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Chronic Ordinary Urticaria: A Clinico-Epidemiological Study in Iraqi Patients

Medical Science

KEYWORDS : urticaria, autoimmune , idiopathic.

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ABSTRACT

Background: Chronic ordinary urticaria is a fairly common disorder. A diversity of factors and causes may contribute in their provocation.

Objectives: To evaluate the clinical and epidemiological aspects of chronic ordinary urticaria, and to estimate the frequency of causes of this problem among Iraqi patients.

Patients and Methods: Sixty one patients having chronic ordinary urticaria,
43 females and 18 males had been recruited from the out patient clinic Department of dermatology and venereology Baghdad Hospital, Baghdad. History and physical examination were performed. All patients were sent for laboratory investigations to evaluate the causes of urticaria.

Results: A total of 61 patients with chronic ordinary urticaria, (70.5%) were females and (29.5%) were males. Their ages ranged from 13-65 years with a mean + SD 36.38 + 14.90 years. Depending upon the various provoking factors and the presence of circulating auto antibodies, patients were divided into three subgroups; chronic idiopathic urticaria (50.8%) patients, chronic urticaria with auto-immune bases(autoimmune urticaria) (27.9%) patients, of which anti-Helicobacter pylori antibodies were found in (19.7%) patients (two patients of this subgroup had also insulin dependant diabetes mellitus, and other two patients had also vitiligo which constituted (33.3%) out 12 patients). Antithyroid autoantibodies were found in (8.2%) patients; without thyroid diseases in (4.91%) patients, and with thyroid disease (hypothyroidism) in (3.3%) patients. Chronic urticaria with potential provoking factors (21.3%) patients. Forty seven (77.0%) patients with chronic ordinary urticaria had also angioedema (ordinary acquired angioedema). Different types of physical urticarias occurred in (73.8%) patients.

Conclusion: 50.8% of chronic ordinary urticaria patients were idiopathic, 27.9% with autoimmune bases and the remaining were with potential provoking factors . Full history taking remains the first most essential step to find the types and causes of chronic ordinary urticaria (as all patients with identified causes were symptomatic in this study).

Introduction:

Urticaria is a group of skin eruption characterized by well circumscribed, raised, usually pruritic, transient erythematous and/or oedematous swelling of the dermis or subcutaneous tissue, where it is called angioedema[1].The term ordinary urticaria can be used when predominantly physical, vasculitic and contact urticarias have been excluded[1]. Ordinary urticaria is either acute or chronic. Chronic ordinary urticaria is defined as the daily, or almost daily, occurrence of urticarial wheals for at least six weeks[1, 2]. Chronic ordinary urticaria (COU) is a fairly common disorder occurring in 0.5% to 3% of the population[3]. At least 50% of chronic ordinary urticaria is idiopathic[3, 4]. About 30% - 50% of chronic urticaria patients have evidence of an autoimmune basis[3]. There does not appear to be an increased incidence of atopy[5].

Regarding the pathogenesis of chronic ordinary urticaria, cutaneous mast cells release more histamine spontaneously and in response to non – specific degranulating agents such as morphine and codeine, and cutaneous vasculature is more responsive to histamine than skin of normal persons, also with intrinsic abnormalities of basophils or mast cells[6].

In autoimmune chronic urticaria, activation occurs by cross – linking autoantibodies IgG directed against the alfa subunit of high affinity IgE receptor (FC epsilon R1 alfa) or less commonly against IgE bound to receptor,leading to histamine release from mast cell and basophils[7, 8]. Cellular infiltrate, releases a variety of cytokines that may enhance and perpetuate the whealing response. Blood basophils numbers are substantially reduced in chronic ordinary urticaria, and they may contribute to prolongation of urticarial wheals by active recruitment from the circulation[4, 9]. Chronic ordinary urticaria may be precipitated by potential provoking factors like drugs, food and food additives, infections, infestations, systemic diseases, psychological causes and other possible factors[1, 2].

The aim of the present work is to evaluate the epidemiological and clinical aspects of chronic ordinary urticaria, and to estimate the frequency of causes of this problem among Iraqi patients.

