Original Article

Epidemiology of urticaria in Spain

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Summary

Background: In spite of the frequency of chronic urticaria there are very few epidemiological studies of its prevalence and distribution.

Objective: We wanted to approach the real prevalence of chronic urticaria in a population-based study and to depict demographic distribution and personal perception of the disease. We also wanted to describe the frequency of acute urticaria episodes in the population studied.

Methods: We conducted a population-based study among adults in Spain. We questioned 5003 individuals after calculating a sample size for a maximum variability (conservative approach p=q=0.5)

Results: We found a 0.6% (95% CI: 0.4-0.8) prevalence of chronic urticaria. The prevalence is significantly higher in women than in men with a OR=3.82 (95%CI 1.56-9.37). Chronic urticaria is a self-limited disease, yet in 8.7% of cases chronic urticaria lasts from one to 5 years and in 11.3%, for more than 5 years. The average age of onset is 40 years.

Conclusions: We offer large epidemiology study data on the prevalence of chronic urticaria. The prevalence of chronic urticaria has not yet been defined in an adult population-based study. With this work we offer such data to describe the prevalence and features of this disease.

Keywords: Chronic urticaria, prevalence, population based survey study, phone interview, epidemiology

Introduction

Chronic urticaria can be defined as the occurrence of widespread daily or almost daily wheals for at least 6 weeks [1], which may be accompanied by angioedema. While the wheals are transient, the resolution of angioedema is slower than wheals and could take up to 72 hours. The natural course of chronic urticaria is self-limited, with spontaneous remissions and occasional relapses[2].

Clinical subtypes consist of physical urticarias, which account for 35% of patients with urticaria, urticarial vasculitis which accounts for less than 1%, while the rest belong to chronic idiopathic urticaria. In recent years it has been shown that 35 to 40 percent of these patients have a circulating antibody directed against the α subunit of the high affinity IgE receptor [3-5] while an additional 5 to 10 percent that have antibodies against IgE [6]. Some of these types can overlap. However, in 60% the origin remains unknown.

Although it was described for the first time by Hippocrates and it is a frequent reason for visiting emergency departments[7], general practitioners, dermatologists and allergists, there is hardly any population-based study on the prevalence of chronic urticaria. Since the much-quoted Champion study [8] based on a review of 554 patients carried out in 1969, and the study performed by Hellgren in 1972 [9], there have been very few retrospective case review studies [10,11] and there is a lack of cross sectional studies.

Chronic urticaria is one of those diseases which constitutes a relatively low threat to health yet has a greater impact on the quality of life[12,13] and presents a major challenge to the physician. On the other hand, a lack of knowledge of its real aetiology and the perception both by the patient and the doctor of an underlying disease or a hidden allergy as the cause, often leads to performance of multiple and expensive tests on these patients, which produce consistently normal results[14].

In the present study we found a 0.6% prevalence of chronic urticaria. We hope this study will serve as an initial step to update the epidemiology of chronic urticaria. We also expect this study will help to fulfil the requirement for objective data to communicate to the patients.

Objectives

In this study we hoped to establish the prevalence of chronic urticaria in a sample of adult general population. We then wanted to describe the profile of population who suffers from this disease, establish the age and sex differences, and to also depict the perception of the patient suffering from chronic urticaria.

Material and Methods

An epidemiological transversal study was performed.

Sample: Sample size was calculated for a maximum variability (conservative approach p=q=0.5), assuming a 1.4% error for global results and a 95% confidence interval. Five thousand and three individuals agreed to take part from a larger population sample of 105.603 randomly selected from a national telephone directory. The rate response was 99%. We interrogated 2436 men and 2567 women with an age distribution showed in Table 2. Social status was calculated depending upon the family income.

The individuals questioned were stratified according to sex, age and location. The phone survey was performed with each individual employing the Computer-assisted Telephone Interview technique [15-18] and was supported by the Taylor Nelson Sofres Market Research Omnibus Phonebus company (Barcelona, Spain).

