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Clinical Profile of Chronic Urticaria: A Retrospective Observational Study from Farwaniya Hospital, Kuwait

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Abstract

Background: Between 15 and 25 percent of people will experience urticaria at some point in their lives. It is characterized by the development of wheals (hives), angioedema, or both. Different types and subtypes of urticaria have a very broad range of clinical manifestations. The Farwaniya Region is the most populated of Kuwait's six governorates, and Farwaniya Hospital is one of the country's main general hospitals. In February 2023, the Farwaniya Hospital's Department of Dermatology established a Urticaria Unit. The specific objective of this study was to delineate the demographic and clinical characteristics of chronic urticaria within our population and to compare these findings with published data from diverse geographic regions. **Methods:** Based on an analysis of a database of patients who were seen at the specialized urticaria outpatient clinic between February 2023 and June 2024, the study was retrospective in nature. In addition to the demographic profile, laboratory parameters and the existence of comorbidities were examined in the records. Only a descriptive analysis was carried out because of the heterogeneity of the data. **Results:** 720 new urticaria patients were registered during the study period. Of these, 629 (87.4%) were diagnosed with chronic urticaria (CU); 515 (81.9%) had CSU; 34 (5.4%) had isolated chronic inducible urticaria (CIndU); and 80 (12.7%) had CSU with CIndU. An average diagnostic delay of 11 months was noted, and the mean age at symptom onset was 32.7 years (range 14 - 88). A subgroup of patients had elevated serum IgE levels and anti-TPO antibodies. Many patients had comorbidities and atopic diathesis. **Conclusions:** According to the majority of previously published research, the clinical profile of chronic urticaria appears to be comparable here. Compared to similar published reports from other locations, a smaller proportion of patients (where data was available) in our population had elevated IgE levels. Although not as prevalent as in

other populations, atopic diseases were linked to chronic urticaria patients in our population. Only a small proportion of patients had *H. pylori* infection (where data was available). Additionally, drugs were not identified as a common precipitating factor.

Keywords

Chronic Spontaneous Urticaria, Chronic Inducible Urticaria, Comorbidities

1. Introduction

A condition that affects 15% to 25% of people at some point in their lives, urticaria is characterized by the development of wheals (hives), angioedema, or both [1]. The range of clinical manifestations of various urticaria types and subtypes is extremely broad. Furthermore, a patient may have two or more distinct urticaria subtypes. Urticaria is divided into two categories based on how long it lasts: acute (lasting six weeks or less) and chronic (lasting more than six weeks) [2]. The prevalence of chronic urticaria is estimated to be between 0.5% and 5% in the general population, but the incidence is thought to be around 1.4% annually [3]. Chronic urticaria (CU), which is defined as symptoms that last longer than six weeks, is divided into two categories: chronic spontaneous urticaria (CSU), which has a known or unknown cause, and chronic inducible urticaria (CIndU), where the development of lesions is caused by identifiable, definite and subtype-specific triggering factors [1]. Etiological investigation and treatment are difficult for both patients and doctors, as approximately 50% of patients present with CSU of unknown reasons, which causes a great deal of frustration. Numerous theories have been proposed to explain the pathogenesis of CSU, with evidence suggesting that up to 50% of patients may have an autoimmune etiology. Two endotypes have been identified: type I auto-allergic CSU, which is linked to IgE antibodies against autoantigens, and type IIb aiCSU, which is caused by autoantibodies that activate mast cells, such as anti-FcεRI and anti-IgE [4]-[6]. Recent data indicate that CU is not only a disease of the mast cells but also a systemic autoimmune disease [7]-[9]. CU has various effects on patients' health and is linked to several comorbidities.

CU patients are also more likely to have other autoimmune diseases, which may be linked to urticaria or make them more susceptible to CU.

The Farwaniya Region is the most populated of Kuwait's six governorates, and Farwaniya Hospital is one of the country's main general hospitals [10]. A urticaria unit was established in the Department of Dermatology, Farwaniya Hospital, in February 2023. This study was conducted with the objective of focusing specifically on characterizing the demographic and clinical profile of chronic urticaria in our population and comparing it with the published data from different geographic areas [11]-[16].