Patients & Methods:

Sixty one patients having chronic ordinary urticaria had been recorded from the out patient clinic- department of dermatology and venereology- Baghdad Hospital,Baghdad. Data including age, sex, residence, occupation, duration of urticaria, duration of each lesion, diurnal variation, seasonal variation, recurrences,distribution of the lesions, associated angioedema, associated physical urticarias,associated symptoms, aggravating factors, relieving factors, history of atopy, familyhistory of atopy, drugs history, past medical history, past surgical history and reviewof systems. All patients were sent for following laboratory investigations :- complete blood picture (CBP) and erythrocyte sedimen-

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tation rate (ESR), antinuclear antibodies test (ANA), general urine examination (GUE), general stool examination (GSE), liver function tests(LFT), renal function tests (RFT), fasting blood sugar (FBS), latex fixation test, ELISA test for ***Helicobacter pylori*** antibodies, antithyroid antibodies tests, thyroid function tests, and tissue typing test for HLA –DR4 and –DQ8 associated allele.

Abdominal ultrasound examinations were done for 38 patients in whom compliants or suspicions of internal diseases. Chest x-ray films were done for 39 patients, in whom positive history of old or recent respiratory tract or cardiovascular problems or positive signs on chest examination. X-ray films of nasal and paranasal sinuses were done for 21 patients, in whom positive history of nasal sinuses problems, or on examination there was palpable tenderness over the maxillary or ethmoid sinuses. Dental x-ray films were done for 14 patients, in whom there was a history of chronic dental or gingival problems.

Urine cultures were done for patients, in whom significant clinical or laboratory findings regarding urinary tract were found (12 patients). The test for dermographism was done for all patients, and also done for sixty one healthy controls.

All patients were tested for the presence of delayed pressure urticaria, by strapping a marble onto the forearm for 5 minutes, a positive response was recorded when indurated lesions were present at test sites at 6 hours (Empirical test) [(1)], and on examination there were wheals and indurations at pressure sites. Highly restricted diet test [(2)], was prescribed for four patients with chronic ordinary urticaria. In this test patients were fed lamb, rice, sugar, salt, and water for 5 days. The occurrance of new hives after 3 days suggested that foods have no role. If hives disappeared, a new food is re introduced every other day until hives appear.

Questionnaire were obtained from a control group of 142 individuals about Personal and family history of atopy and compared with all those with chronic ordinary urticaria.

All patients with positive laboratory findings were sent for further confirming Laboratory .investigations, as mentioned above, then sent (depending on their discovered problems) for consultations to the following departments; internal medicine, general surgery, ear nose throat (ENT), maxillary-facial surgery, urology, and gynecology departments, and the appropriate treatments were given.

Results:

A total of 61 patients with chronic ordinary urticaria, 43 (70.5%) were females and 18 (29.5%) were males. Their ages ranged from 13-65 years with a mean $\pm$ SD 36.38 $\pm$ 14.90 years. Depending upon the various provoking factors and the presence of circulating auto antibodies, chronic ordinary urticaria can be further divided into three subgroups:

1. Chronic urticaria with autoimmune bases (autoimmune urticaria) in whom circulating autoantibodies were demonstrated, these were found in 17 patients(27.9%).
2. Chronic urticaria with potential provoking factors, these were found in 13 patients (21.3%).
3. Chronic idiopathic urticaria, when neither circulating autoantibodies nor potential provoking factors could be found, in 31 patients (50.8%).

The age of patients in each group at presentation and at onset of COU are illustrated in table (1).

(1) Chronic urticaria with autoimmune bases, anti-***Helicobacter pylori*** antibodies were found in 12 patients (two patients of this subgroup had also insulin dependant diabetes mellitus, and other two patients had also vitiligo which constituted 4 out 12 patients). Patients with positive ELISA test for ***Helicobacter pylori*** received a one-week course of triple therapy (omeprazole +amoxicillin+ clarithromycin), despite that, the course of their COU was not changed. Antithyroid autoantibodies were found in 5 patients; without thyroid diseases in 3 patients, and with thyroid disease (hypothyroidism) in 2 patients, and treatment of hypothyroidism with thyroxin orally did not affect the course of chronic urticaria, in those patients.

