Review Article

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A Dual Perspective on Chromic Urticaria: Insights from a Retrospective Study and Systematic Review and Meta-Analytical Evaluation

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Abstract

Background: Chronic urticaria (CU) is a common skin condition that causes hives and swelling, lasting for six weeks or longer. This condition can really take a toll on people's lives, causing physical discomfort, mental stress, and social difficulties. ***Aim and Objective:*** The primary aim of the study was to answer the question: "How do the prevalence rates and related comorbidities of chronic urticaria vary among different populations, and what do these variations imply for clinical management?". ***Methods:*** A systematic review and meta analyses was conducted by selecting studies from the period 2015 to 2024 on the prevalence of spontaneous urticaria and the associated risk factors from PubMed, Embase and Scopus. In addition to this, a retrospective study was conducted alongside including 664 patients with 332 patients each in the control (diagnosed with chronic urticaria) and case group. ***Results:*** The review looked at 12 studies and found some noticeable differences in prevalence rates across different regions, with an overall pooled estimate of 0.12. The retrospective study pointed out that chronic urticaria is more common in women and also noted that conditions like obesity, thyroid issues, and diabetes are often linked to it. ***Conclusion:*** The findings highlight the importance of thorough clinical evaluations and personalized management plans for patients dealing with chronic urticaria. More research is needed to look into the long-term impacts of related health issues and to better grasp how this condition affects different populations.

Keywords: ***Chronic urticaria, Prevalence, Comorbidities, Systematic review, Meta-analyses, Retrospective***

Introduction

Chronic urticaria (CU) is a common skin condition marked by the regular emergence of wheals, angioedema, or both, lasting for six weeks or more (Maurer M *et al,* 2015). This condition can greatly affect the quality of life for those who suffer from it, leading to physical discomfort, mental stress, and social challenges. The causes of chronic urticaria are complex and can involve both autoimmune reactions and non-autoimmune factors. Various triggers, such as environmental allergens, medications, and other health issues, can also play a role (He L *et al,* 2021). Despite how frequently it occurs, the exact prevalence of chronic urticaria is still not well understood, with estimates differing widely among various populations and regions (Mosnaim GS *et al,* 2022).

The primary aim of the systematic review and meta-analyses was to collect and analyze studies based on the prevalence of chronic urticaria to understand its occurrence across various demographic groups. This meta-analysis was designed to assist healthcare professionals by serving as a guide in order to enhance the identification and management of chronic urticaria in their clinical practices.

In addition to this, a retrospective study from our hospital to explore the patient characteristics of those suffering from this condition was conducted. Our study included a case group of 332 people diagnosed with the condition, categorized by gender and age, alongside a control group of individuals who do not have chronic urticaria. This setup allowed us to compare the occurrence of related health issues, such as diabetes, hypertension, and hyperthyroidism, between the two groups.

Materials and Methodology

The retrospective study was conducted using case records of OPD attendees of Karuna Medical College, Vilayodi from February 2020 to January 2025. The total sample size was 664 of which 332 people belonged to case group and the rest 332 people belonged to control group. Ethical approval was obtained from the committee.

Demographic data like age, gender, occupation, comorbidities such as metabolic syndrome, diabetes mellitus, dyslipidaemia, thyroid disease were taken. We adopted WHO criteria (1999) for metabolic syndrome which include the presence of diabetes mellitus, impaired fasting glucose or together with two of the following -elevated blood pressure, dyslipidaemia, obesity and microalbuminuria(urinary albumin excretion ratio more than or equal to 20micro gram/min or albumin-creatinine ratio> or=30microgram/kg).Diabetes was diagnosed according to one of the following criteria: (i) two random tests of blood glucose greater than 200 mg/dL, (ii) fasting glucose tests over 125 mg/dL. Diagnosis of hypertension in patients with two or more measurements of systolic blood pressure higher than 140 mmHg or diastolic above 90

mmHg during at least a one-month period of follow-up. BMI >25 was considered as obese as per ICMR.

Prevalence of investigated morbidities were calculated in cases and controls and compared. Continuous variables were compared using t tests and dichotomous variables were compared by Pearson-chi square test. A p value <0.05% was considered significant. Females were 212 and males were 120 for both the case as well as control groups.

The systematic review and meta-analyses followed the Preferred Reporting Item for Systematic Review and Meta-Analyses (PRISMA) guidelines (Figure 1 a) (Page MJ *et al,* 2021).