2. Methods

Based on a database analysis of all consecutive patients seen at the specialized urticaria outpatient clinic between February 2023 and June 2024, the study was retrospective in nature.

A thorough clinical history was used to determine the diagnosis and etiology of chronic urticaria, which was then categorized using the World Allergy Organization (WAO) guidelines, the European Dermatology Forum (EDF), the EU-funded Global Allergy and Asthma European Network (GA2LEN), and the international European Academy of Allergology and Clinical Immunology (EAACI) [17].

In patients with CSU, in addition to basic tests including differential blood count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), thyroid laboratory tests (TSH, free T4 (FT4), and thyroid autoantibodies (TAA)), namely thyroid peroxidase antibody (anti-TPO), were requested, as well as antinuclear antibodies (ANA) and serology to determine the diagnosis of *Helicobacter pylori* (*H. pylori*) infection. In our lab, the normal reference values for the immunoglobulin E (IgE) quantitative assay are 0 - 100 (kilo-units per liter) (kU/L). The typical range for the anti-TPO antibody quantitative assay is less than 50 IU/mL (international units per milliliter). The normal range for TSH and FT4 quantitative assays is 0.38 - 5.33 micro-international units per milliliter (μIU/mL) and 7.86 - 15.96 micromols per litre (μmol/L), respectively. The titer ratio for the quantitative ANA test is reported, and the normal range is less than 1/80 (<1/80). A quantitative serological test measuring immunoglobulin M, immunoglobulin G, and immunoglobulin A is used to test for *Helicobacter pylori* infection. The results are provided in units per milliliter and are either positive or negative for the three types of immunoglobulins.

The multiple antigen simultaneous testing assay (MAST) was also used to test the patients for different specific serum IgE antibodies, as well as total serum IgE. The following clinical information was documented in addition to sociodemographic details like age and gender: comorbidities (atopic, cardiovascular, psychiatric, rheumatologic, endocrinological, and oncological diseases), the duration between the onset of symptoms and the initial visit to the doctor, the presence of angioedema, and urticaria subtypes (CSU, CIndU).

History and clinical evaluation were used to diagnose chronic inducible urticaria (CIndU).

After receiving approval from the Ministry of Health's Standing Committee for Coordination of Health and Medical Research (approval number 2794/2024), data was gathered from Farwaniya Hospital's Hospital Information System (HIS). As part of the urticaria specialized outpatient clinic's clinical routine, the study's clinical component and laboratory testing were conducted. Clinical data from patients was interpreted while maintaining total anonymity and confidentiality. The Declaration of Helsinki's ethical guidelines were followed when treating each patient.

Statistical analysis

Since this is a retrospective descriptive study aimed at describing the clinico-

epidemiological profile of urticaria patients in our setting, and not at testing a hypothesis or establishing associations/causality, only a descriptive analysis was carried out due to the heterogeneity of the data.

3. Results

720 new urticaria patients were registered during the study period. 629 (87.4%) of them had a chronic urticaria (CU) diagnosis (Table 1). Of the remaining 91 patients, 20 had acute urticaria, 3 had hereditary angioedema, and 68 had other diagnoses (contact dermatitis in 9 cases, chronic pruritus from known or unknown causes in 32 cases, and papular urticaria in 27 cases). These patients were not included in the analysis of this study.

503 (80%) of the 629 patients were referred by the general practitioner, 76 (12%) by other specialties, and 50 (8%) by dermatologists.

The majority of CU patients were female (497, 79%) (Table 2).

The group of CU patients had an average diagnostic delay of 11 months (range 0 - 2 years) and a mean age at symptom onset of 32.7 years (range 14 - 88) (Table 2). 320 (51%) of the patients had symptoms for less than a year prior to diagnosis at our consultation or earlier, 270 (43%) for one to five years, and 39 (6%) for more than five years (Table 1). Many of these patients had a history of atopic disease, with 69 (11%) having atopic dermatitis, 38 out of 329 (11.6%) having a positive result for one or more allergens in their food allergy test, 35 out of 498 (7%) having bronchial asthma, and 70 out of 498 (14%) having allergic rhinitis (Table 1).

