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Clinicodemographic Profile of Adult Patients With Chronic Urticaria in an Allergy Specialty Clinic: A Five-Year Review (2019 to 2023)

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ABSTRACT

Background: There is variability among the prevalence and characteristics of chronic urticaria.

Objectives: This study aimed to determine clinicodemographic characteristics of adult patients diagnosed with chronic urticaria in an allergy clinic in Metro Manila, Philippines, from 2019 to 2023.

Methodology: A cross-sectional review of medical records from patients aged 19 and above at an allergy clinic in Metro Manila was conducted from 2019 to 2023. Clinicodemographic features, along with their frequencies and percentages, were obtained.

Results: Seventy-five patients with chronic urticaria were investigated. The majority were women (72%) aged 30 to 39 (30.7%) from the National Capital Region (85.3%). Most were married (36%), college graduates (30.7%), and employed (54.7%), with 62.7% seeking their initial consultation 2 to 12 months after the onset of the disease. Fifty-seven percent of patients had a personal history of atopy and 54.7% had a family history of atopy. Thirty-seven percent of patients had comorbidities, with hypertension as the most frequent (18.7%). Thirty-three percent of patients were suspected with chronic inducible urticaria with dermographism as the most common suspected trigger (21.3%). Fifty-eight percent of patients had urticaria before COVID-19 vaccination, while 42% had a previous history of COVID-19 vaccine before the onset of symptoms. However, no further tests were done to confirm its association with the disease. Fifteen patients underwent skin prick tests, and all demonstrated positive skin test reactivity to some form of aeroallergen or food allergens. All patients were given second-generation H1-antihistamine at varying doses. The majority of patients (65.3%) reported an improvement in symptoms. Only 26.7% of patients used the 7-day Urticaria Activity Score, while 29.3% used the Urticaria Control Test to monitor their symptoms.

Conclusion: The prevalence of chronic urticaria (13%) was higher than the global estimate of 1%. Most chronic urticaria patients were female, aged 30 to 39, married, college graduates, and employed who showed symptoms within 2 to 12 months after the onset of the disease. Approximately 50% of them had a personal and family history of atopy. Most patients do not have comorbidities and suspected inducible triggers. All patients who underwent skin prick tests showed reactivity to some allergens (aeroallergens, food allergens). All patients were given second-generation H1-antihistamines at varying doses. Many patients experienced symptom improvement with the prescribed medications despite poor compliance with the recommended monitoring tools. According to clinical history, the onset of chronic urticaria was not attributed to COVID-19 vaccination in most cases.

Keywords: urticaria, prevalence, clinicodemographic features



INTRODUCTION

Chronic urticaria (CU) is a skin condition that appears worldwide, affects all ages, and may last up to several years.¹ It is an inflammatory mast cell-derived disorder that presents with recurrent transient pruritic wheals, with or without angioedema, lasting more than six weeks.^{2,3} It is classified into chronic spontaneous urticaria (CSU), wherein the etiology is either uncertain or of a possible autoimmune origin, and chronic inducible urticaria (CIU), wherein physical factors such as contact, pressure, vibration, heat, cold, or aquagenic may be responsible.⁴ CSU is further classified into chronic spontaneous urticaria autoimmune type I (Type I aiCSU) and chronic spontaneous urticaria autoimmune type IIB (Type IIB aiCSU). Other possible triggers for chronic urticaria include infections and food proteins.²

Though wheals may be seen as a superficial problem in the dermis, urticaria is still a burdensome disease for patients and health systems. For patients, quality of life can be significantly impaired, manifesting with bothersome pruritus, struggles in sleep, compromised work and productivity, and even difficulties in social interactions. This may result in significant limitations in daily life.^{1,5} Chronic urticaria, a prolonged disease, can take up medical resources and incur significant treatment costs, leading to other direct and indirect socioeconomic effects.⁵

In 2018, urticaria was previously estimated to have a prevalence rate of 2.29% in the Philippines, although more recent data assessing its local prevalence has been lacking.^{1,6} Urticaria is estimated to affect 1% of the world's population, 0.1% in North America, 0.5% in Europe, 1.4% in Latin America, and 1.5% in Asia. Global trends, however, imply that the prevalence may be greater, having increased by 2- to 10-fold worldwide in the previous 10 years. All ethnicities are affected, but different populations may yield different frequencies due to genetics or lifestyle.⁵ Environmental factors, such as geographical characteristics, may play a role in chronic urticaria, as can a history of atopy and autoimmunity.⁷

Additionally, since 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections have triggered the COVID-19 pandemic, further exacerbating global public health crises and affecting patients with chronic urticaria.⁸

Exploring the underlying cause of chronic urticaria is crucial, as addressing the root problem and potential risk factors may alleviate symptoms.⁹ However, local data on this issue are currently lacking.² This study assesses the clinical and demographic characteristics of adult patients diagnosed with chronic urticaria in a local allergy specialty clinic from 2019 to 2023.