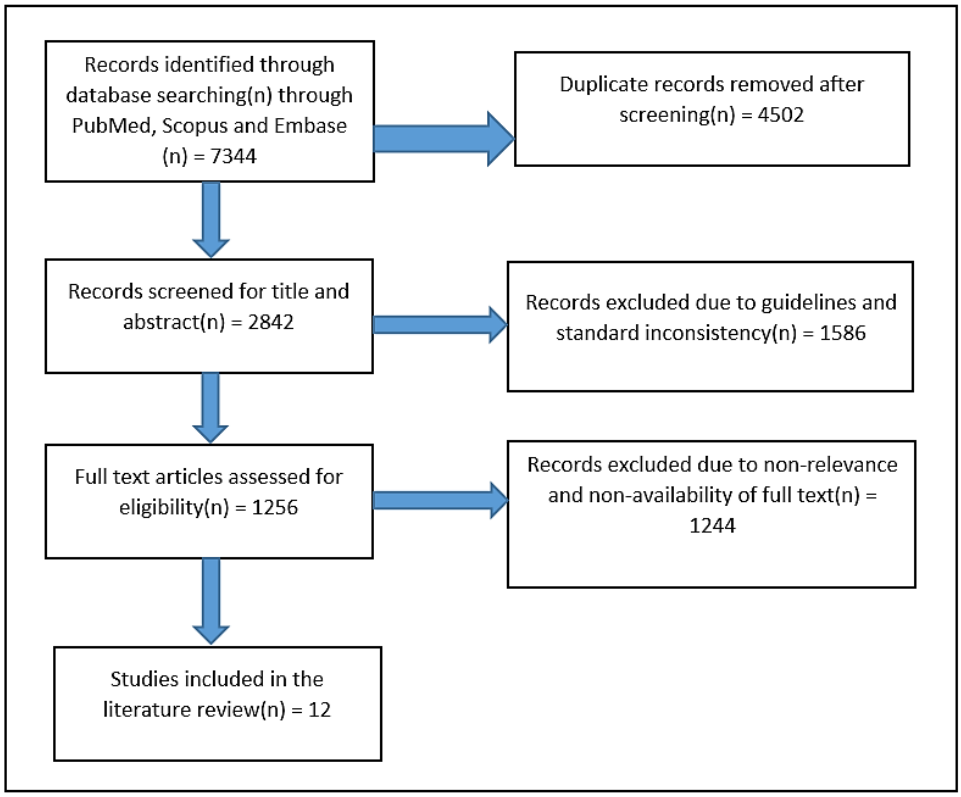

Figure 1a: Flowchart for selection of studies

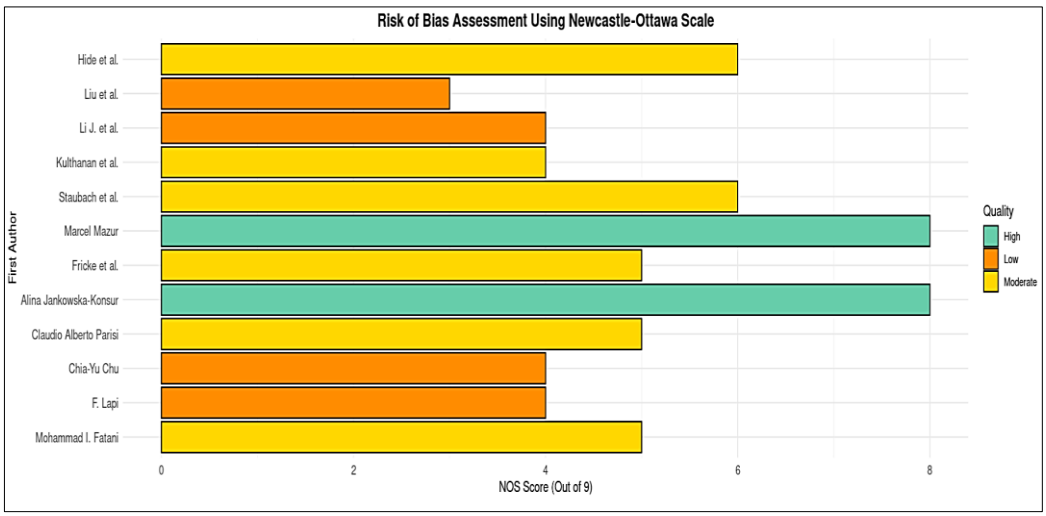

Figure 1b: Risk bias chart

Literature search

A comprehensive literature search was done to find out studies published between 2015 to 2024 on the prevalence of chronic spontaneous urticarial and its risk factors. Electronic database search was done in PubMed, Scopus and Embase using the keywords "Prevalence" and "Chronic Spontaneous Urticaria".