The questionnaire was previously validated with 27 patients with previously diagnosed chronic urticaria and 26 healthy controls. It rendered a sensitivity of 0.92 and specificity of 0.98. We included three different synonyms for the word "hives" used in different regions of Spain. The questionnaire is shown in Table 1.

Chronic urticaria was defined as the presence of hives with or without angioedema daily or more than twice a week for at least 6 weeks[19]. We defined prevalence as the number of cases with the disease active at the present moment (questions number 11 and 12: Have you had hives during this week? and Are you currently receiving treatment?)

Table 1. Questionnaire

1. Have you ever had hives? Yes/No
2. Have you ever experienced angioedema or swelling of lip, eyelid or other body parts? Yes/No
3. Did the hives last more than 6 weeks?
4. How long did they last?
5. At what age did you have it?
6. Do you know what the cause was?
7. If yes, please specify which do you believe it was:
8. Which specialist did you seek?
   - General practitioner
   - Dermatologist
   - Allergist
   - ER
   - Other
9. Which tests were performed?
10. Which treatment did you receive?
11. Have you had hives during this week?
12. Are you currently receiving treatment?

Statistical analysis

In the descriptive analysis relative and absolute frequencies were computed. We calculated the prevalence of chronic and acute urticaria and their 95% confidence interval (CI 95%). For the bivariate analysis we used the Pearson test and calculated the Odds Ratio (OR) for 95% confidence interval (95% CI). A "P" value lower than 0.05 was considered statistically significant. The statistical software program SPSS 6.1 was used for statistical analysis.

Results

Cumulative incidence of acute urticaria

The cumulative incidence by ages of acute urticaria is given in Table 2, with an average of 18.72% (95% CI: 22.3-15.19).

Sex, age and demographic differences in acute urticaria

Table 2 shows the demographic distribution of people affected. In acute urticaria we found a significantly higher prevalence in women (OR=1.64; 95%: CI 1.4-1.9). We also found a higher significant frequency of acute urticaria in cities with more than 500.000 inhabitants and in the central southern region of Spain. These data are summarised in Table 2.

Table 2. Cumulative incidence and demographic distribution of acute urticaria

	n = 5003	n = 1044	
		n	%
Age (years)			
18-24	633	127	20.06
25-44	1946	434	22.30
45-64	1377	249	18.08
>65	1047	159	15.19
Sex#			
Men	2436	408	16.7
Women	2567	636	24.7
City population*			
< 10.000	1218	242	19.9
10.000-50.000	1213	233	19.2
50.000-500.000	1666	338	20.3
>500.000	906	232	25.6
Social status			
High	1110	243	21.9
Medium	2083	394	18.9
Medium-low	1267	269	21.2
Low	543	138	25.4
Geographical region*			
Barcelona	370	79	21.3
Catalonia - Aragon	632	101	15.9
Levant	699	135	19.3
South	993	256	25.7
Madrid	594	149	25.1
Center	479	101	21.1
North east	544	114	20.9
North center	495	73	14.7
Canary islands	197	36	18.3

# p < 0.0001; * 0.001

Actual prevalence of chronic urticaria

One hundred forty seven individuals (2.9%) acknowledged having had hives which lasted more than 6 weeks, 30 of them were having active disease during the study. We estimated the prevalence of chronic urticaria to be 0.6% (95% CI: 0,4%-0,8%).

Duration of chronic urticaria

In 52.3% of patients who had suffered from chronic urticaria in the past (n=147) it lasted from 6 to 12 weeks, in 18.5% from 3 to 6 months, in 9.4% from 7 to 12 months, in 8.7% from 1 to 5 years and finally in 11.3% of patients the urticaria lasted for more than 5 years. (Figure 1)

Sex, age and demographic differences in chronic urticaria

When comparing between sexes we found a significantly higher prevalence of chronic urticaria in women (0.48%) than in men (0.12%) (OR 3.82; 95% CI: 1.56-9.37). The age of onset followed the same profile in men as in women (Figure 2). We found no differences regarding to economic status, geographical location, or size of city. These data are summarised in Table 3.