Pathogenesis of Chronic Urticaria

Chronic Urticaria is primarily an illness that is mast cell-driven. Histamine and other mediators (i.e., cytokines and platelet-activating factor) released from skin mast cells lead to the activation of sensory nerves, vasodilation, plasma extravasation, and cell recruitment to the sites of the urticarial lesions. The signals activating mast cells are heterogeneous and diverse, including T cell-driven cytokines and autoantibodies. Wheals have shown a mix of inflammatory perivascular infiltrates: T cells, eosinophils, basophils, and other cells. Non-lesional skin of CU patients has shown increased adhesion molecules, infiltrating eosinophils, altered cytokine expression, and occasionally a mild-to-moderate proliferation of numbers of mast cells. This highlights the complex nature of urticaria pathogenesis. Some of these features of urticaria are also present in other inflammatory conditions and may be neither of specific nor of diagnostic value; thus, a search for more specific histological biomarkers to identify varying urticaria subtypes and to distinguish urticaria from other conditions is needed.¹⁰

Clinical and Demographic Data in Different Regions

Global trends have consistently shown that chronic urticaria is more common among women, with female to male ratio reported around 2:1.^{1,5,11-15}

The average age of onset appears to be late twenties to forties.⁴ In Spain and Korea, it is at approximately 40 years of age.^{12,16} In a Portugal study, the median age of onset was 44.5 ± 14.9 years of age.¹⁴ In Nigeria, the median age of onset was 31.1 ± 13.3 years, with peak age at onset around 30 years old.² In the United States, the age of onset has been averaged to be around the thirties to fifties.¹¹

Allergic disease exists in patients with CU at a higher rate than in the general population, but rates appear to vary. Co-expression of allergic diseases is more common in patients with chronic urticaria than in the general population in the United States.¹¹ In Portugal, they found that the frequency of comorbid allergic diseases was 21.3% for asthma, 29.5% for patients with rhinitis, and 32.8% for those with asthma and allergic rhinitis.¹⁴ In Korea, when analyzing CU patients, the allergic disease was present more often in children (15.7%) than in adults (7.1%). In comparison, a family history of atopic diseases was found in 16.2% of children with CU and 2.6% of adults with CU.^{12,17} In Taiwan, the rate of allergic diseases in CU patients was much higher. Fifty percent of patients had allergic diseases, with the most common allergic disease being allergic rhinitis (45.2%), followed by asthma (8.1%), allergic conjunctivitis (8.1%) and atopic dermatitis (4.8%).¹³ Although both are Asian countries, it remains unclear whether the large difference in the rates of allergic diseases in chronic urticaria is due to regional and environmental differences.

Studies have shown that the most common type of CIU is symptomatic dermatographism, followed by cold and delayed pressure urticaria.^{5,7} The median age of onset was usually 40 years old.⁵

Autoimmune thyroid disease is the most common autoimmune disease associated with CU globally. Other autoimmune diseases that appear to have higher prevalence among CU patients are systemic lupus erythematosus (26.7 times greater risk), type I diabetes mellitus (1.8%), vitiligo (0.4%), celiac disease and rheumatoid arthritis (0.6%).⁵

Other comorbidities associated with chronic urticaria include depression, with or without anxiety disorder, as seen in 48 of 61 patients with refractory chronic urticaria in Portugal.¹⁴ Given the debilitating nature of CU, this finding is not surprising and reflects a global trend.⁵

In another study carried out in Portugal, hypertension, type 2 diabetes, and obesity were detected in 19 out of 61 patients.¹⁴ Potential links among hypertension, obesity, and chronic urticaria have been observed globally, and some reports have indicated a higher frequency in dyslipidemia and metabolic syndrome.^{5,18}

Infections have also been linked to CU, such as but not limited to infections with *Helicobacter pylori*, parasites, and chronic viral infections (Hepatitis B and C viruses, Human Herpes virus).^{5,9,14} With the recent onset of the COVID-19 pandemic, little is known about its association with chronic urticaria.¹⁹ However, when assessing patients with a prior diagnosis of CU who were later infected with the SARS-CoV-2 virus, 44% developed greater severity of their urticarial symptoms.¹⁵ Likewise, not much is known if COVID-19 vaccines would have any effect on chronic urticaria. A case series reported that eight patients were diagnosed with CU following vaccination against COVID-19 disease. Wheals with or without angioedema were first noted in 6 patients after the first dose and two after the second dose. Three patients had received BNT162b2 vaccine (Pfizer/BioNTech), four had received ChAdOX1 nCoV-19 vaccine (AstraZeneca), and one had received messenger RNA-1273 vaccine (Moderna). However, due to a lack of data, the researchers concluded that disease onset post-vaccination could still be coincidental.²⁰ A study assessing patients previously diagnosed with CSU before vaccination against COVID-19 disease found that of 130 vaccinated, approximately 15% noted exacerbation of urticaria after the first dose. In that study, sixty-five percent received Adenoviral vaccines, and 34.6% received inactivated vaccines.²¹

There have also been reports that hematologic, papillary thyroid, and lung cancers may be linked to CU, but these are allegedly rare.⁵

Diagnostic Tests

In studies evaluating allergen sensitization in CU patients, house dust mites were the most common allergen in Taiwan and Colombia.^{7,13} Sensitization to milk, egg, pork, fruit, and vegetables was also assessed in Colombia; however, no clinical relevance was found.⁷

In chronic inducible urticaria, testing is limited to confirmation of the suspected trigger by provocation testing.¹⁰ Burks et al. stated that among CIU patients, there are two subsets of physical urticaria: 1) those elicited by dermatographism, cold, heat, delayed pressure, solar, and vibration that tend to localize to the area of stimulus, and 2) those elicited by contact, aquagenic and cholinergic stimuli that tend to be generalized.

Most cases of chronic urticaria, however, have no discernible nor definitive external allergic cause or contributing disease process. These are referred to as chronic spontaneous urticaria (CSU).¹¹ In CSU, the diagnostic workup aims to (1) confirm the diagnosis while excluding differential diagnoses; (2) identify underlying causes; (3) detect pertinent conditions that could modify disease activity; (4) assess comorbidities; (5) note potential consequences of CSU; (6) evaluate predictors of the course of the disease and response to treatment; and (7) monitor and control the disease activity and its impact on daily life.^{10,21}

The diagnostic workup for CSU includes a thorough history, physical examination, and basic tests, which may consist of differential blood count, C-reactive protein level (CRP), erythrocyte sedimentation rate (ESR), total immunoglobulin E (IgE), and immunoglobulin G (IgG)-anti-thyroid peroxidase (TPO) levels. Further diagnostic evaluations can be pursued after completing the history, physical examination, and basic tests.