(2) Chronic urticaria with potential provoking factors 13 (21.3%) patients, who went into complete remission of COU ; i.e. disappearance of urticaria; either with discontinuation of the offending drugs (if the drug was the cause), or with special treatment of related conditions, except for 3 patients only, in whom the conditions were chronic relapsing or incurable, as in one female patient with systemic lupus erythematosus, one male patient with hepatitis –C infection & chronic active hepatitis, and one female patient with breast cancer, as shown in table (2).

Regarding the presence of other forms of urticaria in our patients with COU.Forty seven (77.0%) patients with chronic ordinary urticaria had also angioedema (ordinary acquired angioedema); 38(80.8%) were females and 9 (19.1%) were males, distributed as following ; 27 (87.1%) patients with chronic idiopathic urticaria, 14 (82.3%) patients with autoimmune urticaria, and 6 (46.1%) patients with chronic urticaria of potential provoking factors .

Different types of physical urticarias occurred in 45 (73.8%) patients with COU.

Delayed pressure urticaria occurred in 21 (34.4%) patients with COU in whom the wheals were more prevalent and gathered frequently under tight clothing, at sites of bra clips and belts, on the hands after manual work,on the buttocks and lower back after sitting and on the feet after walking. Dermographism is the next common, found in 16 (26.2%)cases followed by cholinergic urticaria 7 (11.5%) cases, and cold urticaria one case (1.6%).

The study showed no statistically significant difference regarding the personal and family history of atopy between control group and chronic ordinary urticaria, as shown in table (3).

Table (4) shows possible exacerbating and relieving factors for all types of COU. Night exacerbation was found in 34 (55.7%) patients with chronic ordinary urticaria, and day exacerbation was found in 12 (19.7%) patients, while in 15 (24.6%) patients there was no much difference in their complaint throughout the whole day. There was no seasonal variation in 47 (77.0%) patients, whereas 14 (22.9%) patients had summer exacerbation mainly. Psychological disturbances (in the form of emotional tension and/or chronic anxiety, depression) were reported to exacerbate urticaria in 39 (63.9%) cases. Other factors that exacerbated COU were as following; heat 38 (62.3%) cases, drugs 18 (29.5%) cases (aspirin as an exacerbating factor rather than as a direct cause, and other NSAID in 10 (16.4%) cases, penicillins in 8 (13.1%) cases), food 11 (18.0%) cases (as spices, egg, sweets, fruits and fruit juice, tommato, tommato paste, cheese and fish), and exercise in one case. In this study cold water was found to relieve pruritus and erythema in 38 (62.3%) cases while different types of antihistamines were relieving factors in 36(59.0%) cases and physical rest in one case, as also shown in table (4).

Regarding associated symptoms, pruritus was usually severe in all patients. Psychologic disturbances were recorded in all patients. They took the form of emotional tension with nervousness, and/or extrinsic (neurotic) depression, anxiety, phobia from having a serious disease, and obsession. Sleep disruption was found in 50(82%) patients, fatigue was complained of by 45 (73.8%) patients. Arthralgia, abdominal pain, nausea and vomiting, diarrhea, and respiratory symptoms (cough, wheezing and dyspnea), were mentioned by only small percentages of patients, as shown in table (5).

