

Levels of depression, anxiety and behavioural problems and frequency of psychiatric disorders in children with chronic idiopathic urticaria

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Summary

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Accepted for publication

1 November 2010

Funding sources

None.

Conflicts of interest

None declared.

DOI 10.1111/j.1365-2133.2010.10138.x

Background Several studies reported that adults with chronic idiopathic urticaria (CIU) frequently exhibit psychiatric comorbidity, most commonly depression and anxiety disorders. However the literature about children is limited.

Objectives To investigate the frequency of psychiatric disorders and to determine the levels of depression, anxiety and behavioural problems in a group of children with CIU.

Methods The study included 27 children with CIU and 27 age- and sex-matched healthy subjects. Psychiatric assessment was done by using the Schedule for Affective Disorders and Schizophrenia for School Age Children—Present and Lifetime Version (K-SADS-PL). The State-Trait Anxiety Inventory for Children (STAI-C), Children's Depression Inventory (CDI) and Child Behavior Checklist (CBCL) were used to examine the levels of depression, anxiety and behavioural behaviours, respectively.

Results The study group had more frequent psychiatric diagnoses than the control group (70% vs. 30%) and the most common psychiatric disorders were social anxiety disorder, separation anxiety disorder and specific phobia. Depression, trait anxiety, internalizing problems, somatic complaints and anxiety/depressed scores were significantly higher in children with CIU. No correlation was found between the severity and duration of illness and psychological functioning.

Conclusion This study showed that children with CIU had high psychiatric morbidity. The results suggest that the psychological status of children with CIU should be screened by clinicians and that an interdisciplinary approach combining dermatological and psychiatric evaluations is necessary for the management of CIU.

Chronic urticaria is defined as the daily or almost daily occurrence of recurrent, transitory and itchy weals with or without accompanying angio-oedema for more than 6 weeks.¹ It is a common and extremely distressing dermatological disease causing severe impairment in many facets of everyday life.² However it still remains as a major health problem in terms of aetiology, investigation and management.^{1,2}

Chronic urticaria is less common in children than adults, affecting 0.1–3% of children.³ Causal factors such as physical factors, infections and allergies can be identified in only about 20% of cases. When a possible cause cannot be determined, the diagnosis of chronic idiopathic urticaria (CIU) is made. The most common type of chronic urticaria in children is CIU.⁴

As a chronic and distressing illness, it would not be a surprise to find psychological problems in this group of patients.

Recent studies showed that adults with CIU frequently exhibit psychiatric comorbidity, most commonly depression and anxiety disorders.^{5–8} These findings support the claim that dermatological diseases and psychiatric disorders are often related.⁹ On the other hand, according to our knowledge, there is no study investigating the psychological functioning of children with CIU.

In this study, we used an interdisciplinary approach combining interview and questionnaire-based psychiatric and dermatological evaluations to assess the psychological status of children with CIU. There were two aims of this present study. The first was to investigate psychiatric comorbidity and levels of depression, anxiety and behavioural problems in children with CIU. The second was to identify factors associated with the presence of psychiatric problems.

Materials and methods

Subjects

Children with CIU were recruited from the Pediatric Allergy Out-Patient Clinic of Istanbul University Faculty of Medicine from January 2007 to August 2007. Twenty-seven consecutive paediatric patients were referred to the clinic who met the inclusion and exclusion criteria (see below). Children and their parents were invited to participate in the study, and the purpose and procedures of the study were explained to them. Upon their agreement, written consent of the children and their parents was obtained. The study protocol was approved by the Ethics Committee of Istanbul Faculty of Medicine.

Inclusion criteria were as follows: (i) having a diagnosis of CIU as defined below; (ii) being between 7 and 18 years of age; and (iii) being able sufficiently to read, write and comprehend the Turkish language. Exclusion criteria were: (i) having cognitive impairment due to psychotic illness or mental retardation; (ii) having current psychiatric treatment; (iii) having an additional chronic illness; and (iv) having received corticosteroid medication within the last 4 weeks.

Twenty-seven healthy children (with no history of urticaria or other skin diseases) from a local school were included in the study as the control group. They were matched in age and sex with the study group. They had the same exclusion criteria as those of the study group.

Procedures

A semi-structured interview form developed by the investigators was used to determine the demographic characteristics of the participants. The duration and severity of disease were also recorded. A paediatric allergist assessed the severity of CIU using the urticaria activity score (UAS) according to the European Academy of Allergology and Clinical Immunology/Global Allergy and Asthma European Network/European Disability Forum [EAACI/GA(2)LEN/EDF] guideline.¹⁰ Psychiatric assessment of the children was done by using the Schedule for Affective Disorders and Schizophrenia for School Age Children—Present and Lifetime Version—Turkish Version (K-SADS-PL) during their last visit to the hospital. Parents of the children were invited to complete the Child Behavior Checklist for 4–18 years of age (CBCL) and the children were asked to complete two self-report inventories, the State Trait Anxiety Inventory for Children (STAI-C) and the Children's Depression Inventory (CDI).