Among 245 patients with CSU in a study conducted in Colombia, 93 patients tested positive for autologous serum and plasma skin tests when evaluated for self-reactivity.⁷ Five of 60 patients (8.3%) in Taiwan have been noted to have autoantibodies to the thyroid, while 29.6% of patients had elevated inflammatory markers.¹³ Autoimmune markers were found in 45.2% of 42 tested adult patients in Portugal who had chronic urticaria, with one-third testing positive for anti-nuclear antibodies (ANA). Among those who were ANA positive, 21.4% of patients had autoimmune thyroid disease.¹⁴ Autoimmune thyroid disease was noted in 6.7% (4 of 60) of patients with CU in a study conducted in Nigeria.²

Biopsy of urticarial lesions showed the presence of mast cells that have degranulated in the dermis and perivascular leukocyte infiltrates comprising eosinophils, basophils,

neutrophils, and lymphocytes. Histamine levels were also elevated in these biopsied samples.

Treatment

The primary goal of treatment is to achieve complete relief of symptoms. However, according to a consensus by the Asian Academy of Dermatology and Venereology Study Group in collaboration with the League of Asian Dermatological Societies in 2010, spontaneous remission can occur at any time despite the variations in severity.⁹

In patients with chronic spontaneous urticaria (CSU), on average, only about half may have a satisfactory response to non-sedating antihistamines at standard or even up to fourfold doses. This percentage may be even lower in the presence of angioedema, as response rates vary significantly across different studies. CSU patients with high-normal or elevated IgE levels have been found to respond more effectively to omalizumab. In contrast, those with low or very low serum IgE levels tend to have a slower response to omalizumab but respond well to cyclosporine.⁵

Due to recurrent exacerbations, variable responses to treatment, and fluctuating signs and symptoms, patient-reported outcome measures (PROM) have been developed to assess the disease impact, activity, and control of chronic urticaria.²² PROMs are tools for patients to evaluate their health status from their perspectives and improve the accuracy of disease evaluation, treatment outcomes, and prognosis of patients.^{22,23} The 7-day Urticaria Activity Score (UAS7) and the Urticaria Control Test (UCT) have been among the PROMs of choice for chronic spontaneous urticaria in the EAACI/GA²LEN/EDF/WAO guidelines in 2014 and 2018, respectively. However, literature regarding their validity in the Philippines appears to be lacking.^{22,25-27} For the UAS7, patients score the severity of their hives and pruritus, then calculate the sum after seven days.^{25,28,29} The UCT questionnaire is a 4-item retrospective tool used to assess urticaria control over the past 4 weeks.^{25,26} Despite guidelines recommending these PROMs, in a global study investigating real-world use of PROMs-related chronic urticaria in dermatology and allergology clinics, only 15% of physicians used PROMs for chronic urticaria due to the time constraints in assessing patients and the impression that patients dislike PROMs.²² However, in an American study analyzing patient's willingness to accomplish PROMs for breast cancer, 88% of patients were amenable to using PROMs, contradicting the idea that patients have a general dislike for PROMs.³⁰ A single hospital study on patients' compliance with UAS7 in Korea found that the average compliance rate of their subjects with UAS7 was 29.8%.²⁴ In the Philippines, data regarding patients' compliance towards chronic urticaria PROMs appear lacking.

OBJECTIVES

General Objective

To determine the demographic and clinical characteristics of adult patients (19 years old and above) diagnosed with chronic urticaria in an allergy specialty clinic in Metro Manila from 2019-2023.

Specific Objectives

1. To describe the demographic profile of patients with chronic urticaria:
 - A. Age
 - B. Sex
 - C. Residence
 - D. Marital status
 - E. Educational attainment
 - F. Employment status
2. To describe the clinical profile of patients with chronic urticaria:
 - A. Disease duration at the time of the initial consult
 - B. Suspected inducible triggers
 - a. None
 - b. Dermographism
 - c. Heat
 - d. Cold
 - e. Cholinergic
 - f. Aquagenic
 - g. Vibratory
 - h. Solar
 - i. Delayed pressure
 - j. Contact
 - C. History of angioedema
 - a. Present
 - b. Absent
 - D. Personal history of atopy
 - a. None
 - b. Atopic dermatitis
 - c. Asthma
 - d. Allergic rhinitis
 - e. Both allergic rhinitis and atopic dermatitis
 - f. Both asthma and allergic rhinitis
 - g. Both asthma and atopic dermatitis
 - E. Family history of atopy
 - a. Present
 - b. Absent
 - F. Comorbidities as diagnosed by a physician
 - a. None
 - b. Hypertension
 - c. Dyslipidemia
 - d. Diabetes mellitus type 2
 - e. Autoimmune diseases such as autoimmune thyroiditis
 - f. Thyroid disease without workup for autoimmunity
 - g. Malignancy