Inclusion and exclusion criteria for systematic review and meta-analyses

The inclusion criteria were: 1.) Population based studies cross-sectional or cohort in nature 2.) Published in English. 3.) Studies based on health insurance and physician databases 4.) Studies comprising of adults and/or children diagnosed with chronic urticarial 5.) Studies utilizing standardized diagnostic criteria like ICM-9-CM codes for urticarial 6.) Studies reporting prevalence/incidence rates of chronic urticarial providing demographic data, clinical characteristics and treatment patterns related to chronic urticaria

The exclusion criteria were: - 1.) Case series, reports. 2.) Intervention studies not focusing on prevalence or epidemiology 3.) Studies published before 2015 4.) Studies lacking clear methodology for the diagnosis of chronic urticaria 5.) Studies published in languages other than English

Data extraction

The eligibility of the article based on criteria search was completed by two authors (P.P and D.G) and the full text of the studies was analyzed by using Microsoft Excel 2016. The two authors assessed the methodology and the quality of the articles by using the New Castle Ottawa assessment scale (Peterson J *et al,* 2011) (Figure 1 b). Finally, a total of 12 studies met the quality of assessment. The data shows different studies from different parts of the world. The first author name with publication year, country of study, study design with period of study, sample size, study sample characteristics and prevalence were tabulated (**Table 1**).

Results

Screening flow

A total of 7344 articles were retrieved from Pubmed, Embase and Scopus of which 4502 duplicates were excluded. During the title and abstract screening phase, from a total of 2842 articles 1586 records were removed. A total of 1244 articles were excluded from 1256 articles during the full text screening phase. Finally, 12 articles were included in the systematic review of which 10 articles were included in the meta-analyses.

The forest graph plotted for the prevalence of chronic spontaneous urticaria depicted a heterogeneity of 100% with a pooled estimate of 0.12[95% CI: -0.01,0.26] (**Figure 2**).

The bubble meta-regression graph was plotted (**Figure 4**).

Funnel and Egger's Test

The funnel plot showed asymmetry attributed to the chronological differences, varying geographical locations and huge sample sizes in most studies (**Figure 3**). Egger's test showed p value <0.001 indicating publication bias (Egger M *et al,* 1997).

Analysis of the data showed that the highest number of cases were found in the age group 40-50 followed by 50-60 and 30-40 (**Table 2**). Lowest number of cases were found in children less than 10 years of age. Females exhibited higher prevalence rate of the condition in comparison to males. As for the comorbidities, BMI, thyroid disorders and hyperthyroidism showed significant association with the condition with p values less than 0.05 while obesity, metabolic syndrome and hypothyroidism failed to show significant association due to values higher than 0.05 (**Table 3 and Figure 5**).

Table 1: Characteristics of the various studies selected for systematic review and meta analyses

S No	First Author's Name	Study Design	Period of Study	Country of Study	Sample Size	Study Characteristics
1	Mohammad I. Fatani (2015)	Retrospective review	2008-2012	Saudi Arabia	201 patients	Mean Age: 32.9 years; Gender: 74.6% female; Comorbidities: Atopic diseases (30.1%), food allergy (25.4%), bronchial asthma (18.7%), allergic rhinitis (13.6%), allergic conjunctivitis (6.1%)
2	F. Lapi (2016)	Nationwide, population-based study	2002-2013	Italy	14,859 patients	Mean Age: 46.43 years; Gender: Not specified; Comorbidities: Obesity, anxiety, dissociative and somatoform disorders, malignancies, use of immunosuppressive drugs, chronic use of systemic corticosteroids
3	Chia-Yu Chu (2017)	Nationwide population-based study	2009-2012	Taiwan	1429289	Mean Age: Not specified; Gender: 56% female; Comorbidities: Psychiatric disorders, rheumatic diseases, thyroid disorders, inflammatory diseases
4	Claudio Alberto Parisi (2018)	Epidemiological study	2012-2014	Argentina	463	Mean Age: 38 ± 12 years; Gender: 66.7% female; Comorbidities: Allergic diseases (asthma, rhinitis, dermatitis), hypothyroidism
5	Alina Jankowska Konsur (2019)	Nationwide multicenter study	2017-2018	Poland	1,091 patients	Mean Age: Not specified; Gender: 64.8% female; Comorbidities: Other allergic diseases
6	Marcel Mazur (2020)	Epidemiological study	2016-2018	Poland	536	Mean Age: 7-8 years (children), 16-17 years (adolescents); Gender: Not specified; Comorbidities: Not specified
7	Fricke *et al*. (2020)	Systematic Review & Meta-Analysis	Not specified	Global (multiple countries)	86,632,267 (across 11 studies)	Mixed (adults and children)
8	Staubach *et al*. (2021)	Retrospective Study	2010-2015	Germany	313,581 (children under 18)	Mean Age: Not specified; Gender: 153,214 females, 160,367 males
9	Kulthanan *et al*. (2022)	Systematic Review	Until February 2021	Thailand, USA	1,112,066 (elderly patients)	Mean Age: 70.4 years; Gender: 57.4% female
10	Li J. *et al*. (2022)	Population-based Survey	Not specified	China	41,041	Mean Age: 33.5 years; Gender: 57.21% female, 42.79% male
11	Liu *et al*. (2023)	Systematic Analysis	1990-2019	Global (multiple countries)	65140000	Mean Age: Not specified; Gender: Higher prevalence in women
12	Hide *et al*. (2024)	Cross-Sectional Study	2019	Japan	334	Mean Age: 50.8 years; Gender: 62.3% female