Type of physician sought and treatment received

Finally, we studied the type of physician visited by the patients who had suffered or were suffering from

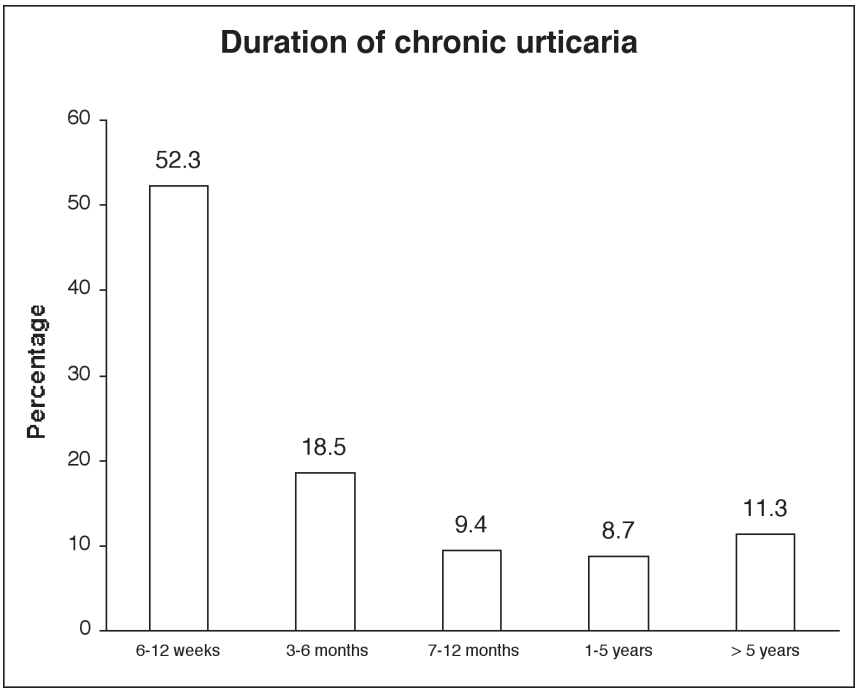

Figure 1. Percentage of duration of chronic urticaria (n= 147).

chronic urticaria (n=147) to resolve the problem. One hundred thirty-three (90.4%) needed medical attention, 35 (23.8%) were referred to an allergist, 71 (48.2%) to the dermatologist and 3 (1.8%) sought alternative medicines. We include the remaining answers in Table 4.

When urticaria lasted less than three months, patients tended to visit a general practitioner or a dermatologist, and a small proportion (15.6%) required visits to Emergency departments. With larger symptomatic periods, there was a significantly higher proportion of patients who went to the allergist and Emergency visits decreased. Interestingly, there is a frequency association (χ^2 $p<0.01$) between the group of patients whose urticaria did not disappear in 5 years and the number of specialists visited.

Figure 2. Age of onset. Three men and a woman did not recall the age of onset and so they were not

