Data from the literature also emphasize diagnostic difficulties, as well as frequent idiopathic background [6]. In the case of the patients included in the research, 35% indicated the cause. Most often these were drugs — levothyroxine, diclofenac, clindamycin, rosuvastatin and non-steroidal anti-inflammatory drugs, as well as a dietary supplement containing glucosamine sulphate derived from crustaceans, chondroitin sulphate and vitamin C. Nettis [6] stated that non-steroidal anti-inflammatory drugs, antibiotics and convertase inhibitors as the most common cause of acute urticaria. The second factor causing urticaria among the

study patients was food, which is also consistent with the literature. Three patients reported infection before the onset of the first episode of urticaria. Respiratory tract infections are also indicated as a possible cause of acute urticaria in the literature in children and adults [6, 22]. Schaefer also points to bacterial, viral, fungal and parasitic infections as possible causes of urticaria. Another factor may also be an increase in body temperature, which often accompanies infectious diseases [3].

Food allergies are common in patients with acute urticaria. Poowuttikul et al. [8] believe they are the most frequent cause of urticaria. As the second factor, they mention drugs, which is different from the obtained data. In the study patients, 38% were previously diagnosed with allergies, most often to drugs. It was mainly antibiotics — 57% of all allergies (including  $\beta$ -lactams), followed by ketoprofen, drotaverine, iron preparations, xylocaine, anagrelide, hydroxycarbamide and pantoprazole. Poowuttikul et al. [8] also stated that antibiotics as the most common drug cause of urticaria, followed by NSAIDs. In the literature, among the drugs that most often cause urticaria and angioedema, Antia et al. [22] point out angiotensin-converting enzyme inhibitors and NSAIDs. It is worth mentioning that medications containing NSAIDs are freely available without a prescription in many stores, which may lead to a belief that these products are completely safe and their consequent abuse. Antia et al. [22] mentioned that in their studies they were also the cause of angioedema, which lead to health and life-threatening conditions in 0.68% of cases. In patients suspected of urticaria, it is advisable to discontinue such medications permanently and not only during the occurrence of symptoms [11].

Among the analysed patients, angioedema that required the use of angiotensin-converting enzyme inhibitors was 1.46%. It is estimated in the literature that ACEIs are taken by 40 million patients worldwide, and in 0.1–0.7% of patients in this group they are the cause of angioedema [23]. This reaction was more often observed in African Americans, women, the elderly and smokers [23]. It has been observed that angioedema may appear at any time during the use of ACEIs and also occur after discontinuation of their use [24]. In children, there were also grass and grain, animal hair and mites. The main food allergens are tomatoes, rye, bananas, milk, fish, hot spices, cherries, radishes and strawberries. The results of this analysis are not entirely consistent with the data from the literature, where hazelnut, potato, apple, oatmeal, beef and seafood are usually responsible for causing the allergic reaction [22]. For children, cow's milk, peanuts and shellfish, and hot spices are the most common [8].

Changes in the laboratory tests were noted among patients with urticaria such as an increase in the concentration of inflammatory parameters, which is related to

the mechanism of the formation of urticarial lesions [25]. In the study by Criado et al. [14], in most patients, the blood counts did not differ from the normal state, and the parameters of inflammation did not show abnormalities. The literature emphasizes the lack of the need to perform additional laboratory tests, which, however, should be ordered when another cause of changes is suspected in order to establish a diagnosis [3]. Performing complete blood count, Biernacki's test, CRP, TSH, liver tests and general urine tests should be considered [3]. Some reports found that positive rheumatoid factor and antinuclear antibodies are more common in patients with urticaria [14]. However, none of these abnormalities were observed in the analysed patients. The concentration of d-dimers may also be elevated [14], which was observed in 3 of the study patients.

Criado et al. [14] reported that urticaria was mainly accompanied by hyperthyroidism and hypothyroidism, which occurred in 5.1% of the study patients, rheumatoid arthritis, Sjögren's disease, celiac disease, type 1 diabetes, and systemic lupus erythematosus. Data suggesting that among patients with urticaria, the incidence of thyroid diseases may even exceed 50% can be found in the literature. The obtained data depend on the fact that in some studies, the criteria for qualifying a patient to the group with thyroid diseases was the presence of antithyroid antibodies [26]. There was also an increase in the incidence of psychiatric disorders in these patients, such as anxiety disorders and depression, which were reported in up to 60% of the patients [26]. This relationship can be explained by a significant deterioration in the quality of life in patients with urticaria associated with pruritus, deterioration of sleep quality, the visibility of changes that may affect professional and social life, and the unpredictability of symptoms for which it may be difficult to determine the cause [26].

The analysed patients were treated with second-generation antihistamines and systemic glucocorticosteroids-as a short course, one patient was qualified for treatment with omalizumab, which is in accordance with the current guidelines of the Polish Society of Dermatology [4]. Patients hospitalized at the Clinic between 2015 and 2020 were included in the study, the drug program for the treatment of urticaria with omalizumab was introduced in January 2020, hence only one patient was qualified for this therapy.

## CONCLUSIONS

Urticaria is a common dermatosis affecting people of all ages, both adults and children, more than twice as often in women than men. There is a noticeable increase in the number of patients with urticaria living in urban areas. Patients with episodes of acute urticaria in March and in June require hospitalization more often. Often, despite numerous attempts, the cause of urticaria cannot be determined, which

indicates the need for the development of new diagnostic methods and the provision of broader, interdisciplinary medical care. Antihistamines remain the recommended treatment for patients with urticaria. However, in patients with treatment-resistant chronic urticaria, eligibility for omalizumab therapy should be considered.

## Article information and declarations

### Data availability statement

No new data was generated.

### Ethics statement

The paper reflects the authors' own research based on medical records of patients hospitalized at the Department of Dermatology.

### Author contributions

Conceptualization, investigation, writing — review and editing, and project administration: AS, AM, BP, JKG and AB. Methodology, data curation, resources, writing — original draft preparation, and visualization: AS, AM, BP, JKG. Validation: IF. Supervision: AB and IF. All authors have read and agreed to the published version of the manuscript.

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None.

### Conflict of interest

We declare no conflict of interest.

### Supplementary material

None.

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