Table 2: Case vs control group comparison based on demographics for our retrospective study

Age in years	Case	Chronic urticaria patients (%)	Control	Patients without chronic urticaria (%)
<10	4	1.20	4	1.20
10-20	22	6.63	22	6.63
20-30	24	7.23	24	7.23
30-40	68	20.48	68	20.48
40-50	86	25.90	86	25.90
50-60	72	21.69	72	21.69
60-70	42	12.65	42	12.65
>70	14	4.22	14	4.22
Gender				
Female	212	63.85	212	63.85
Male	120	36.14	120	36.14

Table 3: Case vs control group comparison based on comorbidities for urticaria patients from retrospective data

Comorbidities	Cases	Control	P value	Chi Square Value
BMI	28(8.43%)	25(7.53%)	0.0041	4.1295
Obesity	118(35.4%)	73(21.98%)	0.0614	3.5000
Hyperlipidemia	126(38%)	98(29.5%)	0.3173	1.0000
Diabetes	78(23.49%)	66(12%)	0.1216	2.3960
Hypertension	112(33.13%)	90(27.1%)	0.0861	2.9455
Metabolic syndrome	64(19.27%)	46(14%)	0.0961	2.7692
Thyroid disease	32(9.63%)	20(6.02%)	0.0308	4.6667
Hypothyroidism	28(8.43%)	14(4.216%)	0.5271	0.4000
Hyperthyroidism	4(1.205%)	6(1.807%)	0.0011	10.6021

Table 4: Important findings for various studies for systematic review and meta-analyses

S No	First Author's Name	Important Findings
1	Mohammad I. Fatani (2015)	44.3% CSU patients reported, 40.3% acute spontaneous urticarial and 7.5% physical urticarial found, 66.2% patients aged 21-50 yrs mostly affected, there was minimal elevation in the erythrocyte sedimentation rate (45%). 42.2%, 22.5% and 35.3% patients had urticaria for less than 6 weeks, between 6 weeks and for 6 months respectively. Angioedema was associated with 19.7% of all urticaria cases, normal thyroid stimulating hormone found in 80% of patients.
2	F. Lapi (2016)	Most patients were above 20 yrs and showed a greater risk. There was increased risk in patients aged 50-74 yrs, those above or at 80 showed lower risk. The ratio of female to male in terms of urticaria prevalence was approx 2:1. There were significant associations regarding risk factors like obesity (aHR 1.40), anxiety (aHR 1.22), malignancies (aHR 1.14), immunosuppressive drugs (aHR 2.19) and corticosteroids (aHR 1.95). Smoking was negatively correlated with the condition (aHR 0.75)
3	Chia-Yu Chu (2017)	There was increased prevalence of psychiatric disorders, inflammatory diseases, thyroid disorders and rheumatic diseases and repeated occurrence of itchy hives or angioedema for 6 weeks or more among the CU patients
4	Claudio Alberto Parisi (2018)	Prevalence of 0.29% for CU reported with CI 95%: 0.26-0.31%, Adults showed prevalence of 0.34% (95% CI: 0.31-0.38%), Prevalence of 0.15% (95% CI: 0.11-0.2%) depicted in paediatric population. Spontaneous CU cases 67% on the whole. The duration of CU was 6-12 weeks, 3-6 months, 7-12 months, 1-5 years and over 5 years in 52.8%, 18.5%, 9.4%, 8.7% and 11.3% respectively
5	Alina Jankowska-Konsur (2019)	CU and inducible spontaneous urticarial rates: 61.1% and 35.1% respectively, 12.1% CSU patients had family history for urticaria, Absenteeism of 16.3% observed in CU patients. Generalized wheals were more common in CU rather than IU patients (57.9% vs 45.2%)
6	Marcel Mazur (2020)	3.3% lifetime occurrence of urticarial (3.6% in children, 2.8% in adolescents), 2.1% and 1.1% in children and adolescents respectively.
7	Fricke *et al.* (2020)	Prevalence was higher in Asia compared to Europe and Northern America (1.4% vs 0.5% and 0.1%). Females demonstrated to be affected more than males.
8	Staubach *et al.* (2021)	1.7% prevalence in urticaria patients, Highest prevalence of 3% noted in 0-3 years, Comorbidities that were observed in the patients were atopic diseases (16% in case vs 8% in control), autoimmune diseases, mental health disorders and obesity
9	Kulthanan *et al.* (2022)	0.2-2.8% prevalence of CU in the elderly population, Higher prevalence of 73.9% for wheal alone, comorbidities: gastrointestinal disorder(71.9%), autoimmune diseases and malignancies associated
10	Li J. *et al.* (2022)	Factors associated with condition reported as urban living, pollutants, depression and anxiety, family history of allergies. Prevalence by age group was reported for children(7-11 years), adolescents(12-17 years) and adults(≥18 years) as 5.17%, 5.6% and 8.19% respectively