Table 1. Chronic urticaria diagnoses of the studied patients.

Chronic urticaria subtypes	CU patients (n = 629), n (%)
A. Isolated chronic spontaneous urticaria	515 (81.9%)
B. Chronic inducible urticaria	34 (5.4%)
Symptomatic dermographism	25
Cholinergic urticaria	6
Solar urticaria	2
Heat urticaria	1
C. Chronic spontaneous urticaria + Chronic inducible urticaria	80 (12.7%)
Symptomatic dermographism	71
Cholinergic urticaria	7
Solar urticaria	2

Abbreviations: CU, chronic urticaria.

Of the CU patient subtypes, 515 (81.9%) had isolated chronic spontaneous urticaria (CSU), 34 (5.4%) had isolated CIndU, and 80 (12.7%) had concomitant CSU with CIndU. Twenty-five (73.5%) of the 34 patients who had only CIndU

had symptomatic dermographism, while the remaining 6 patients had cholinergic urticaria, 2 patients had solar urticaria, and 1 patient had heat urticaria.

Table 2. Demographic and clinical profile of our patients.

Characteristics	Chronic Urticaria patients (n = 629)
A. Gender, n (%)	
Male	132 (21%)
Female	497 (79%)
B. Mean age, years (range)	
At the onset of symptoms	32.7 (14 - 88)
Average diagnostic delay	11 months (0 - 2)
C. Duration of disease before diagnosis, n (%)	
Less than 1 year	320 (51%)
1 - 5 years	270 (43%)
More than 5 years	39 (6%)
D. Tests	
Anti-TPO test†, n positive result/total (%)	19/434 (4.4%)
Serum Immunoglobulin E, n high/total (%)	83/524 (15.8%)
E. *Helicobacter pylori* infection, n positive result/total (%)	37/411 (9%)
F. UAS‡ at diagnosis, n (%)	
Score < 4	509 (81%)
Score ≥ 4	120 (19%)
G. Comorbidities	
Atopic	
Atopic dermatitis	69/629 (11%)
Food allergy	38/329 (11.6%)
Asthma	35/498 (7%)
Allergic rhinitis	70/498 (14%)
Others, n (%)	
Hypertension	44 (7%)
Diabetes mellitus	56 (9%)
Hyperlipidemia	50 (8%)
Coronary artery disease	11 (1.7%)
Depression	32 (5.1%)
Rheumatologic diseases	47 (7.5%)
Hypothyroidism	15 (2.4%)
Oncologic diseases	8 (1.3%)
H. Drug allergy	46 (7.3%)
NSAIDS⁋	26
Antibiotics	11
ACE-inhibitors¶	9

Abbreviations: †Anti-TPO, Anti-Thyroid Peroxidase; ‡UAS, Urticaria Activity Score; ⁋NSAIDS, Non-Steroidal Anti-Inflammatory Drugs; ¶ACE-inhibitors, Angiotensin Converting Enzyme inhibitors.

The majority of the 80 patients (12.7%) who presented with concomitant CSU and CIndU had symptomatic dermographism (89 percent, 71 patients), followed by cholinergic urticaria (8.7 percent, 7 patients) and solar urticaria (2.5 percent, 2 patients) (Table 1).

A laboratory profile was requested for all patients; however, a significant number of them had not yet completed it by the date data was collected. Consequently, the denominators for the cohorts where anti-TPO testing results, serum immunoglobulin E results, *Helicobacter pylori* infection results, and atopic comorbidities were identified vary. The record lacked pertinent information for certain patients. Fifteen of the 629 patients had changes in TSH and FT4 that were consistent with hypothyroidism, and 19 (4.4%) of the 434 whose anti-TPO antibodies test report was available, came back positive. Out of the 524 patients for whom this report was available, 83 had elevated serum immunoglobulin E (IgE) levels.