- h. Anxiety
- i. Depression
- j. Infection
- G. Patient compliance with UAS7 and UCT monitoring
 - a. Done
 - b. Not done
- H. Outcome as reported by the patient in terms of improvement of symptoms (pruritus or wheals)
 - a. Improved
 - b. Not improved
 - c. Lost to follow up
- I. Dosage of **second-generation** H1-antihistamines on last follow-up
- J. Allergy test
 - a. Skin prick test
 - i. Done
 - ii. Not done
 - b. Serum-specific IgE (ImmunoCAP FEIA)
 - i. Done
 - ii. Not done
- K. Autologous serum skin test
- L. COVID-19 vaccine prior to symptom onset
 - a. None
 - b. COVID-19 mRNA Vaccine (nucleoside modified) [Pfizer-BioNTech/Comirnaty®]
 - c. ChAdOx1-S (recombinant) [Vaxveria™]
 - d. SARS-CoV-2 Vaccine (Vero Cell), Inactivated [CoronaVac™]
 - e. COVID-19 mRNA Vaccine (nucleoside modified) [COVID-19 Vaccine Moderna]
 - f. COVID-19 Vaccine Ad26.COV2-S (recombinant) [Janssen]
 - g. Sputnik V/Sputnik Light Gam-COVID-Vac
 - h. Whole Virion, Inactivated Corona Virus Vaccine [COVAXIN®]
 - i. SARS-CoV-2 rS Protein Nanoparticle (Recombinant) [Covovax™]
- M. To determine the prevalence of urticaria (acute and chronic) among adult patients seen at the allergy clinic

METHODOLOGY

Study Design

This is a cross-sectional design chart review of patients' medical records from an allergy specialty clinic in Metro Manila.

Study Population and Data Collection

Adult patients aged 19 and above diagnosed with chronic urticaria at an allergy specialty clinic in Metro Manila from January 2019 to December 2023 were included in the study, and their charts were reviewed. Patients were interviewed and followed up by fellows-in-training within the clinic. Patients with incomplete charts were excluded.

The following data were obtained:

1. Age
2. Sex
3. Residence
4. Disease duration at the time of consult
5. Suspected inducible triggers
6. History of angioedema
7. Personal history of atopy
8. Family history of atopy
9. Comorbidities as diagnosed by a physician
10. Patient compliance with UAS7 and UCT monitoring, as noted in the patient's charts
11. Outcome, as reported by the patient
12. Diagnostic tests:
 - Skin prick test
 - Serum-specific IgE (ImmunoCAP FEIA)
 - Autologous serum skin test
13. COVID-19 vaccine prior to symptom onset

Skin Prick Test

A trained allergist and/or fellow-in-training performed a skin test with certain-aeroallergens and food allergens. Physiologic saline was utilized as the negative control, and histamine (1.0 mg/mL) as the positive control.

The skin of the volar arm, at least 3 cm distal to the antecubital fossa and 5 cm proximal to the wrist or the upper back, was sterilized with alcohol and air-dried. Marks were placed 2 to 2.5 cm apart on the skin to indicate where the saline, histamine, and allergens would be applied. Separate sterile blood lancets were dipped into the allergen extracts and positive and negative controls and then gently pressed into the skin at a 45 to 60-degree angle. The skin was gently lifted to create a break where the solutions could penetrate the epidermis. After 15 to 20 minutes, the wheal diameter was measured horizontally and vertically and recorded in millimeters.

Statistical Analysis

A total enumeration of cases was conducted to determine the sample size. Frequencies and proportions were used to assess the prevalence of chronic urticaria and the various clinicodemographic characteristics of the patients.

Ethical Considerations

The study protocol was reviewed and approved by the ethics committee of the allergy clinic's institution before implementation. The privacy and anonymity of the patient subjects were maintained during the study, and data were stored and disposed of securely. This study followed the National Ethical Principles for Health and Health-Related Research 2017, the Declaration of Helsinki, Good Clinical Practice, and other national and international principles governing research involving human subjects.

RESULTS

Five hundred fifty-seven adult patients were seen at the Allergy Unit's outpatient department from 2019 to 2023. One hundred seventy-one were diagnosed with urticaria (31%).

Figure 1 shows the number of patients seen yearly from 2019 to 2023. Most patients were seen and assessed as having urticaria in 2022 (n = 56, 32.7%).

As shown in Figure 2, 17% (n = 96) were diagnosed with acute urticaria and 14% (n = 75) with chronic urticaria.

Table 1 shows the demographic data of patients seen and assessed with chronic urticaria. Of these, 28% were male, while 72% were female. Most patients were from the National Capital Region (n = 64, 85.3%).

Twenty-three patients diagnosed with chronic urticaria (30.7%) were 30 to 39 years old at the time of the initial consult. Many of them were married (n = 27, 36%), employed (n = 41, 54.7%), and college graduates (n = 23, 30.7%).

Table 2 shows the frequency of patients' disease duration at the initial consult and the presence or absence of angioedema. Forty-seven patients (62.7%) sought consultation within 2 to 12 months after the onset of the disease. Fifty-three patients (70.7%) did not have coinciding angioedema.

Table 3 shows patients' comorbidities, personal history of atopy, family history of atopy, and COVID-19 vaccination prior to the onset of symptoms. Forty-three patients (57.3%) had some form of personal history of atopy, with allergic rhinitis (n = 18, 24%) as the most common

Table 1. Demographic data of patients with chronic urticaria from 2019 to 2023

Characteristics	N=75	
	Frequency (n)	Percentage (%)
Age (years)		
19 to 29	18	24.0
30 to 39	23	30.7
40 to 49	19	25.3
50 to 59	5	6.7
≥60	10	13.3
Sex		
Male	21	28.0
Female	54	72.0
Residence		
National Capital Region (NCR)	64	85.3
Outside of NCR	11	14.7
Marital status		
No answer	32	42.7
Single	16	21.3
Married	27	36.0
Widowed	0	0.0
Employment status		
No answer	26	34.7
Employed	41	54.7
Unemployed and looking for work	1	1.3
Student	3	4.0
Housewife	2	2.7
Retired	2	2.7
Educational attainment		
No answer	45	60.0
Elementary undergraduate	0	0.0
Elementary graduate	0	0.0
High school undergraduate	0	0.0
High school graduate	1	1.3
College undergraduate	2	2.7
College graduate	23	30.7
Graduate degree acquired	4	5.3