11	Liu *et al.* (2023)	Notable increase in prevalence rates and incidence since 1990. Variations across regions observed with highest rates observed in low-middle SDI regions. Central Europe had the highest prevalence regarding age standardization
12	Hide *et al.* (2024)	High anxiety and depression rates associated with the condition (41.3% vs 44%). SF-12 PCS and MCS reported as 50.3(7.0) and 45.1(10.0). 90% patients visited healthcare providers. The average monthly out-of-pocket costs:JPY 1-999 for 16.5% patients highlighted to evaluate the economic as well as human burden

Table 5: Strengths and weaknesses for various studies

S No	First Author's Name	Merits	Gaps
1	Mohammad I. Fatani(2015)	Comprehensive prevalence and clinical pattern data in particular region presented	Limited generalizability
2	F. Lapi (2016)	Crucial epidemiological data on CSU in Italy provided	There was limited data regarding laboratory findings
3	Chia-Yu Chu (2017)	Significant associations with different comorbidities in Taiwan highlighted	Lack of data regarding particular demographics for sample
4	Claudio Alberto Parisi (2018)	Valuable epidemiological data regarding the condition provided for better effective management	Selection bias might be there
5	Alina Jankowska-Konsur (2019)	Robust dataset on epidemiology and clinical characteristics for CU in Poland	Less age distribution and comorbidities data regarding demographics
6	Marcel Mazur (2020)	The impact of air pollutants on the progression of the condition investigated	Data on demographic gender and comorbidities was lacking
7	Fricke *et al.* (2020)	Comprehensive systematic review with large sample size	There was high statistical heterogeneity noted (I^2=100%)
8	Staubach *et al.* (2021)	Huge sample size, comprehensive analysis of comorbidities performed	Lack of detailed age classification
9	Kulthanan *et al.* (2022)	Large sample size, detailed review on clinical features and treatment performed	Study focused only on the elderly
10	Li J. *et al.* (2022)	Large sample size covering numerous regions, detailed analysis of risk factors comducted	Lack of data regarding age stratification
11	Liu *et al.* (2023)	Global data utilized for the study to perform analysis	Variations in diagnostic criteria across multiple studies, national data lacked granularity
12	Hide *et al.* (2024)	Comprehensive evaluation of economic and human burden performed	Longitudinal data was lacking,