Measures

The K-SADS-PL is a semi-structured interview designed to assess 32 psychiatric disorders in children and adolescents on the basis of DSM-IV diagnostic criteria.¹¹ The current and past symptoms of the child were asked about and recorded, and lifetime diagnoses were determined. The Turkish version of K-

SADS-PL was reported to have good test–retest and inter-rater reliability.¹²

The CBCL is one of the most widely accepted and well validated rating scales that includes 20 competence items and 118 problem behaviour items.¹³ In this study, only the problem items were used. Parents are asked to score each item that describes the child's behaviour over the previous 6 months on a three-point scale: 0 = not true; 1 = somewhat or sometimes true; 2 = very or often true. Previous studies confirmed its acceptable reliability and discriminant validity in Turkish children.¹⁴ The CBCL does not generate a diagnosis, but instead suggests cut-off scores for problems in the clinical range. A *t*-score > 63 is considered clinically important.

The CDI is a 27-item, self-report questionnaire that measures cognitive, affective and behavioural symptoms of depression in children.¹⁵ Each item has scores ranging from 0 to 2 and the total score ranges from 0 to 54. The validity and reliability study of the Turkish version was carried out by Oy¹⁶ and the cut-off point was determined as 19.

The STAI-C is a self-report questionnaire consisting of two 20-item subscales that evaluate the state and the trait anxiety in children.¹⁷ The State subscale examines the shorter-term anxiety that is commonly specific to situations. The Trait subscale measures longer-term anxiety which addresses how the child generally feels. Each item is scored from 1 to 3 and for each scale the total score ranges from 20 to 60. The higher scores indicate higher levels of anxiety. The validity and reliability study in the Turkish paediatric population was performed by Ozusta.¹⁸

Diagnosis of chronic idiopathic urticaria

The medical history was recorded and a physical examination was performed. Skin prick tests with inhalant and food allergens, and provocation tests for physical urticaria were done to diagnose allergic and physical urticaria. To investigate the other causes of chronic urticaria, patients underwent additional laboratory examinations including the following: (i) blood tests for complete blood count, erythrocyte sedimentation rate, blood chemistry, liver function tests, serum levels of complement C3, C4 and C1 inhibitor, free thyroxine, thyroid stimulation hormone, total serum IgE; (ii) an autoimmune panel (antinuclear antibody, antithyroid peroxidase antibodies, antithyroglobulin antibodies); (iii) an infection panel (hepatitis surface antigen, antibody titres for hepatitis B and C viruses, urine analysis and culture, throat swab culture, *Helicobacter pylori* IgG antibodies, microscopic investigation of stool for parasite ova); and (iv) an autologous serum skin test (ASST).¹⁹ The ASST was performed while the urticaria was active, as previously defined by Sabroe *et al.*²⁰

Identification of severity of chronic idiopathic urticaria

The clinical details we noted were the duration of the urticaria in months and their distribution in the body. Moreover the number and size of the weals and severity of the itching were

scored. CIU activity was monitored using the urticaria activity score (UAS) according to the EAACI/GA(2)LEN/EDF guidelines.¹⁰ The UAS consisted of the sum of the wheal number score and the itch severity score. As urticaria scores frequently change in intensity during the course of a day or week, overall disease activity is best measured by advising patients to document 24-h self-evaluation scores for several days.¹⁰ However, in our study we used the 1 day value of UAS because not all patients were able to measure multiple scores due to the educational and social problems of some of the families.

Statistical analysis

Demographic and clinical data were shown as means and standard deviations (SD) or percentages. For comparisons between children with CIU (study group) and healthy children (control group), McNemar's test was used for categorical variables and the Wilcoxon signed ranks test was used for continuous variables. Spearman's correlation analysis was used to establish the association of CBCL, CDI and STAI-C scores with age, gender, duration of the disease and UAS in the study group. A probability level of $P < 0.05$ was used to indicate statistical significance. Two-tailed significance values were reported throughout. Data were analysed using the SPSS (Statistical Package for the Social Sciences), version 16.0 (SPSS, Inc., Chicago, IL, U.S.A.).

Results

Characteristics of the sample

There were no significant differences with respect to subjects' age and gender between the study and control groups, as summarized in Table 1. The mean duration of illness was 17.8 ± 15.9 (2–60) months and the mean UAS was 3.5 ± 1.0 (2–6) in children with CIU.

Prevalence of psychiatric disorders

Table 2 shows rates of psychiatric diagnosis in the study and control groups. Nineteen children with CIU had at least one psychiatric disorder. The most common psychiatric diagnoses were social anxiety disorder and specific phobia. In the control group seven children had at least one psychiatric diagnosis and the most common psychiatric disorder was attention defi-

cit hyperactivity disorder. Anxiety disorders were significantly more frequent in the study group.

Levels of depression, anxiety and behavioural problems

When compared with healthy controls, children with CIU had significantly higher depression and trait anxiety scores. The study group had higher total, internalizing, somatic and anxious/depressed but lower delinquent scores in the CBCL. The externalizing score in the study group was higher but this was not statistically significant (Table 3).

