

Epidemiology of urticaria: a representative cross-sectional population survey

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Summary

Aim. To investigate the prevalence of urticaria with a focus on chronic urticaria (CU) in a general German population.

Methods. A questionnaire survey was sent to a representative cross-sectional sample of 13 300 inhabitants of Berlin, Germany, of whom 4093 responded. All respondents who stated ever having had weals or angio-oedema ($n = 767$) were interviewed by telephone. Any interviewees with recent symptoms (within the previous 3 years) were invited for personal investigation including allergy tests; double-blind, placebo-controlled food challenge tests; and quality of life (QOL) assessment. Reported prevalence rates were weighted with regard to age, gender and education so that they were representative of the total population of Berlin.

Results. Lifetime prevalence rate of urticaria was 8.8% (95% CI 7.9–9.7%) for all types of urticaria. Lifetime prevalence for CU was 1.8% (95% CI 1.4–2.3%), and prevalence for the 12 months before assessment was 0.8% (95% CI 0.6–1.1%), and 70.3% were female. QOL was markedly reduced for people with CU. Unlike other allergic diseases, there was no increased risk associated with higher education or social status. Prick tests found sensitization of ≥ 1 for type 1 allergens in 39.1% of patients. These were related to comorbidities such as allergic rhinitis or oral allergy syndrome, but were never the underlying cause of CU, as proven by double-blind, placebo-controlled provocation tests.

Conclusion. Urticaria is a common disease with marked effects on QOL. The lifetime prevalence of 8.8% for urticaria must be regarded as a lower limit as it is based on conservative prevalence rate calculations, and under-reporting of previous disease can be expected in a questionnaire-based study.

Introduction

Urticaria is a heterogeneous group of diseases defined by the appearance of weals and angio-oedema.^{1,2} It is one of the 10 most common dermatoses. Owing to its chronic course and to difficulties in treatment and diagnosis, urticaria causes a high burden for the patient,

with a reduction in quality of life (QOL) and performance.³ Published data on the epidemiology have almost always involved selective populations, usually patients attending clinics. In this report, we present the largest recent population-based study of urticaria worldwide, to our knowledge. In a representative cross-sectional survey of the population of the city of Berlin, the prevalence of the disease in the total population was determined. This paper concentrates on chronic urticaria (CU), which, in accordance with the current guidelines was defined by at least 6 weeks of continuous or recurrent weals and/or angio-oedema,^{1,2} excluding non-histamine-mediated angio-oedema.

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Methods

Study population

The PANE study is a cross-sectional epidemiological study analysing the prevalence of adverse reactions to food in Germany⁴ and is based partly on results from a doctoral thesis.⁵ The study reported here used a subset of people assessed in PANE. It was approved by the responsible Charité ethics committee and the data-protection representative of Berlin. In a representative cross-sectional survey, the prevalence of urticaria within the population of Berlin was determined, using a representative random sample of 15 000 people, all German citizens. Of these, 13 300 people were contacted by repeated subsampling in batches until the statistical threshold of 3500 respondents was exceeded; in total, 4093 responded and gave informed consent, a response rate of 30.8%. Besides age and gender, education levels were taken into consideration, because the frequencies of some allergic diseases are positively associated with the level of education.

For the initial contact, a standardized questionnaire based upon elements and questions of the Federal Health Survey of 1998 was used.⁶ It recorded frequency, symptoms, clinical features and reproducibility of reactions to food intolerance. In addition, this questionnaire asked if respondents had ever experienced any of a list of diseases and symptoms often associated with urticaria, and recorded their eating habits and demographic data. All other items were related only to the PANE study. A slightly altered questionnaire, which was answered by a parent, was used for children aged < 14 years.

All respondents ($n = 767$) who reported ever having had weals or angio-oedema were interviewed by telephone. Of these, any who reported active symptoms in the previous 3 years ($n = 247$) were invited for a personal investigation.