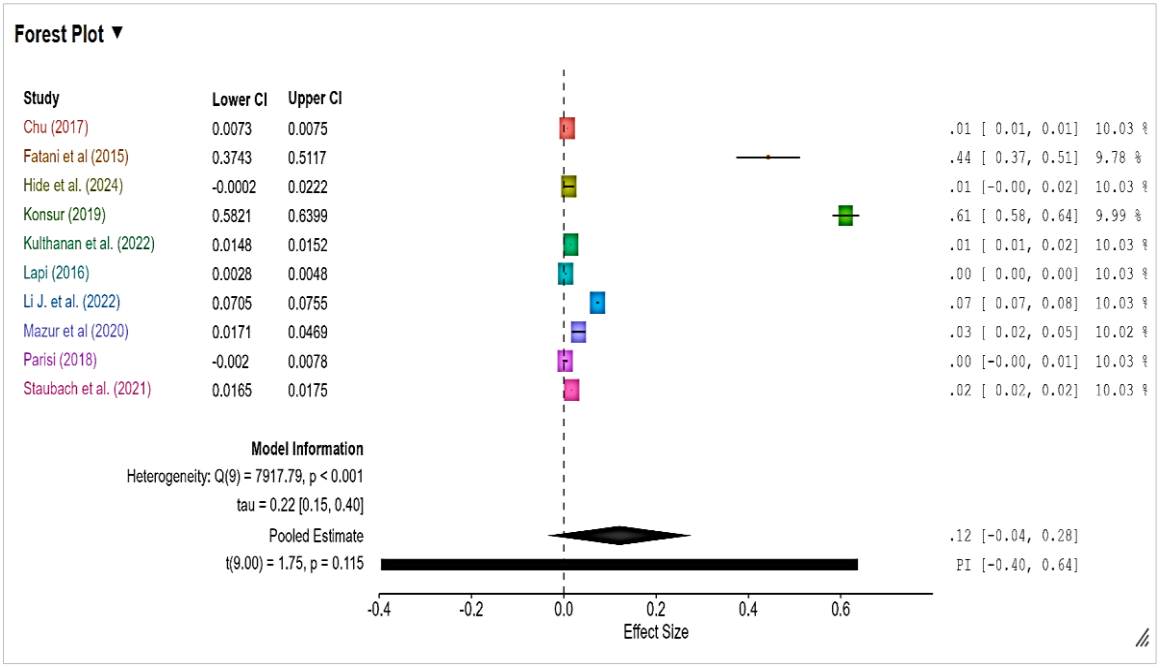

Figure 2: Forest plot for prevalence of chronic urticaria across studies for systematic review and meta-analyses