Helicobacter pylori test result was available for 411 patients; 37 (9%) had Helicobacter (*H. pylori*) infections (Table 2).

Antibiotics caused urticaria in 11 patients, ACE inhibitors in 9 patients, and non-steroidal anti-inflammatory drugs (NSAIDs) in 26 patients (Table 2).

When the CU group was explored, the following comorbidities were noted (Table 2): coronary artery disease (1.8%), depression (5.1%), rheumatologic diseases (7.5%), hypothyroidism (2.4%), hypertension (7%), diabetes mellitus (9%), hyperlipidemia (8%), and oncologic diseases (1.3%).

4. Discussion

In our study, we reported a large cohort of CU patients (n = 629) who were followed up with over a period of one year and five months at a specialized urticaria outpatient clinic of the Department of Dermatology, Farwaniya Hospital, Kuwait. These patients' clinical, laboratory, and demographic profiles are presented here.

12.7% of the evaluated patients had CIndU, while the majority had CSU. According to Maurer *et al.*'s evaluation of the prevalence and distribution of chronic urticaria in multiple countries, 66 to 93% of patients who presented with non-acute urticaria had CSU, 4 to 33% had CIndU, and cholinergic urticaria ranged from 1 to 7% [18]. The majority of patients who showed both CIndU and CSU also had symptomatic dermographism.

As observed, in our population, more than half of the patients were referred by general practitioners directly. We assume this trend might be due to the fact that, in our country, they represent primary health care and frequently the first medical contact, regardless of the severity of the disease. Additionally, data revealed referrals from a wide range of specialties, indicating that urticaria accounts for a sizable percentage of doctor visits and, as a result, its significance in routine practice across numerous specialties. This aligns with the findings of Caldeira LE *et al.* [16].

Most previous reports have demonstrated that women suffer from urticaria about twice as often as men do, based on highly selected patients from specialized

urticaria treatment centers [19]-[21]. In contrast, we identified that female patients outnumbered men by more than three times. The female preponderance might accurately reflect the demographic distribution, or it might be a reflection of women's superior health-seeking behavior. In addition, women might visit the clinic more frequently than men because they are more likely to be concerned about skin problems. Because adult men may not be able to attend special clinics or take part in active studies in medical centers during regular working hours, the prevalence of CU in men may be underestimated. Additionally, it has been noted that ill men often delay seeking help, which could lead to an underestimation of the proportion of male urticaria. Furthermore, the fact that female sex is recognized as a risk factor for autoimmune disease cannot be disregarded [22].

In our study, the average age at which CSU was presented was 32.7 years. According to a review by Niu *et al.* [23], this is comparable to other research done in hospital settings, indicating that CSU is primarily an adult-onset illness.

In a study conducted in Spain, Gaig *et al.* reported that 8.7% of patients had symptoms between one and five years, and 11.3% had symptoms longer than five years [24]. A prospective study involving 139 patients by Toubi *et al.* found that urticaria had lasted more than one year in over 70% of patients and over five years in 14% of the patients studied [25]. In our study, although slightly more than half of the patients received a diagnosis within a year of the onset of symptoms, the remaining patients experienced a diagnostic delay, with 43% of them experiencing symptoms for one to five years before a diagnosis of CSU was established, demonstrating the difficulty of appropriately diagnosing and managing this disease.

As mentioned before, in result section, certain laboratory results and data for the atopic comorbidities was not available at the time the record was accessed. For this reason, when discussing results pertaining to these laboratory parameters and for the cohort showing atopic diatheses, the percentages do not reflect the full cohort; the discussion merely refers to that cohort only, for which the result was available.