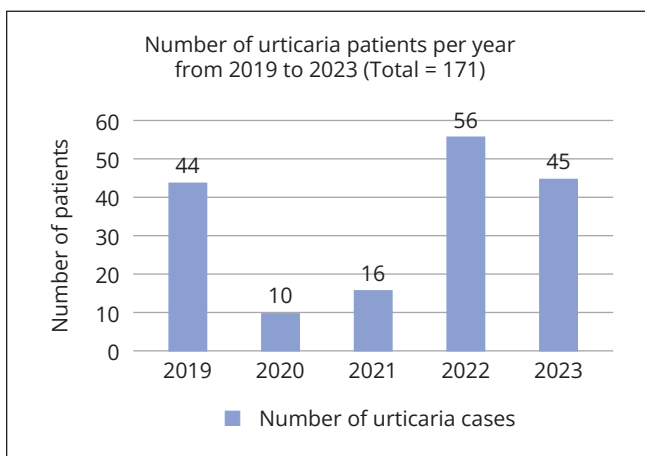


Figure 1. Number of urticaria patients seen per year from 2019 to 2023.

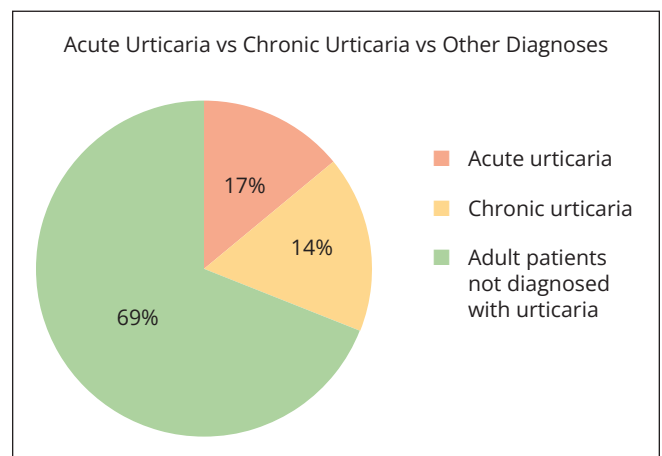


Figure 2. Acute vs chronic urticaria.

Table 2. Disease duration at the time of initial consult and history of angioedema

	Frequency (n)	Percentage (%)
Disease duration at the time of initial consult (months)		
2 to 12	47	62.7
13 to 24	4	5.3
25 to 36	3	4.0
37 to 48	2	2.7
49 to 60	1	1.3
61 to 72	3	4.0
>72	15	20.0
History of angioedema		
Present	22	29.3
Absent	53	70.7

concurrent atopic disease, followed by bronchial asthma (n = 9, 12%), patients with both bronchial asthma and allergic rhinitis (n = 6, 8%), patients with both allergic rhinitis and atopic dermatitis (n = 5, 6.7%), and then patients with atopic dermatitis (n = 4, 5.3%). Likewise, forty-one patients (54.7%) had a family history of atopy. Forty-seven patients (62.7%) had no other comorbidity. Of the other comorbidities present, hypertension was the most common (n = 15, 18.7%), followed by DM type 2 (n = 4, 5.3%), and at equal numbers, dyslipidemia, autoimmune diseases (autoimmune thyroiditis and antiphospholipid antibody syndrome), hypothyroidism, and malignancy (n = 2, 2.7%), then depression (n=1, 1.3%). Two patients with breast cancer were incidentally noted. Patients who were seen to have a personal history of hypothyroidism were not reported to have had previous workups for autoimmune thyroiditis. Forty-four patients (58.7%) were not vaccinated before the onset of the disease, with 32% seen before the COVID-19 vaccine rollout in March 2021 and 26.7% seen after the rollout. Twenty patients (26.7%) were vaccinated before the onset of symptoms. One of them developed urticaria within 24 hours after the 2nd dose of the vaccine (ChAdOx1-S[recombinant] VAXZEVRIA™).

Table 4 shows the frequency of suspected inducible triggers. Fifty patients (66.7%) had no suspected inducible triggers. For patients suspected of having chronic inducible urticaria, dermographism was the most common trigger (n = 16, 64%), followed by delayed pressure (n = 4, 16%), cholinergic (n = 3, 12%), cold (n = 1, 4%), and heat (n = 1, 4%). Table 5 shows the frequency of positivity to the skin prick test. Fifteen patients with chronic urticaria underwent a skin prick test. No patients underwent testing for serum-specific IgE (ImmunoCAP FEIA) or total IgE. Ten patients (66.7%) who underwent skin prick tests had concomitant atopic disease. All patients who underwent skin prick test had multiple sensitizations with grass pollen as the most common positive finding (73.3%), followed by house dust

Table 3. Comorbidities as diagnosed by a physician, personal and family history of atopy, and COVID vaccine prior to symptom onset

	N = 75	
	Frequency (n)	Percentage (%)
Family history of atopy		
Present	41	54.7
Absent	34	45.3
Personal history of atopy		
None	32	42.7
Atopic dermatitis	4	5.3
Bronchial asthma	9	12.0
Allergic rhinitis	18	24.0
AR + AD	5	6.7
BA + AR	6	8.0
BA + AD	1	1.3
Comorbidities as diagnosed by a physician		
None	47	62.7
Hypertension	15	20.0
Dyslipidemia	2	2.7
DM type 2	4	5.3
Autoimmune disease (Antiphospholipid antibody syndrome; autoimmune thyroiditis)	2	2.7
Thyroid disease (Hypothyroidism)	2	2.7
Malignancy	2	2.7
Anxiety	0	0.0
Depression	1	1.3
Infection	0	0.0
COVID-19 vaccine prior to symptom onset		
None (seen before March 2021)	24	32.0
None (seen after March 2021)	20	26.7
No answer	15	20.0
Pfizer-BioNTech/Comirnaty® COVID-19 mRNA Vaccine (nucleoside modified)	9	12.0
ChAdOx1-S[recombinant] VAXZEVRIA™ (COVID-19 Vaccine AstraZeneca)	2	2.7
SARS-CoV-2 Vaccine (Vero Cell), Inactivated [CoronaVac™]	3	4.0
COVID-19 mRNA Vaccine (nucleoside modified) [COVID-19 Vaccine Moderna]	5	6.7
Janssen COVID-19 Vaccine (Ad26.COV2-S (recombinant))	1	1.3
G. Sputnik V/Sputnik Light Gam- COVID-Vac /Sputnik Light	0	0.0
Whole Virion, Inactivated Corona Virus Vaccine [COVAXIN®]	0	0.0
SARS-CoV-2 rS Protein Nanoparticle Vaccine [[Covovax™]]	0	0.0