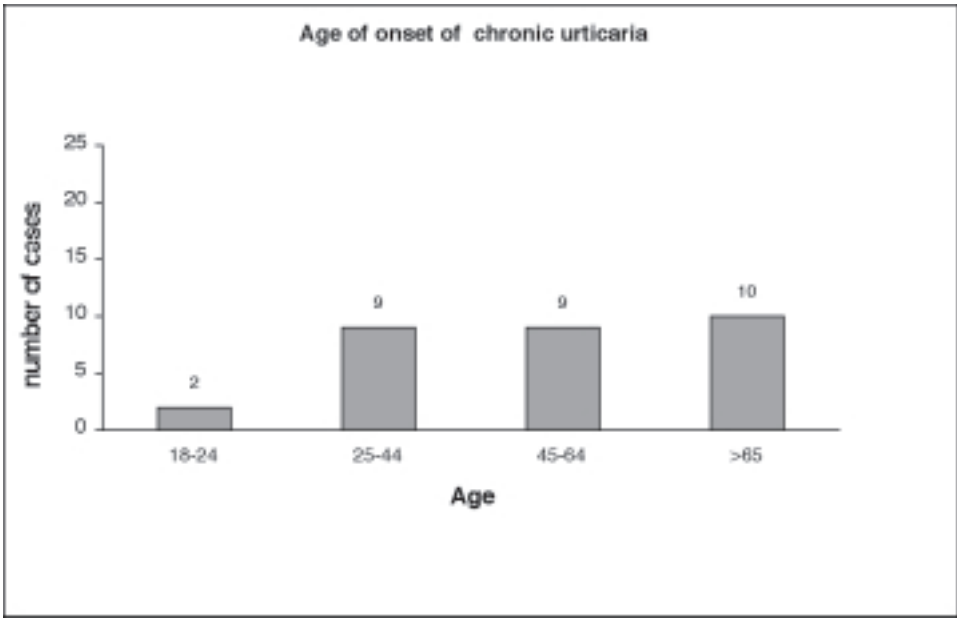

Table 3. Actual prevalence and demographic distribution of chronic urticaria

	n = 5003	n = 30	
		n	%
Age (years)			
18-24	633	2	0.32
25-44	1946	9	0.46
45-64	1377	9	0.65
>65	1047	10	0.96
Sex[#]			
Men	2436	6	0.12
Women	2567	24	0.48
City population			
< 10.000	1218	6	0.49
10.000-50.000	1213	7	0.58
50.000-500.000	1666	14	0.84
>500.000	906	4	0.44
Social status			
High	1110	2	0.18
Medium	2083	15	0.72
Medium-low	1267	10	0.79
Low	543	4	0.74
Geographical region			
Barcelona	370	0	0
Catalonia - Aragon	632	2	0.04
Levant	699	4	0.08
South	993	7	0.14
Madrid	594	4	0.08
Center	479	4	0.08
North east	544	3	0.06
North center	495	3	0.06
Canary islands	197	3	0.06

# $p < 0.0001$

Discussion

We understand that our data cannot be compared with similar statistics since there are no recent population-based studies. Moreover, in spite of many efforts over the last two decades to identify causes of different types and subtypes of urticaria there is no agreement on its classification. Furthermore, due to the heterogeneity of the disease and the different mechanisms involved, it is even more difficult to reach authoritative conclusions. Yet surprisingly, our data on acute urticaria agree closely with previous results based on retrospective case review studies. Sheldon pointed out[20] in 1954 that 15% of the population had an episode of urticaria at some time in their lives, Hellgren [9] in 1972 gave a figure of 17.02%, Champion in 1969 found 20% [8] and we report 18.72% average of cumulative incidence.

Neither can we compare our results on chronic urticaria with prior studies since previous work did not distinguish between acute and chronic urticaria, they included both children and adults, and were mostly based upon retrospective or prospective case reviews. We only included in our study those patients who acknowledged having had hives with or without angioedema for more than 6 weeks. From our results, we can conclude that chronic urticaria has a prevalence of 0.6% in our adult population. These results have the limitations of a phone survey. Some patients might have identified other skin conditions than urticaria, yet examining each patient is not feasible for large population studies, and it must be