Histamine and other proinflammatory mediators are released by activated skin mast cells, which causes urticaria symptoms. Most forms of urticaria have unidentified underlying causes and mechanisms of mast cell activation. CU and autoimmunity are linked, as evidenced by the presence of IgG autoantibodies against IgE receptors or IgE and IgE anti-autoantigens, such as thyroid peroxidase (TPO), on the membranes of basophils and cutaneous mast cells [26] [27]. Given that autoimmune factors may be shared by both thyroid autoimmunity and urticaria, it is likely that both conditions will coexist in the same patient. Serum levels of thyroid autoantibodies were elevated in 4.4% of the patients for whom the report was available. The authors of a systematic review on CSU and autoimmune thyroid diseases discovered that the prevalence of elevated thyroid autoantibodies ranged from 3.7% to 37.1% [28].

Elevated serum IgE levels were documented in 83/524 (15.8%) of patients with available data on serum IgE levels. It is well known that mean IgE levels vary be-

tween men and women, between children and adults, and among populations with different genetic backgrounds and exposure to environmental factors [29]-[32]. More recent publications have shown that approximately half of CSU patients have higher than normal total IgE levels, ranging from 18% to 82% in various studies using different tests and cutoff levels [29]. It is also known that total IgE levels in patients with CSU are not as high as those in patients with allergies or atopic diseases. In our cohort of 524 patients, the prevalence of elevated total IgE was lower than that reported in some studies, which is consistent with the recognized heterogeneity of chronic urticaria; three factors could explain these findings. The predominance of type IIb autoimmune CSU, driven by IgG autoantibodies against IgE or FcεRI in our cohort, could explain the low prevalence. Our cohort had a low background rate of atopy, which may have reduced the proportion with elevated IgE. Third, geographic and population factors influence IgE. Studies from the MENA region have reported lower mean IgE in CSU compared to European cohorts, possibly reflecting differences in parasitic exposure, atopy prevalence, and genetic background [29].

In our study, *H. pylori* infection testing report was available for 411 patients and infection identified in 37 (9%). A study found that the prevalence rate of *H. pylori* infection was 40.81% in controls and 49.74% in the chronic urticaria group [33]. Nevertheless, the correlation between *H. pylori* infection and CSU has a lot of disagreement. A higher prevalence of *H. pylori* infection has been reported in chronic urticaria patients in several studies, and some studies have documented skin lesion remissions following eradication therapy [34]-[36]. Other studies, however, corroborated the idea that there is no connection between *H. pylori* infection and CU, while other research revealed no association between *H. pylori* and alleviation of urticarial symptoms [37].

Even though *H. pylori* eradication has been recommended as part of routine chronic urticaria management by multiple authors, the evidence that *H. pylori* eradication leads to improvement of chronic urticaria outcomes is weak and conflicting [38]. Considering the low prevalence of *H. pylori* infection in our 411-patient cohort with chronic urticaria, we concur with Shakouri *et al.* [38] that before assessing and treating *H. pylori* the possible risks, costs, and advantages of this therapeutic intervention as well as the values and preferences of the patient must be taken into account. Additionally, we presume that instead of being a standard recommendation, *H. pylori* eradication should be carefully and individually considered. Low prevalence of *H. pylori* infection in our cohort suggests it is unlikely to be a major driver of chronic urticaria in our population; or at least it is not a predominant trigger. The pathogenesis of chronic urticaria in our cohort is more likely related to other mechanisms-autoimmune type I/type IIb, etc.

Up to 40% of CSU patients have exacerbations after taking NSAIDs [39]. In our study sample, we have verified NSAIDs were a trigger to urticaria in 26 (4%) patients; ACE inhibitors and antibiotics were among the other medication triggers found. There have been previous reports of a similar range of drug triggers [11].

CU patients have a significant overrepresentation of atopic diseases [40]. In our study, among the various atopic disorders documented, atopic dermatitis was identified in 69/629 (11%), food allergy in 38/329 with available data on food allergy (11.6%), asthma in 35/498 with available data on asthma (7%) and allergic rhinitis in 70/498 with available data on allergic rhinitis (14%). In our study, the percentage is significantly lower than the over 90% of CU patients who had a personal history of atopic disease reported by Nassif *et al.* [41]. Although the percentage in our study was lower, our findings are consistent with those of others who have documented links between CU and atopic conditions, such as atopic dermatitis, allergic rhinitis, and asthma [16]. Significant correlations between CU and asthma, atopic dermatitis, and allergic rhinitis were found in two recent cross-sectional studies involving 11,217 and 12,185 patients, respectively [40] [42].