Urticaria questionnaire

Based on the routine questionnaire described above, a specific urticaria questionnaire was developed.⁷ It contained 34 main questions and several subordinate items. The questions in the first section related to the first appearance of the disease, its duration, and its relevance to the patient's life at the time of the questionnaire. An open question asked the patient what they thought was the likely cause of the disease. Thus, a rough differentiation between acute and chronic urticaria and between current and past conditions was possible. Questions 2–8 concerned the symptoms, the extent

and duration of the weals/swellings, the most frequently affected parts of the body, the frequency of appearance of the symptoms, and whether the patient had noticed a connection to the time of day or any association with possible causes based on their simultaneous occurrence, e.g. infection. Questions 9–18 asked about possible triggers. Questions 19–21 asked the patient if their urticaria interfered with sleep, holidays or habits. Ten further questions were taken from a validated Dermatology Life Quality Index (DLQI) (German translation).⁸

These questions could be classified into six categories: (i) extent of the symptoms and influence on well-being; (ii) limitations in household activities and clothing; (iii) limitations in social and sporting activities; (iv) limitations in the workplace or with daily tasks; (v) interference with sexual life; and (vi) problems related to treatment.

Examination of subjects and investigation of eliciting factors for urticaria

During the personal interview, the answers given on the urticaria questionnaire were discussed with the subject. A third questionnaire was completed by the doctor and subject during the consultation to elicit any history of allergies, and this was followed by a physical examination.

If physical urticaria was suspected, appropriate provocation tests were performed. All examined subjects underwent a blood test to determine the total IgE and specific IgE levels (Cap; Pharmacia, Freiburg, Germany) for latex, inhalant allergens and basic foods in the serum. The nutrient allergens were mostly tested as native fresh food samples because of their better sensitivity.⁹ The choice of the inhalant allergens was based on the subject's atopy status and to ensure detection of pollen-associated food allergies.

In addition, a prick test was performed with common nutrient and inhalant type 1 allergens (kindly provided by ALK-Scherax, Hamburg, Germany and Bencard, Munich, Germany) in all subjects who reported having symptoms in the 12 months before the investigations. A prick test was regarded as positive when the resulting weal was > 60% of a weal induced by histamine.

If adverse reactions to food were suspected, a double-blind, placebo-controlled food challenge (DBPCFC) test was performed. The following products were used as placebo and to mask the colour, smell and taste of the tested food: non-dairy milk substitute (Sinlac®; Nestle, Munich, Germany), orange flavouring (Modjul; SHS International, Liverpool, UK), cereal flakes, carotene

and/or cocoa powder. These oral provocation tests took place after a special elimination diet avoiding the suspected type1 allergens. In cases where a non-IgE-mediated pseudo-allergic reaction to food was suspected, an elimination diet followed by a double-blind oral provocation test (the only one possible) was used to confirm the diagnosis.¹⁰ For this purpose, subjects were

put on a pseudo-allergen-free diet¹¹ for 3 weeks before double-blind oral provocation tests were performed with food additives in capsules (mannitol and silicon dioxide serving as placebo). If natural foods were suspected to be the trigger, an oral, double-blind, placebo-controlled provocation test was performed as described above for IgE-mediated allergy.

Table 1 Patient demographics.

	Unweighted, %	Weighted, %
Gender, M/F	54.2/45.8	52.3/47.7
Age, years		
0–19	20.1	17.9
20–39	28.1	28.5
40–59	28.5	29.3
60–79	20.6	21.0
≥ 80	2.7	3.3
Education		
Completed university/vocational college	34.4	22.9
Completed second-level education*	29.1	27.9
Compulsory second-level education only†	15.6	25.9
Other	20.9	23.3

*Gained second-level graduate qualification; †up to the age of 16 years.