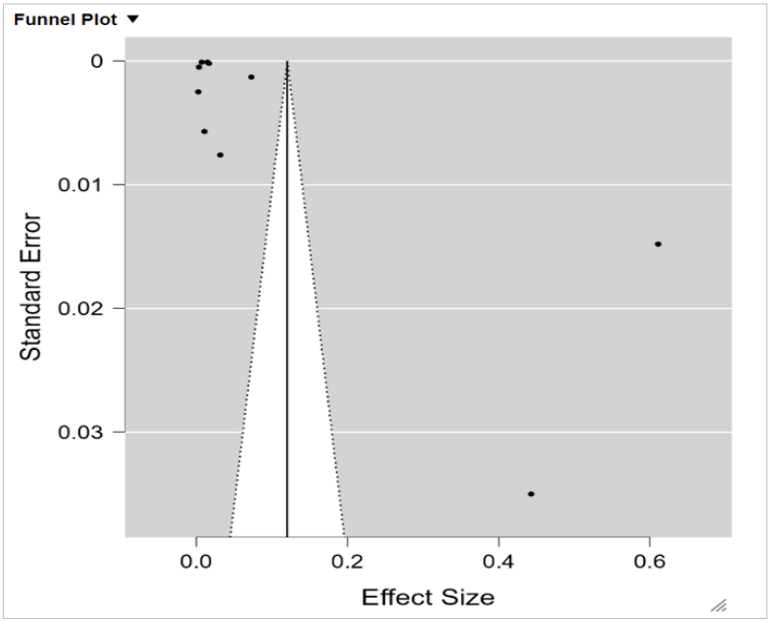

Figure 3: Funnel plot for various studies

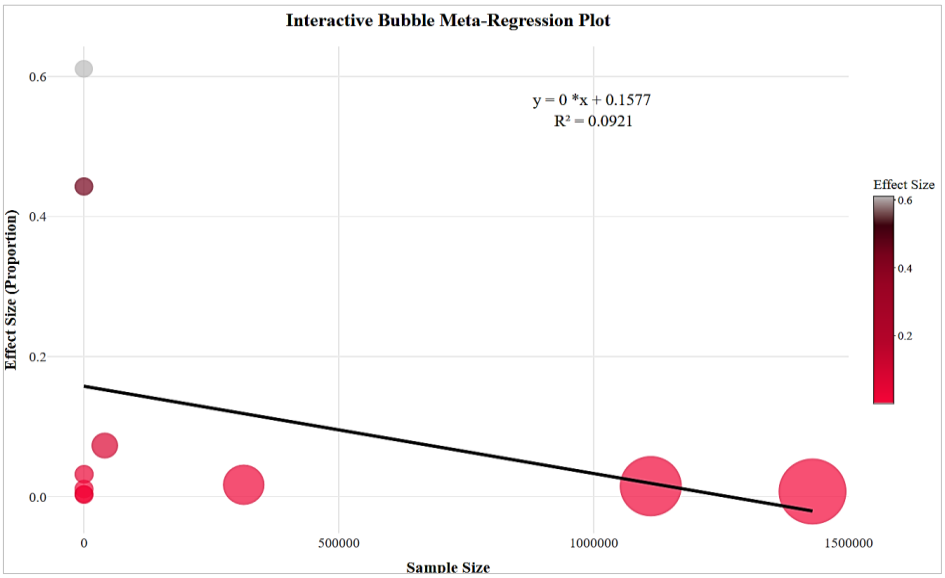

Figure 4: Bubble meta regression analyses of the various studies

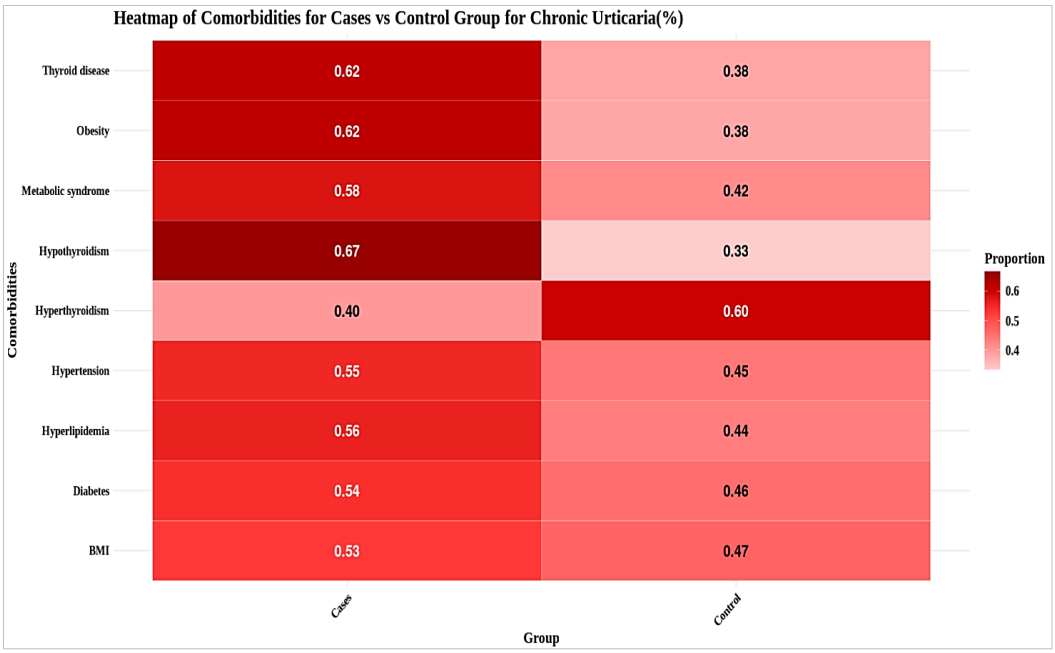

Figure 5: Heat map for cases vs control group for comorbidities association with urticaria based on retrospective data

Statistical Analysis

SPSS version 28 was used for data analysis and R Studio for plotting graphs.

Discussion

A study by an author showed a prevalence rate of 44.3% for chronic spontaneous urticaria in 201 patients with 66.2% aged from 21 to 50 years (Fatani MI *et al,* 2015). Around 30.1% and 25.4% patients had atopic diseases and food allergies respectively. This was further supported by another author (Lee SJ *et al,* 2017). The study depicted that the condition continued to persist in the patients for more than six months stressing upon the association between morbidity and the condition.

Another author reported an annual prevalence of CSU increasing from 0.2% to 0.38% from 2002 to 2013 showing a 19-fold rise (Lapi F *et al,* 2016). Obesity and anxiety disorders were identified as risk factors resonating with the previous author's findings (Fatani MI *et al,* 2015) on comorbidities. This was further corroborated on by another author (Telia Z, 2022). The burden of CU was further depicted with higher risks showed in younger patients based on demographic trends.

