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Original Research Article

# A case control study of risk factors in chronic urticaria

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ABSTRACT

**Background:** Urticaria presents as erythematous, often pruritic, raised transient wheals. The aetiology of Chronic Urticaria (CU) is not well understood. Autoimmunity, chronic infections, allergens and metabolic syndrome are some known implicated factors. But the role of life style factors like diet, smoking, alcohol, occupation, family
history etc is relatively unknown. This study aims to uncover the role of these modifiable factors in causation of CU.

**Materials and Methods:** Data from 20 individuals with chronic urticaria (duration <1 year) and 20 age and sex matched Controls (healthy/patients without chronic urticaria) was collected using questionnaires to assess lifestyle and risk factors like diet, alcohol consumption, smoking, medications, stress, sleep etc in the implication of CU.

**Result:** Our study revealed notable if not significant associations. Out of these, 6 cases (30%) had a family history of CU, while 10 cases (50%) had a prior history of acute urticaria episodes. Additionally, 6 cases (30%) reported food allergies, and 10 cases (50%) had a documented medical history. Furthermore, 7 cases (35%) reported insect bites as a factor, while 1 case (5%) was linked to H. Pylori infections. Notably, 12 cases (60%) showed a lower consumption of fruits, while 9 cases (45%) exhibited a relatively higher intake of foods containing dyes and additives. These findings collectively suggest some potential connections in the development of CU.

**Conclusion:** This study underscores the intricate connections between risk factors, lifestyle choices, and CU. Differences in sleep quality, food allergies, dietary habits, and seafood consumption provide potential insights into associations. This investigation may contribute to improved CU management approaches.



## 1. Introduction

William Cullen introduced the word "urticaria".[1] Urticaria may present with short-lived, itchy, red and mildly swollen wheals and/or angioedema[2] (deep swelling of the dermis or subcutaneous tissue). Urticaria can affect any race or ethnic group & has a female preponderance. Urticaria can present in persons of any age, with a lifetime prevalence of approximately 20%. Chronic urticaria has a lifetime prevalence of approximately 0.5% to 5%.[3] Depending on its duration, urticaria can be categorized into two types: acute urticaria (AU), which lasts for less than six weeks, and chronic urticaria (CU), persisting for more than six weeks. Chronic Urticaria can further be subdivided into Chronic Inducible Urticaria (CIndU) and Chronic Spontaneous Urticaria (CSU). CU is often a multifactorial disease which include IgE mediated allergy, autoimmunity, infections and infestations, drug intake, diet etc. Autoimmune conditions such as thyroid disease and type 1 diabetes are factors that increase the odds of having urticariaand hence, it is believed that almost 45 per cent of patients with urticaria

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have autoimmune chronic urticaria (CU) and the rest are truly idiopathic.[4] Infections by a variety of organisms have also been associated with CSU. These include bacteria (Helicobacter pylori, Streptococci, Staphylococci, Yersinia, Mycoplasma pneumoniae), virus (Hepatitis virus, Norovirus, Parvovirus B19), and parasites (Giardia lamblia, Entamoeba spp., Anisakis simplex). Causality remains unproven but may involve infection-mediated autoimmune response and molecular mimicry.[5] Urticaria results from the release of vasoactive substances (histamine, bradykinin, kallikrein) from mast cells (MCs). MC-derived histamine and cytokines such as IL-4, IL-13, and IL-31 stimulate peripheral sensory neurons, which leads to itch. In concert, MC mediators released by degranulation mainly promote vasodilation and vascular permeability, whereas de novo produced and released cytokines and chemokines recruit leukocytes (eosinophils, basophils, T cells, neutrophils) from the bloodstream to form wheals and angioedema.[6] In CSU, symptoms can appear suddenly without clear triggers, although stress, infections, diet, sleep and other factors can affect their severity.

Activation of H1 receptors in the skin causes itch, erythema, flare and whealing. Whereas, H2 receptor activation causes erythema and whealing. Release of histamine from mast cells can occur spontaneously as well as in response to non-specific degranulating agents. Several studies have demonstrated elevations of histamine levels but not MCs in the skin of CSU patients.[7]

## 2. Materials and Methods

This was an observational study. The data collection was done through questionnaires for cases and controls.

The data collected from patients with chronic urticaria (CU) was compared to that from a control group to identify any factors linked to a higher risk of CU.

### 2.1. *Inclusion criteria*

Cases of CSU, CINDU, or both, aged 18 years or older with CU episode lasting no more than 12 months.

Each CU patient was matched with a control of the same age and gender. Control patients could include those seeking cosmetic procedures, individuals with nevi, hair loss. Healthy individuals were also eligible.