The results of investigations showed that ESR was raised in 10 patients with COU (more than 20 mm/L), their ESR ranged between 30 – 90 mm/hr. with a mean of 47.5 mm/hr. These patients had the following underlying diseases; metastatic breast carcinoma (1 case), SLE (1 case), hepatitis-C infection with chronic active hepatitis(1 case), purulent chronic cholecystitis (2 cases), recurrent UTI (1 case), chronic sinusitis with recurrent sinus abscess formation (1 case), chronic periapical infection with recurrent abscesses and granuloma (1 case), chronic anaemia(2 cases). Eosinophilia (more than 3%) was detected in 8 (13.1%) patients, six patients had intestinal amoebiasis while two patients had giardiasis. Leucocytosis (more than 11000/c.m.m.) was present in 6 (9.8%) cases; one case had chronic active hepatitis two cases had chronic cholecystitis, one case had UTI, one case had chronic sinusitis, and one case had chronic periapical infection. Normochromic normocytic anaemia (Hb. less than 14 g/dL in men, and less than 12 g/dL in women) were found in 3 (4.9%) patients. Leucopenia (less than 4000/c.m.m.) was demonstrated in 2 cases, one case with SLE and one case had breast cancer. Thrombocytopenia (less than 250.000 /c.m.m.) in one patient who had breast cancer.

- General stool examination results were as follow; nine (14.7%) patients had Entamaeba histolytica, nine (14.7%) cases had intestinal moniliasis, and 4 (6.5%) cases had Giardia lamblia.

- By general urine examination, RBC more than 1/HPF in urine was found in 12 (19.7%) cases, pus cells (more than 5/HPF) were found in 10 (16.4%) patients and Trichomona vaginalis was found in 4 (6.5%) patients. Other important results of investigations, were as following;

-Chronic sinusitis in 4 (19.0%) out 21 patients of chronic ordinary urticaria who were sent for x- ray films of nasal and paranasal sinuses.

-Growth of pathogenic bacteria in 2 (16.7%) out 12 patients of chronic ordinary urticaria who were sent for urine culture.

-Renal stones with hydronephrosis in 2 (5.3%) out 38 patients of chronic ordinary urticaria who were sent for abdominal ultrasound.

-Chronic cystitis in 1 (2.6%) out 38 patients of chronic ordinary urticaria who was sent for abdominal ultrasound.

-Chronic cholecystitis with gall stones in 2 (5.3%) out 38 patients of chronic ordinary urticaria who were sent for abdominal ultrasound.

-Positive ANA was found in one (1.6%) patient out of 61 patients who were sent for this test, (a case with SLE).

-Tissue typing test (HLA-DR4, and-DQ8) were found to be positive in 9 (14.7%) out 61 patients with chronic ordinary urticaria, of which 7 (41.2%) out 17 patients had chronic urticaria of autoimmune bases (autoimmune urticaria).

-Fasting blood sugar was abnormal in two patients of the autoimmune urticaria group.

-The result of skin biobsy which was taken from patient with SLE (to exclude urticarial vasculitis) was of chronic urticaria (interstitial dermal oedema and a perivascular and interstitial cellular infiltrate mainly of lymphocytes, with few eosinophils).

In the control group dermographism test was positive in (3.06%) 3 persons only. While it was positive in (26.22%) 16 cases with COU. P-value = 0.0001.

Highly restricted diet (empirical test) was done for only 4 patients (who gave a history of exacerbation with food or food additives). The hives still occurred after 3 days of diet restriction which suggested that food had no role in their urticaria.

Discussion:-

Urticaria is one of commonest diseases in dermatology[1]. It is stated that it affects about 20% of the population at one time in their lives[1, 2]. Acute urticaria is usually self limiting. However chronic urticaria poses the great burden on the life of the affected individuals[9, 10]. Often such patients are subjected to a lot of investigations hoping to find the cause[11].

In the present study careful history,and physical examination were utilized to guide us in performing specific investigations for the purpose of finding the cause of urticaria. It was found that despite of these procedures, the cause in more than half of the patients could not be found. However, an immunological abnormality(circulating autoantibodies) were demonstrated in 27.9% of our patients, and in 21.3% a potential provoking factors could be found. And towards these two subgroups treatment aimed at the cause of urticaria should be directed.

It is interested to note that most of the provoking factors were discovered by history taking alone (like patients in whom the cause was drug), or by using simple investigations like GSE, GUE, chest X-ray and so on. Other investigations were guided by the results obtained by a detailed history and physical examination, for example, sinus X-ray, dental X-ray, abdominal ultrasound and urine culture. It is also interesting to note that the frequently requested tests for connective tissue diseases were not useful as antinuclear antibodies (ANA) was positive in one case out of 61 patients, and this patient was already known to have SLE. Other demographic factors were similar to what is published in literatures, for example females outnumber males with COU [9, 12]. In the present study no association between COU and personal and family history of atopy and it is similar to what is reported before [5].