There is growing evidence that abnormal immune function is linked to CU and atopic conditions. Although there are studies that refute these theories [43], its association might be a reflection of abnormal crosstalk between mast cells and T-helper cells [44]. We believe that these conditions may have complex interrelationships that need further study.

According to a prior study, the CU group had higher rates of depression (4.4%), osteoporosis (2.9%), atopic dermatitis (2.5%), rhino-conjunctivitis (2.9%), and diabetes mellitus (2.3%) [40]. We discovered that diabetes mellitus, hyperlipidemia, rheumatologic disorders, and hypertension were more common in our CU patients. According to a systematic review by Kolkhir *et al.*, hypothyroidism is more prevalent than hyperthyroidism at CSU [28], which is consistent with our results. According to reports, 6.6% to 29.4% of people have mood disorders, including depression [45] [46]; in our study, we discovered signs and symptoms of depression in 5.1% of cases. According to reports, patients with chronic spontaneous urticaria have a higher risk of solid cancer (4.9% vs. 2.6%) than age- and sex-matched controls without urticaria [8]. Oncologic diseases were found in 1.3% of our study participants.

5. Conclusion

According to the majority of previously published research, the clinical profile of chronic urticaria appears to be comparable here. Compared to similar published reports from other locations, a smaller proportion of patients in our population had elevated IgE levels among the patients whose data was available. Atopic diseases were associated with chronic urticaria patients among our population; however, they were not so overrepresented as in other populations. *H. pylori* infection was identified in a small percentage of patients where the data was available. Additionally, drugs were not identified as a common precipitating factor. Due to varying completeness of documentation, frequencies are reported with their specific denominators. While these percentages allow us to describe the clinical profile of patients with chronic urticaria presenting to this single center, they do not allow for assessment of risk, association, or causality, and any extrapolation beyond this

setting should be made with caution. Although it is important to explore precipitants peculiar to this environment, as such knowledge may help in abating the symptoms in affected patients, a thorough history is still the most important guiding factor in the assessment of patients with chronic urticaria, as this approach will reduce the need for extensive investigations.

6. Study Limitations

This study may be more representative of individuals with more severe and prolonged disease because it was conducted in a tertiary care hospital; the circumstances may differ from those available for a community-based study. Additionally, the absence of provocative tests may lead to an inaccurate representation of the physical factors.

Ethics Approval

This study was conducted in accordance with the Declaration of Helsinki and received approval from the Ministry of Health's Standing Committee for Coordination of Health and Medical Research [approval number: 2794/2024].

Patient Consent

Written informed consent was obtained from all participants prior to enrollment, allowing the use of their clinical data for research purposes. All data were anonymized to protect patient privacy.

Permission to Reproduce Material

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Clinical Trial Registration

This study is observational/descriptive and not a clinical trial; therefore, registration was not required.

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Author Contributions

AAA, AKS and MRA designed the study and wrote the manuscript. MRA contributed to data collection. All authors read and approved the final manuscript.

Conflicts of Interest

The authors have no financial support or relationships that may pose a conflict of interest.

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Abbreviations

CU, chronic urticaria;
CSU, chronic spontaneous urticaria;
CIndU, chronic inducible urticaria;
IgE, immunoglobulin E;
aiCSU, autoimmune chronic spontaneous urticaria;
FcεRI, high-affinity receptor for the Fc region of immunoglobulin E;
ESR, erythrocyte sedimentation rate;
CRP, C-reactive protein;
TSH, thyroid-stimulating hormone;
FT4, free T4;
TAA, thyroid autoantibodies;
TPO, thyroid peroxidase;
ANA, antinuclear antibodies;
MAST, multiple antigen simultaneous testing;
NSAIDs, non-steroidal anti-inflammatory drugs;
ACE, angiotensin-converting enzyme;
HIS, hospital information system.