### 2.2. *Exclusion criteria*

Cases of Chronic Urticaria for more than 12 months Controls were excluded if they had a history of chronic urticaria. Patients with Chronic inflammatory skin conditions like psoriasis, atopic dermatitis, or lichen planus and allergic conditions like Asthma, atopic dermatitis, drug allergies, or other allergies were also excluded.

### 2.3. *Questionnaire*

Participants were requested to fill out a set of questionnaires. The process of filling was done face to face with a clinician. The questionnaires covered a range of topics, including family and social life, occupation, diet, alcohol and tobacco use, caffeinated beverages, herbal teas, herbal supplements, turmeric, vitamins, physical activity, stress, sleep, psychological well-being, as well as other medical conditions and medications. Responses were based on the last 3-6 months leading up to the onset of urticaria, with variations in question content.

### 2.4. *Statistical analysis*

The collected data were transformed into variables, coded and entered in Microsoft Excel. Data were analysed and statistically evaluated using SPSS-PC-25 version. Normal distribution of different parameters was tested by the Shapiro-Wilk normality test. Quantitative data was expressed in mean±standard deviation and depends on normality difference between mean of two groups were compared by unpaired t test or Mann Whitney U test. Qualitative data were expressed in frequency and percentage and statistical differences between the proportions were tested by chi square test or Fisher exact test. p value less than 0.05 was considered significant

## 3. Results

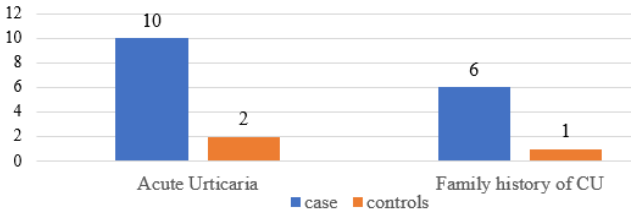


**Figure 1:** Clinical and family history

A previous history of acute episodes and a family history of CU was noted more in cases than controls

Apart from 35% cases suffering from insect bites as compared to only 15% controls, no significant differences in the living conditions are noted in the two groups.

No correlation was found between CU and work-related psychosocial stressors and allergen exposures.

50% of controls mostly slept well as compared to only 15% cases.

Diabetes and Hypertension show equal distribution among both groups. Dental, Respiratory and H.Pylori infections as well as allergies noted more in the cases.

More cases were seen to be on medications than controls. Transfusions and vaccines showed equal distribution in the two groups

**Table 1:** Comparison of living conditions between both groups

| **Number of members living in same household** | | | |
|---|---|---|---|
| | **Cases (n=20)** | **Controls (n=20)** | **p value** |
| No | 0 | 2 | |
| 1-3 | 10 | 11 | 0.26 |
| >3 | 10 | 7 | |
| **Presence of pets in House** | 5 | 5 | **-** |
| **Financial strains in the household** | | | |
| No | 12 | 12 | |
| Often | 3 | 0 | 0.16 |
| Sometimes | 5 | 6 | |
| Always | 0 | 2 | |
| **Changes in residential area** | 8 | 6 | 0.74 |
| **Insect bite** | 7 | 3 | 0.27 |

**Table 2:** Comparison of sleep between cases and controls

| **How often did you get amount of sleep you needed?** | **Cases (n=20)** | **Controls (n=20)** | **p value** |
|---|---|---|---|
| All the time | 7 | 4 | |
| Mostly | 3 | 10 | |
| Good bit | 3 | 3 | 0.10 |
| Sometimes | 3 | 0 | |
| Little | 4 | 3 | |

**Table 3:** Comorbidities and allergies in both groups

| | **Cases** | **Controls** | **p value** |
|---|---|---|---|
| Hypertension | 1 | 1 | - |
| Diabetes | 1 | 1 | - |
| Thyroid disease | 1 | 2 | 1.0 |
| Migraine | 4 | 6 | 0.71 |
| Dental infections | 2 | 0 | 0.49 |
| H.Pylori infection | 1 | 0 | 1.0 |
| Respiratory infections | 5 | 3 | 0.69 |
| Mental disorders | 7 | 4 | 0.48 |
| Contact dermatitis | 1 | 2 | 1.0 |
| Food allergies | 6 | 2 | 0.23 |
| Drug allergies | 1 | 0 | 1.0 |
| Others | 7 | 2 | 0.12 |

**Table 4:** Iatrogenic factors

| | **Cases** | **Controls** | **p value** |
|---|---|---|---|
| Medication history | 10 | 6 | 0.33 |
| Vitamins & supplements | 8 | 10 | 0.52 |
| Vaccines | 5 | 5 | - |
| Blood transfusion | 0 | 0 | - |

Cases of CU show moderate to high consumption of Fish/Seafoods, white meats, red meats, sweets and foods with food dyes and additives whereas relatively lesser consumption of fruits and dietary fibre.