Another study depicted a prevalence of CU ranging from 0.69% to 0.79% from the year 2009 to 2012(Chu). The correlation of psychiatric disorders showed in the study aligned with the previous author's study (Lapi F *et al,* 2016) demonstrating the mental health implications of CU. This was further stated by another study (Konstantinou GN *et al,* 2019). Yet, the chances of potential misclassification prevailed due to reliance on ICD-9-CM codes similar to the gap observed in the previous author's study (Lapi).

A prevalence of 0.29% was depicted by another author with 67% spontaneous cases (Parisi CA *et al,* 2018) complementing the findings of the previous two authors (Fatani MI *et al,* 2015; Lapi F *et al,* 2016) in different regions.

The absenteeism of 16.3% reported in 61.1% of CSU cases was further demonstrated by an author (Jankowska-Konsur A *et al,* 2019). The study's socioeconomic impact aligned with one of the previous author's (Fatani MI *et al,* 2015) findings on healthcare utilization. This was reported by another study. (Gabrielle PE *et al,* 2021).

Another author highlighted on paediatric considerations in CU research by reporting a lifetime occurrence of urticarial in 3.3% paediatric population aligning with the findings stated by the previous author(Jankowska-Konsur A *et al,* 2019) especially in the younger people(Mazur M *et al,* 2020). This was further elucidated upon in another study (Netchiporouk E *et al,* 2017).

The global variances in prevalence of CU stated in the previous studies was further complemented by another author's study in spite of high heterogeneity observed posing a challenge in drawing definite conclusions (Fricke J *et al,* 2020). The rates were comparatively higher in Asia when compared to Europe (1.4% vs 0.5%). This was further depicted in another study (Tiongco-Recto M *et al,* 2024).

Another study focused on comorbidities like atopic diseases reporting a prevalence of 1.7% with highest rates observed in children (3%) aged 0 to 3 years aligning with the previous two author's studies (Fatani MI *et al,* 2015; Jakowska-Konsur *et al,* 2019) indicating and reinforcing correlation between CU and allergic conditions.

A study showcased the prevalence of CU ranging from 0.2% to 0.8% in the old population (Kulthanan K *et al,* 2022). This was stated by another author (Khaliliya R *et al,* 2023). Higher rates of comorbid gastrointestinal disorders were associated with CU underscoring the crucial need for targeted research in the elderly demographic that was less explored in the previous studies. Similar findings were reported by another study (Aitella E *et al,* 2018).

A study revealed the factors such as urban living and anxiety as well as depression associated with CU aligning with previous author's studies (Lapi F *et al,* 2016; Chu CY *et al,* 2017) pinpointing on the influence of mental health on CU patients by reporting a lifetime prevalence of 7.3% vs a point prevalence of 7.3% (Li J *et al,* 2022). This was further demonstrated in another study (Bud C *et al,* 2017).

A global prevalence estimate of 841.88 per 100000 was reported by an author showing a significant increase since 1990 in CU rates. The higher prevalence in females aligned with the findings stated in all the previous studies reinforcing gender parities in urticaria cases. Similar findings echoed in another study (Goncalo M *et al,* 2021).

Yet another study showed a weighted prevalence of CSU at 1.1% impacting the quality of life (Hide M *et al,* 2025). High rates of psychiatric conditions such as anxiety and depression (41.3 % and 44% respectively) emphasized on the mental burden associated with the condition aligning with the findings of previous studies (Lapi F *et al,* 2016; Chu CY et 2017).

The important findings of each study were tabulated along with the merits and gaps (Table 4 and 5).

Conclusion

Our systematic review and meta analyses coupled with retrospective study set out to shed light on the prevalence and characteristics of chronic urticaria and its related comorbidities. Our results revealed notable differences in prevalence rates and pinpointed important comorbid conditions that can affect how chronic urticaria is managed. To improve management strategies, it's essential for clinicians to devise tailored treatment plans that take into account each patient's unique profile, including the severity of their urticaria and any other health issues they might have.Further future research should be conducted to emphasize longitudinal studies that look into the long-term effects of comorbidities on chronic urticaria and how well-integrated management approaches work.

Declarations

Ethical Considerations, informed consent, and Consent for publication

Informed consent was signed by all study participants. All mentioned ethical aspects and related consents were taken into consideration during the conduct of this study.

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Conflicts of interests

The authors report no conflict of interest.

Author contributions

Conceptualization and methodology, P.P. and D.S.; Formal analysis, P.P., D.S., J.H..; Visualization and writing - original draft P.P., D.S., J.H.; Writing - review and editing, P.P., D.S. and J.H. All authors have read and agreed to the final version of the manuscript.

Article category

Retrospective systematic review and meta-analyses

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