Table 4. Frequency of suspected inducible triggers

	Frequency (n)	Percentage (%)
Presence or absence of suspected inducible trigger		
None	50	66.7
Present	25	33.3
Suspected inducible trigger		
	N = 25	
Dermographism	16	64.0
Heat	1	4.0
Cold	1	4.0
Contact	0	0.0
Cholinergic	3	12.0
Aquagenic	0	0.0
Vibratory	0	0.0
Solar	0	0.0
Delayed Pressure	4	16.0

Table 5. Frequency of positivity to skin prick test

	Positive	Percentage (%)
SPT to Aeroallergens		
Cockroach	8	53.3
House dust mite	9	60.0
Grass pollen	11	73.3
Tree pollen	8	53.3
Kapok	2	13.3
Dog dander	3	20.0
Cat dander	6	40.0
Mixed molds	3	20.0
SPT to Food Allergens		
Shellfish	10	66.7
Fish	3	20.0
Fruit	5	33.3
Vegetable	7	46.7
Peanut	4	26.7
Poultry	4	26.7
Beef	2	13.3
Pork	2	13.3
Total number who were tested for Specific IgE via SPT	15	

mite (n = 9, 60%), cockroach and tree pollen (n = 9, 53.3%), cat dander (n = 6, 40%), mixed molds and dog dander (n = 3, 20%), and kapok (n = 2, 13.3%). Among food allergens, shellfish was the most common positive finding (66.7%), followed by vegetable (n=7, 46.7%), fruit (n=5, 33.3%), peanut and poultry (n=4, 26.7%), fish (n=3, 20%), beef and pork (n=2, 13.3%). Of the 15 patients, only 2 underwent autologous serum skin test, and only one tested positive.

Table 6 shows the outcomes and compliance with the 7-day Urticaria Activity Score (UAS) and Urticaria Control Test (UCT). Forty-one patients (54.7%) were given the regular recommended dose of second-generation H1-antihistamines, ten patients (13.3%) were given twice the

Table 6. Outcomes and compliance with 7-day Urticaria Activity Score (UAS) Urticaria Control Test (UCT)

	N=75	
	Frequency (n)	Percentage (%)
UAS7		
Done	20	26.7
Not done	55	73.3
UCT		
Done	22	29.3
Not done	53	70.7
Dosage of antihistamines on last follow up		
As needed	16	21.3
1x dose	41	54.7
2x dose	10	13.3
3x dose	0	0.0
4x dose	3	4.0
2x dose + Omalizumab	1	1.3
Outcome		
Improved	49	65.3
Not improved	6	8.0
Lost to follow up	20	26.7

regular dose of the antihistamines, four patients (4%) were given 4x the regular dose of the antihistamine. One patient (1.3%) was given omalizumab and 4x the regular dose of the antihistamine. To monitor the treatment outcomes, UAS7 was done by 20 patients (26.7%), while UCT was done by 22 (29.3%). Forty-nine patients (65.3%) improved with the prescribed medications, although 6 of them (8%) did not. Twenty patients (26.7%) were lost to follow-up.

DISCUSSION

The prevalence of chronic urticaria has significant regional differences on an international level.¹ Our study provides new epidemiological information on chronic urticaria. No recently published local data are available to compare our study as of the time of writing.

In 2019, the Asian point prevalence of chronic urticaria for children and adults was estimated to be 1.4%, while the global prevalence was approximately 1%.¹ In our study, the prevalence of chronic urticaria is 13%. There may be some bias in our results, as this data was taken from a clinic that caters specifically to allergies. It has been postulated that chronic urticaria prevalence rates have increased over the years.¹ However, this was not reflected in our data, which may be due to the onset of the COVID-19 pandemic, when access to healthcare services became more difficult.

Our study supports the foreign literature that chronic urticaria is more common in women than in men^{5,11,31} and adults aged 30 to 39.^{5,11,12} Though the reason for the prevalence by age of chronic urticaria remains unclear,

the difference in gender has been postulated to be due to the effects of sex hormones and autoimmunity.¹² Autoimmunity in CSU has been theorized to be due to two mechanisms. Type I autoimmune CSU is due to the release of IgE antibodies to autoantigens, leading to activation of mast cells, while Type IIb autoimmune CSU is triggered by IgG autoantibodies targeting IgE antibodies or their high-affinity receptors.^{5,28}

Our study showed that most patients reside in the National Capital Region (NCR). This may be attributed to the accessibility of our institution, as it is located in the NCR. Most patients were college graduates, married, and employed, which may explain their ability to access healthcare services due to financial stability.³²⁻³⁴

Approximately one-third (33.3%) of our patients were noted to have chronic inducible urticaria, which is in conformity with the data gathered in Poland.³⁵ Likewise, a study in Sao Paulo, Portugal estimated their rate of chronic urticaria at 35.3%.³⁶

Our study demonstrated that dermographism is the most common type of CIU at 60%, supporting other studies with estimated findings of 50–70%.^{5,35-37} Several studies have also estimated cold urticaria to occur in 8 to 37% of CIU patients,^{36,37} which is greater than that observed in our study (4%). Cholinergic urticaria has been estimated to occur in 6 to 13% of CIU patients,^{36,37} which is similar to our study (12%). Delayed pressure urticaria has been estimated to occur in 3 to 20% of CIU patients,³⁴ which is consistent with our study (16%). Limited data on the prevalence of solar, heat, cold, contact, aquagenic, and vibratory urticaria is available.^{36,37} Heat contact urticaria has been estimated in Portugal at 0.8% of CIU patients³⁶ which is much less than that observed in our study (4%).