Addictions showed equal distribution in both groups

This study enrolled 40 participants, evenly divided into two groups: 20 individuals with chronic urticaria (CU) and 20 control subjects. The mean age for both groups was 31.75±8.11 years, with a gender distribution of 12 females (60%) in the CU group and 8 males (40%) in the control group. Notably, there were no significant differences in terms of age, race, or marital status between these two groups.

The primary objective was to identify lifestyle and risk factors contributing to chronic urticaria. Although no significant correlations were found between the examined risk factors and CU, individuals with chronic urticaria were more likely to have a family history of CU and a past

**Table 5:** Food habits related history in both groups

| | Cases (n=20) | Controls (n=20) | p value |
|---|---|---|---|
| **Vegetables** | | | |
| Less | 8 | 9 | |
| Moderate | 12 | 10 | 0.53 |
| High | 0 | 1 | |
| **Fruits** | | | |
| Less | 12 | 7 | |
| Moderate | 6 | 12 | 0.16 |
| High | 2 | 1 | |
| **High fibre cereals** | | | |
| Less | 11 | 8 | |
| Moderate | 3 | 8 | 0.20 |
| High | 6 | 4 | |

**Table 6:** Food habits related history in both groups

| | | | |
|---|---|---|---|
| **Red Meat** | | | |
| Less | 17 | 20 | |
| Moderate | 3 | 0 | 0.23 |
| High | 0 | 0 | |
| **White meat** | | | |
| Less | 14 | 16 | |
| Moderate | 6 | 4 | 0.71 |
| High | 0 | 0 | |
| **Fish/sea food** | | | |
| Less | 15 | 18 | |
| Moderate | 4 | 2 | 0.37 |
| High | 1 | 0 | |

**Table 7: 7:** Food habits related history in both groups

| | | | |
|---|---|---|---|
| **Sweet** | | | |
| Less | 5 | 5 | |
| Moderate | 7 | 12 | 0.30 |
| High | 8 | 3 | |
| **Full-fat dairy products** | | | |
| Less | 7 | 5 | |
| Moderate | 6 | 10 | 0.43 |
| High | 7 | 5 | |
| **Food dye and additives** | | | |
| Less | 11 | 17 | |
| Moderate | 8 | 3 | 0.10 |
| High | 1 | 0 | |

**Table 8:** Smoking and alcohol intake history in both groups

| | Cases (n=20) | Controls (n=20) | p value |
|---|---|---|---|
| **Smoking** | | | |
| No | 17 | 16 | 1.0 |
| Yes | 3 | 4 | |
| **Alcohol** | | | |
| No | 13 | 13 | 1.0 |
| Yes | 7 | 7 | |

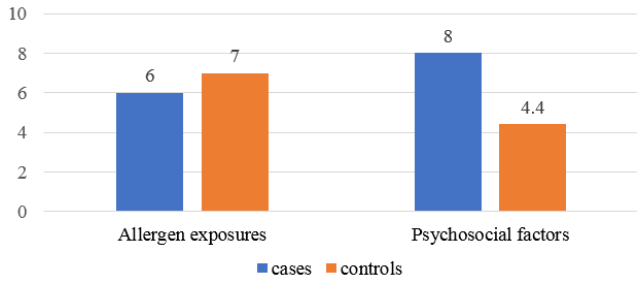


**Figure 2:** Factors at workplace

history of acute urticaria episodes. Cases exhibited a higher prevalence of food allergies, consumption of food with dyes and additives, and lower intake of fruits and dietary fibres.

Regarding environmental factors, 35% of CU cases reported experiencing insect bites, compared to only 15% of controls, with no significant differences in living conditions between the two groups. CU cases were more prone to dental, respiratory, and H. pylori infections, various allergies (food, drugs, others) as well as mental disorders. Only 15% of CU cases reported restful sleep, compared 50% of controls.

Several factors, such as mental stressors like family deaths and financial strains, the presence of pets in the house, residential area changes, workplace exposures, and psychosocial factors, along with habits like smoking and alcohol use, showed no significant association with CU causation. Furthermore, certain medical conditions like diabetes mellitus, hypertension, a history of blood transfusions, and vaccine administration were equally distributed between CU cases and controls.