Results

There was no significant difference in age or gender between respondents and nonrespondents. A comparison of the age distribution of both groups showed only a small deviation for people aged < 30 years responding more and those aged > 65 years responding less. The representativeness of the study was checked by comparison with the Berlin Micro Census of the same year, and data were weighted with regard to age, gender and education levels. Table 1 shows the weighted and unweighted distribution of gender, age and education. As expected, the main differences between weighted and unweighted data for the examined features were associated only with education. The calculation of prevalence rates was based on a conservative approach; cases in which no clear diagnosis could be obtained were regarded as non-CU (Fig. 1).

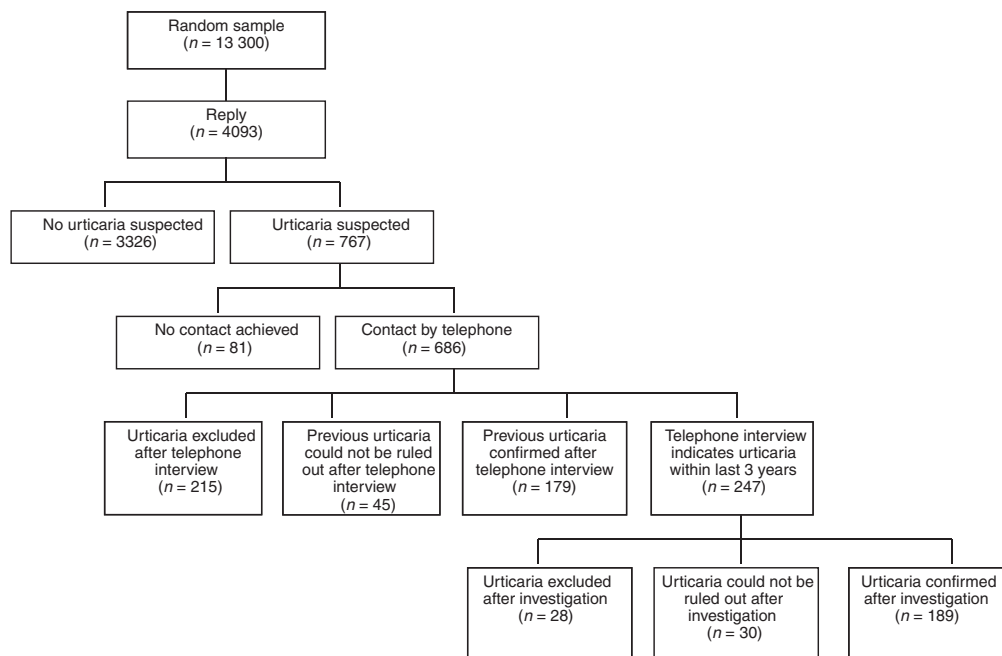


Figure 1 Flow sheet of the study and investigations performed. Patient numbers are unweighted. Patients for whom telephone contact could be achieved ($n = 81$) or in whom urticaria other than chronic urticaria (CU) could not be excluded after telephone interview ($n = 45$) were categorized as non-CU.

A lifetime prevalence of 8.8% (95% CI 7.9–9.7%) was found for all types of urticaria in the whole population (mean age 39 years), the majority of cases being acute and physical urticaria.

Chronic urticaria

Lifetime prevalence for CU was 1.8% (95% CI 1.4–2.3%). A period prevalence for active CU within the past 12 months of 0.8% (95% CI 0.6–1.1%) was calculated, of which chronic recurrent urticaria, with a period prevalence of 0.6% (95% CI 0.4–0.9%), was the most common subtype. Chronic continuous urticaria was found to be significantly less common (period prevalence 0.2%; 95% CI 0.1–0.3%) and there were no subjects with daily symptoms of CU. In 1999, the average age of subjects with CU was 42.8 years, which was greater than the average age of all subjects with urticaria in our study (mean 37.7 years). Women were more likely than men to have CU (70.3% vs. 29.7%). People with higher education had no significantly increased risk for urticaria.