Several studies have demonstrated that chronic urticaria is associated with co-morbidities, such as hypertension (18.7%), dyslipidemia (2.7%), diabetes (5.3%), autoimmune disease (2.7%), thyroid disease (2.7%), malignancy (2.7%), and psychosocial illness (1.3%).^{5,12,38} Hypertension has been reported in as many as 43.5% of CU patients in a study done in Germany, 12% of CU patients in a study done in Sweden, and 1.9% of CU patients in Scandinavia.³⁸ Other studies have estimated that hypertension may occur generally in more than 20% of CU patients.⁵ Hypertension was the most common comorbid illness seen in our study (18.7%). The link between urticaria and hypertension has only been theorized but not confirmed. Systemic hypertension may cause injury to the blood vessels, leading to activation of the coagulation cascade. Elevated levels of prothrombin and D-dimer have previously been observed in other studies to be elevated in chronic urticaria.³⁹ Our study found a dyslipidemia rate of 2.7% among patients,

which is significantly lower compared to other studies in the literature. Dyslipidemia has been reported in 32.1% of adult CU patients in a study conducted in Germany, 17% in Sweden, and 29.8% in Korea.³⁸ Diabetes mellitus has been less frequently noted in CU patients, with a Danish study recording approximately 2.3%.^{38,40} Our study reported a slightly higher prevalence of 5.3%. In some studies, at least one autoimmune disease has been noted in approximately 30% of CU patients.^{4,38} Thyroid diseases are usually the most common autoimmune disease, occurring in as many as 4 to 37.1% of CU patients.² Both hypothyroidism and autoimmune thyroiditis may be associated with chronic urticaria according to literature, as an inflamed thyroid may prompt a generalized inflammatory response with activation of complement system, mast cells, and release of anaphylatoxins.³⁸ Our study estimated autoimmune and thyroid diseases at much lower rates (2.7% each), and this may be mainly due to patients following up to report symptoms but not proceeding with laboratory examinations that would confirm the diagnosis of thyroid or autoimmune diseases. CU has been reported with malignancy in 0.007% of the population in one European study.³⁸ In our study, the two adult CU patients who reported malignancy had breast cancer. Urticaria and cancer can incidentally coexist; further studies would be needed to establish causality.^{38,40,41} Urticaria has been proposed as a possible paraneoplastic syndrome of breast cancer, but this phenomenon has only been described in case reports.⁴² Psychosocial illness has been reported to coexist with CU. Anxiety was estimated to have a prevalence rate with CU at 30.6%, and mood disorders, including depression, have a prevalence rate of 29.4%.³⁸ In our study, one patient reported having been diagnosed with depression before the onset of urticaria. However, it is inconclusive at this time to draw a link between CU and depression.

The presence or absence of angioedema is also noted to be variable across different countries, with global rates of angioedema estimated to be at 40% to 60% of patients with chronic urticaria.⁴ Rate in Korea, however, is estimated to be low at 0.027%.⁴³ Further highlighting this variability, our study showed a prevalence rate of chronic urticaria with angioedema at 29.3%.

Our study confirmed that atopy is frequent in chronic urticaria (57.3%), with a higher prevalence of allergic rhinitis (24%) followed by asthma (12%), as noted in global studies.^{5,13} Similar trends were seen in the pediatric population analyzed in a government hospital in the Philippines. Allergic diseases were reported to coexist with chronic urticaria (79%), with a higher prevalence rate of asthma than allergic rhinitis.⁴⁴ Further studies are needed to investigate whether this discrepancy is related to age.

In our study, 15 patients underwent a skin prick test (SPT). Results of allergy skin prick test positivity and the number of those who underwent allergy skin prick test in our study were likely influenced by the personal and family histories of atopy. Ten patients (66.7%) who underwent SPT also had concomitant atopic diseases, with three patients having atopic dermatitis and seven patients having allergic rhinitis. SPT is useful in identifying IgE sensitization to a specific allergen; however, it is not predictive of clinical relevance without the history.²⁶ All 15 patients who had undergone SPT were found to have multiple sensitizations. Studies have shown that allergen sensitization may occur in CU patients with prevalence rates of 2.3 to 67.9%.⁴⁵ In our study, the most common allergens that our patients are sensitized to are grass pollens (73.3%), followed by house dust mites (60%), and tree pollens (53.3%) among the aeroallergens. Among food allergens, the most common allergens our patients are sensitized to are shellfish (66.7%), followed by vegetables (46.7%), and fruits (33.3%). However, clinically, these patients did not indicate a definitive correlation between exposure to sensitized food and developing urticaria. In a study conducted in Taiwan, house dust mites and shrimp were noted to be the most common allergens that their patients with chronic urticaria are sensitized to.¹³ Likewise, a study in the Philippines noted that house dust mites were the most common aeroallergen that urticarial patients with allergic rhinitis are sensitized to.³⁰ In our study, the greater prevalence of sensitizations to pollens as compared to house dust mites may, in part, be due to the environment of the patients and to the greater number of trees and grass pollens being tested in our allergy clinic.