## 4. Discussion

Chronic urticaria (CU) exerts a substantial impact on both the physical and psychological well-being of those affected. Women have a higher risk of the onset of urticaria than that among men. Urticaria is more common in young adult age groups compared to older age groups.[8] A study indicated that the prevalence of chronic urticaria in children appears to be similar to that reported for adults. Same study also mentioned that Chronic urticaria is influenced by potential irritants in the environment and socioeconomic status, but it is not influenced by the serum vitamin D levels, atopic status and past history, and parental history of allergic conditions.[9] It's worth noting that CU is estimated to affect between 0.5% and 5% of the global population.[10]

Our study explored various lifestyle factors, including dietary choices such as white meat, seafood, full-fat dairy products, the presence of dyes and additives, stress levels, and habits like smoking and alcohol consumption, in relation to CU incidence among participants. The assessment of study outcomes was based on data obtained through a questionnaire, specifically the Simple Lifestyle Indicator Questionnaire (SLIQ).

Upon analyzing the collected data, we noted mental disorders, food allergies, and respiratory infections emerged as potential modifiable risk factors for future studies to explore. Emerging research has shown that skin actively participates in the response to stress through a local hypothalamic-pituitary-adrenal (HPA) axis, peripheral nerve endings, and immune system skin-homing cells, including keratinocytes, mast cells, and T cells.[11] Stress can induce sleep disorders (SD), and sleep deprivation has itself been hypothesized to be a stressor. Therefore, stress may play a major role in SD-related CSU.[12] Interestingly, a higher proportion of CU cases reported insufficient sleep compared to their controls, although it remains unclear whether the lack of sleep directly contributes to the development of urticaria or if CU itself disrupts patients' sleep patterns. Alcohol intake and smoking showed no correlation to the causation of CU in our subjects. Although studies suggest nicotine in tobacco smoke can act as an inhalant allergen and induce urticaria in hypersensitive persons.[13] Alcohol consumption has been implicated as a cause for urticaria in several case reports, but the pathogenesis of mast cell activation remains to be elucidated.[14] Notably, the most significant factor associated with CU was a history of previous acute episodes in the affected individuals, which could progress over time if left untreated. One study identified some predictive factors for progression from acute urticaria AU to CU. It observed that there may be some patient-related factors associated with CU such as NSAIDH or food allergy. The study further suggested that identification of AU patients who have a high risk of progression to CU is important since these patients need a better follow-up.[15]

Another significant association was noted with the presence of family history of CU. Genetic factors play a pivotal role in the pathogenesis of many autoimmune disorders. Recent studies demonstrated that chronic idiopathic urticaria (CIU) is an autoimmune disease at least in a subset of patients, but familial studies have not yet been conducted.[16] There is growing body of evidence that some cases of CIU are associated with thyroid autoimmunity. The first studies of autoimmunity in patients with CIU reported that patients with CIU have an increased frequency of Hashimoto thyroiditis. The association was with the presence of antibodies to thyroglobulin or a microsomal-derived antigen (peroxidase), even in euthyroid patients.[17,18] Hypertension showed no significance as a causative factor of CU in our research, but results from a study in 2009 show that hypertension is associated with extended duration of Chronic Inducible Urticaria[19] We did not identify any specific lifestyle modifications or risk factors that could be definitively linked to the causation of CU in this group of participants. In the future

urticaria would not be seen as disease entity, but as a guiding symptom, which could have multiple underlying (otherwise subclinical) aetiologies, including metabolic disease, intolerance reactions, and dysbiosis. Nonetheless, it is advisable for patients to consider periodic follow up and investigations in case of an acute urticaria episode or if there is a family history. While oral antihistamines remain the mainstay of therapy in CU, education on potential dietary factors may be offered to a selection of the group of patients.[20]

Incorporating more high-fiber options and fruits into their diet, and avoiding food preparations with food preservatives and dyes should be encouraged. Care should be taken as to prevent insect bites. An improvement

in sleeping habits is also recommended. These practices may hold, if not significant but potential benefits for

both patients and healthcare providers in reducing the occurrence of CU.

However, it is crucial to acknowledge the limitations of this study, primarily its small sample size, which prevented the identification of significant correlations between suspected risk and lifestyle factors.

## 5. Conclusion

There is a need for future studies to be conducted, which would explore the relationship of urticaria and extrinsic factors further.[21] People with CU exhibit different levels of engagement with the lifestyle and risk factors in their daily lives as examined in the study. Although the modifiable lifestyle and risk factors did not demonstrate a significant correlation with the presence of CU, but it is important to note that the limited sample size of the study may have impacted the outcomes.

## 6. Source of Funding

None.

## 7. Conflict of Interest

None.

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