Notably, we found that angio-oedema occurred together with weals in one-third of all cases (33.3%). In 6.1% of the respondents, CU appeared only as recurrent angio-oedema. The most frequently reported locations for weals were over the whole body (57.1%), and on the limbs (28.6%), face (14.3%) and trunk (9.5%). Angio-oedema mainly appeared on the face: the eyes were affected in 69.2% of cases, the lips in 61.5% and the whole face in 36.4%. Extracutaneous symptoms were found in over a third of cases (39.4%). Swelling in the oral cavity was the symptom most frequently associated with CU, occurring in 18.1% of subjects. A small group (9.1%) of subjects with CU reported dyspnoea, rhinorrhoea or irritation of the eyes. Almost one-third (31.1%) of subjects with CU reported having an independent episode of acute urticaria before this latest episode. Over half (52.7%) of the subjects had an atopic disease: 41.9% had allergic rhinitis, 18.9% had atopic dermatitis and 17.6% had allergic asthma.

Prick tests were performed in 69.7% of subjects with active CU ($n = 23$). At least one sensitization was detected in 39.1% of the tested subjects, and 18.3% of the people affected had positive prick tests to food allergens. The most common allergens were hazelnut (12.1%), potato (9.1%), apple (6.1%) and oatmeal (6.1%).

The IgE values of 66.7% of the subjects with CU were determined. The median total IgE value was 88.8 kU/L, a significant increase compared with subjects with acute urticaria (median 51.3 kU/L) and all subjects with any

type of urticaria (median 71.4 kU/L), but is within the normal range (< 94 kU/L). An oral DBPCFC proved that IgE-mediated food allergy was not the cause of the disease in any of the subjects with CU. Although in total, 18.2% of subjects with CU had positive reactions to the DBPCFC, none developed weals; only oral allergy syndrome, local itching and dyspnoea were seen, and in one case mild oral angio-oedema without weals occurred. The DLQI showed an impairment of 17.4% in QOL for subjects with CU.

Discussion

In this study, we confirmed the published data for the lifetime prevalence of urticaria: 8.8% (population of Berlin), 7.8% (Germany) and 9.0% (southwest Norway).^{12,13} These three studies, although with different intentions and study populations, were similarly structured: all used questionnaires and the diagnosis was based on a medical interview and/or additional investigations. The estimates in the existing literature for the prevalence of CU range from 0.05% to 3%.^{14–16} In our study, we found a period prevalence of CU within the past 12 months of 0.8%. Further comparisons with reports from the older literature are difficult, as the definitions used and the numbers and grouping of urticaria subtypes vary considerably. For our study, we followed the definitions of urticaria from the current guidelines first published in 2000, and reconfirmed in 2004 and 2008.^{1,2,7}

To date, very few investigations have investigated the incidence of urticaria incidence, except in Sweden,¹⁷ where a rate of 1.9% was found. We confirmed a female predilection for urticaria, but we have no explanation for this. However, similar patterns have been found with other atopic diseases.^{12,13} We found that 39.1% of our subjects with CU had ≥ 1 sensitization as shown by the skin prick and specific IgE tests, a similar proportion to previous studies (34–44%).^{18,19}

Using DBPCFC, we were able to show that none of the patients with urticaria had a food allergy or a non-allergic hypersensitivity to food triggering their disease. This is in contrast to our previous findings in in-patients,¹¹ in which we found a high prevalence of pseudoallergic reactions to food in CU. However, the important difference between these two studies is that the patients studied in our earlier investigation were more severely affected and had daily continuous symptoms, whereas in the present study, not a single case with daily symptoms was found.

The impairment of QOL in our population (17.4%) was not as pronounced as the impairment reported for

patients with urticaria in a dermatological clinic (28%).¹⁹ This difference is probably due to the reduced severity described above. Although we did not use urticaria-specific instruments like those recently developed by Baiardini,²⁰ we consider that our results are a valid reflection of the effect of urticaria on our subjects' lives. Thus, this study emphasizes the burden placed by urticaria on the patient and on society.

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