It has been theorized that antibodies to SARS-CoV-2 can bind to antigens in humans, leading to the development of an autoimmune disease, which can also trigger urticaria.^{18,19} It cannot be determined at this time what larger implications the COVID-19 pandemic has placed on chronic urticaria cannot be determined at this time. In our study, approximately 50% of patients with chronic urticaria had no prior COVID-19 vaccine, while 26.7% of patients reported that they had received the COVID-19 vaccine before the onset of the symptoms. We cannot definitively link COVID-19 vaccines and chronic urticaria in our study, especially when only one patient noted urticaria within the same day after receiving the vaccine. We cannot conclude if a COVID-19 vaccine is a risk factor or another triggering factor is the underlying cause of chronic urticaria. A study conducted in Thailand found that approximately 15% of their CU patients experienced worsening symptoms after receiving COVID-19 vaccines (ChAdOx1 nCoV-19, CoronaVac™, BBIBP-CorV).²¹ Another study noted that less than one percent of patients with CU developed exacerbation of symptoms after vaccination.⁴⁶ In a study done in Switzerland, they found that the crude incidence rate of CSU per 100,000 patients who were vaccinated

with the COVID-19 vaccine booster dose was 19, and the relative risk of developing CSU after the Moderna vaccine was 20.8, which was similar to that of Pfizer-BioNTech vaccine.¹⁹ There is variability in the results, possibly due to the difference in vaccines used and the study type. Many studies on urticaria and COVID-19 vaccination lack a control group,¹⁹ and our study also has that limitation. Pre-existing allergies, concomitant medications, or other comorbid illnesses may also affect the disease activity of CU and confound the results of the data.⁴⁶

In our study, the compliance rates of CU patients using UAS7 and UCT in monitoring their symptoms were 26.7% and 29.3%, respectively. These low compliance rates may be attributed to both monitoring tools being only implemented in 2022. However, such findings are somewhat similar to a study conducted in Korea, where the average compliance rate of subjects using UAS7 in monitoring their symptoms was 29.8%.²⁴ Reasons previously given for poor compliance included 1.) patients finding it cumbersome; 2.) symptoms were very similar from the previous day; and 3.) because there were no symptoms to record.²² Adherence might be improved by emphasizing that recording UAS7 and UCT scores helps communicate their symptom severity to their physicians.²⁴ Research regarding patient compliance to UCT monitoring seems to be lacking, but the number of research papers using UCT, when reviewed in a literature search, has increased from 5.4% in 2016 to 23.4% in 2020 with its introduction into EAACI/GA²LEN/EDF/WAO guidelines in 2018.²⁴

The use of second-generation H1-antihistamines is the mainstay of treatment in CU. Treatment with standard dosing is considered the first line of treatment, and it may be up-titrated to four times the dose. Omalizumab is given as an add-on treatment when an inadequate response is noted with antihistamines.^{47,48} In our study, 65.3% of patients showed improvement in symptoms, specifically hives and pruritus. All patients were treated with second-generation H1-antihistamines. Approximately 50% of patients used the standard recommended daily dose of H1-antihistamine or as-needed dosing (21.3%) during their last follow-up. In a single-center study done in Korea, the majority of adult CU patients (77.4%) were noted to improve with H1-antihistamines.¹² Likewise, in a study done in Taiwan, approximately 60.7% of chronic urticaria patients improved with antihistamines. Most of their non-responders tend to have a history of atopy, particularly allergic rhinitis.¹³ In another study, they found that two-thirds of their subjects, unresponsive to antihistamines, improved with omalizumab and cyclosporin.⁵ Chronic urticaria is still considered a self-limiting disease, though it may persist for a long duration or even recur. Variability in prognosis may be influenced by factors such as race, treatment, and the definition of improvement.¹²

CONCLUSION

This study offers a demographic and clinical profile of adult patients with chronic urticaria seen over five years (2019 to 2023) at a Filipino allergy specialty clinic. The prevalence of chronic urticaria (13%) was higher than the global estimate of 1%. Most chronic urticaria patients were female, aged 30 to 39, married, college graduates, and employed who showed symptoms within 2 to 12 months after the onset of the disease. Approximately 50% of them had a personal and family history of atopy. Most patients do not have comorbidities and suspected inducible triggers. All patients who underwent skin prick tests showed reactivity to some allergens (aeroallergens, food allergens). All patients were given second-generation H1-antihistamines at varying doses. Many patients experienced symptom improvement with the prescribed medications despite poor compliance with the recommended monitoring tools. According to clinical history, the onset of chronic urticaria was not attributed to COVID-19 vaccination in most cases.

While some similarities with existing literature were observed, comparing the study with other studies was challenging due to significant differences in ethnicity, geographic location, environmental conditions, age groups, comorbidities, and treatments, among other factors.

Limitation and Recommendation

Our study has many limitations. It is retrospective, and all data were obtained from only one center specializing in allergy treatment, so that selective bias may have been introduced. The data were also difficult to assess uniformly because they were obtained through retrospective chart review. Given the various mechanisms and potential triggers involved in chronic urticaria, reaching definitive conclusions is challenging without comprehensive testing.

Further multicenter studies with larger sample sizes are needed to characterize patients with chronic urticaria in the Philippines. Additional tests, such as total serum IgE levels, IgG anti-TPO, CRP, and provocation tests, may be necessary to confirm the diagnoses of chronic spontaneous urticaria and chronic inducible urticaria. Furthermore, validated skin tests for COVID-19 vaccines may be required to confirm cases of vaccine-induced urticaria. Patients with associated autoimmune diseases or malignancies may also need more specific tests, such as autoimmune marker assessments.

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Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

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