Table 4. Results of questions regarding age of onset, perception, and treatment received by patients with past or present chronic urticaria

	n = 147	Proportion
Know what is their urticaria caused by		
Yes	73	50
No	74	50
If yes, what was it		
Hidden illness	17	11.6
Allergy	11	7.5
Pollen	6	4.1
Animals	5	3.4
Sun	3	2.0
Drug allergy	3	2.0
Food	14	9.5
Others	10	6.8
Do not answer/do not know	4	1.8
Tests performed		
Blood test	67	45.8
Urinalysis	45	30.6
Skin prick test	46	31.6
Skin biopsy	17	11.8
Stool parasites	16	10.7
X-ray	26	17.9
Other	23	15.8
No test	53	36.0
Treatment received		
Oral antihistamines	34	22.9
Systemic corticosteroids	48	32.9
Topical treatment	79	53.4
Diet	14	9.3
Antidepressants	14	9.3
Other	36	24.3
No treatment	17	11.4
Do not answer/do not know	2	1.7

recognised that the diagnosis of urticaria is primarily historical. However, the sensitivity and specificity of our questionnaire was high and it has the advantage of being a nation-wide sampling. Thus we can conclude that, although this disorder is not life threatening, its prevalence makes chronic urticaria a major human morbidity issue. We asked patients in our study whether they have either hives or angioedema, since angioedema without hives is considered chronic urticaria by several authors [21]. It may also have included patients suffering from delayed pressure urticaria. However, it actually does not impact our data since only four individuals included in the prevalence data had angioedema without hives.

Even though expected, we confirm a significantly higher incidence in women than in men at a proportion of 4:1. We cannot explain this sex difference but it emerged in all the case review studies [8,9,22] This sex difference also holds for acute urticaria, and it continues through all the age groups. One possible explanation could be the 35-40% autoimmune origin of chronic idiopathic urticaria since women have a higher prevalence of autoimmune diseases[23].

We demonstrate herein that chronic urticaria is often a self-limited process (more than 70% patients reported resolution in less than 6 months). We cannot provide data on the percentage of relapses, as a question regarding relapses was not included in the survey in order to simplify the questionnaire and to avoid confusing data. With these results we can offer some useful information to patients with chronic urticaria regarding expectations of remission. In summary, 70.8% are likely to be free of symptoms within 6 months. Yet there are still 9.4% of patients whose chronic urticaria will last at least 7 months to a year and 8.7% that will have it from 1 to 5 years. Finally, there is 11.3% probability of no remission after 5 years. We think that the last 11.3% is the group that needs more attention and intervention, especially when we consider the reported [12,13] high incidence of sleep disturbance, anxiety, and depressive symptoms with a larger impact on work and rest activities.

Moreover, another fact that greatly stresses these patients is their confusion about the aetiology of urticaria. For that reason, we included an open question on the cause they attribute to the chronic hives. Interestingly, the perception was almost identical with half of patients knowing the cause and the other half acknowledging that they did not know it. Likewise, there is a clear perception of two kinds of causes: either an underlying disease, or an allergy to foods, additives or drugs, yet nobody could say precisely which one triggered it. The perception of the cause did not change throughout the duration of the disease. We think this is a first step since we cannot say to what degree this answer was directed by a physician and how much comes from a human desire to associate events.

Concerning tests performed and treatment received, we wanted to reflect the patient's perception. Very few conclusions can be made since the patient usually has little idea as to which tests are performed. It confirms that many tests are indeed performed on these patients; further data and a questionnaire to physicians would help to address this problem. From the data on treatment received there is a surprisingly high frequency of topical treatments prescribed.

Taken all together, these data demonstrate that following recent guidelines[19,24,25], performing a thorough history and physical examination would avoid most of the suffering the patients go through. In the majority of patients symptomatic pharmacological treatment is possible with the new generation of antihistamines. When non-sedating antihistamines are ineffective, the "old" sedative types e.g. Hydroxazine at 25-50mg QID can still be beneficial and

steroid sparing[2]. For severe, non-responding patients, addition of anti H2 antihistamines should be tried and sometimes we should consider corticosteroids [2,26] or other reported therapies [27-29] such as cyclosporine. Usually, what the patient really needs is a detailed explanation of what is known of this disease, what their chances of remission are and what can they expect from a symptomatic treatment that will not cure the cause.

This work will allow physicians to indicate to a concerned patient that his/her disease is more than likely self-limited but there is a small but appreciable chance that it may last five or more years.

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