A number of exacerbating and relieving factors were reported by our patients which are also compatible to what have been mentioned before [1, 13].

It was also demonstrated in the present work that COU has profound effects on life of the affected individuals as psychological disturbances were seen in all patients, sleep disruption was noted in 82% of patients, and fatigue was also noted in 74% of patients. These disabling effects, stressing on the importance of treating perfectly this condition.

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Tables

Table (1): the mean SD of age and the mean SD of age of onset of the patients with chronic ordinary urticaria & mean SD of duration of their disease.

Types of chronic Or dinary urticaria	Age at presentation Mean ± SD and range (years)	Age of onset Mean ± SD and range (years)	Mean ± SD of duration (weeks)
Chronic idiopathic urticaria	36.58 ± 15 .42 Range (14-64)	35.45 ± 14.34 Range (14 – 62)	76.65 ± 70.07
Chronic urticaria with autoimmune bases	35.24 ± 12 .26 Range (17 – 57)	33 . 12 ± 10.95 Range (17 – 54)	84.94 ± 72 .83
Chronic urticaria With potential Provoking factors	37.38 ± 17.68 Range (13-65)	36.38 ± 17 .46 Range (13 – 64)	55.15 ± 41 .47
Total	36.38 ± 14.90 Range (13 – 65)	35.00 ± 14 . 05 Range (13 – 64)	74.38 ± 65 .79

Table (2) : the frequency of types and causes of chronic ordinary urticaria.

Types and causes of Chronic ordinary urticaria	NO	%
I . Chronic idiopathic urticaria	31	50.81
II. Autoimmune urticaria	17	27.86
anti – ***Helicobacter pylori*** antibodies antithyroid antibodies without evident thyroid disease Hypothyroidism	12 5 3 2	19.67 8.19 4.91 3.27
III. Chronic urticaria with potential provoking factors	13	21.31
Drug induced chronic urticaria and angioedema angioedema (with only few wheals) induced by ACE – I : captopril (1) lisinopril (1) chronic urticaria & angioedema induced by aspirin	3 2 1	4.91 3.27 1.63
Intestinal amoebiasis	2	3.27
Intestinal moniliasis	1	1.63
Root canal inflammation with recurrent periapical Abscesses & granuloma formation	1	1.63
Chronic sinusitis & sinus abscess	1	1.63
Recurrent U.T.I. (spina bifida)	1	1.63
Chronic cholecystitis	1	1.63
Hepatitis – C infection & chronic active hepatitis	1	1.63
Systemic lupus erythematosus	1	1.63
Breast carcinoma	1	1.63
Total	61	

Table (3) : the personal and family history of atopy.

Chronic urticaria	Personal atopy		P – value	Family history of atopy		P – value
	No.	%		No	%	
Chronic ordinary urticaria (n=61)	6	9.83	= 0.659	10	16.39	= 0.395
Control (n=142)	17	11.97		25	17.60	

Table (4) : the possible exacerbating and relieving factors of different types of chronic ordinary urticaria.

Exacerbating factors	Chronic ordinary urticaria (n = 16)	
	No	%
Psychological Disturbances	39	63.93
Heat	38	62.29
Drugs	18	29.50
Food	11	18.03
Exercise	1	1.63
Relieving factors		
1. Cold water	38	62.29
2. Antihistamines	36	59.01
3. Physical rest	1	1.63

Table (5) : the associated symptoms with chronic ordinary urticaria.

Associated symptoms	Chronic ordinary urticaria (n= 61)	
	No .	%
1.Psychologic disturbances	61	100.00
2. Sleep disruption	50	81.96
3. Fatigue	45	73.77
4. Arthralgia	3	4.91
5. Abdominal pain	2	3.27
6.Nausea & vomiting	2	3.27
7. Respiratory symptoms	2	3.27
8.Diarrhea	1	1.63

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