Association of variables with psychiatric morbidity

All variables that could potentially affect scores of CDI, STAI-C and CBCL were analysed independently. These variables were age, gender, duration of the illness and the UAS. Spearman correlation analysis revealed that CDI, STAI-C and CBCL scores were unrelated to gender, duration and severity of CIU. However, there was a positive correlation between age and CDI score ($P = 0.05$). On the other hand, correlations between age and anxious/depressed ($P = 0.06$), between age and withdrawn ($P = 0.08$), and between disease severity and state anxiety ($P = 0.06$) were close to significance (Table 4).

Table 2 Frequency of psychiatric disorders in study and control groups (total 27)

Diagnosis	Study group n (%)	Control group n (%)	P value
Any psychiatric disorder	19 (70)	7 (26)	0.002
Anxiety disorders	13 (48)	4 (15)	0.004
Separation anxiety disorder	7 (26)	1 (4)	0.07
Specific phobia	8 (30)	2 (7)	0.11
Social anxiety disorder	9 (33)	1 (4)	0.02
Generalized anxiety disorder	2 (7)	1 (4)	1.0
Obsessive compulsive disorder	3 (11)	0 (0)	0.2
Post-traumatic stress disorder	1 (4)	0 (0)	1.0
Disruptive behaviour disorders	7 (26)	4 (15)	0.3
Attention deficit hyperactivity disorder	7 (26)	4 (15)	0.5
Oppositional defiant disorder	3 (11.1)	2 (7.4)	1.0
Conduct disorder	0 (0)	0 (0)	0.2
Tic disorder	3 (11.1)	1 (3.7)	1.0
Chronic tic	2 (7)	1 (4)	1.0
Transient tic	1 (4)	0 (0)	1.0
Mood disorders	4 (15)	1 (4)	0.2
Major depressive disorder	4 (15)	1 (4)	0.2
Bipolar disorder	0 (0)	0 (0)	1.0
Adjustment disorders	3 (11)	2 (7)	1.0
Depressive	2 (7)	1 (4)	1.0
Anxious	1 (4)	1 (4)	1.0
Elimination disorders	7 (26)	2 (7)	0.2
Enuresis	7 (26)	2 (7)	0.2
Encopresis	0 (0)	1 (4)	1.0

Table 1 Demographic characteristics of study and control groups

	Study group	Control group	P value
Age (years), mean $\pm$ SD	10.5 ± 2.7	10.7 ± 2.5	0.9
Gender, n (%)			
Female	18 (67)	18 (67)	1.0
Male	9 (33)	9 (33)	1.0

Table 3 The Children's Depression Inventory (CDI), State-Trait Anxiety Inventory for Children (STAI-C) and Child Behavior Checklist (CBCL) scores of study group and control group

	Study group	Control group	P value
CDI	9.8 ± 4.3	7.4 ± 3.1	0.02
STAI-C			
State anxiety	31.6 ± 6.3	28.6 ± 4.5	0.1
Trait anxiety	34.9 ± 6.2	30.5 ± 5.4	0.01
CBCL			
Total score	59.5 ± 6.5	54.3 ± 9.0	0.01
Internalizing score	63.9 ± 6.8	56.9 ± 9.7	0.01
Externalizing score	50.0 ± 8.4	53.1 ± 9.4	0.2
Withdrawn	59.1 ± 8.2	55.3 ± 5.9	0.07
Somatic complaints	64.6 ± 7.3	53.9 ± 5.3	0.0
Anxious/depressed	62.1 ± 6.4	58.0 ± 6.4	0.03
Social problems	55.7 ± 5.7	55.1 ± 7.5	0.6
Thought problems	58.4 ± 5.6	57.9 ± 8.1	0.9
Attention problems	57.7 ± 7.0	58.3 ± 8.3	0.9
Delinquent problems	52.0 ± 3.8	55.1 ± 5.1	0.03
Aggressive problems	54.1 ± 6.9	55.2 ± 6.5	0.3

In the study group, 18 children experienced a stressor event within the 6 months before the onset of CIU. The most common reported stressful life events were failure in examinations ($n = 9$), family conflict ($n = 4$), illness of family member ($n = 3$) and moving away ($n = 3$). Psychiatric disorders were more frequent in subjects who had stressful life events ($n = 18$).

Discussion

The results of our small group showed that children with CIU had more frequent psychiatric disorders and higher levels of

depression and trait anxiety when compared with healthy children. Also they had higher internalizing, somatic and anxious/depressed scores in the CBCL. We found no effects of duration of CIU and UAS on the CDI, STAI-C and CBCL scores.

In the literature, data on psychiatric comorbidity in subjects with CIU is limited to the adult population. A study using a structured clinical interview found that 49% of the participants had at least one Axis I diagnosis.⁶ Similarly, Ozkan *et al.*⁷ reported that 60% of their study group had psychiatric comorbidity. Anxiety and depressive disorders were the most common psychiatric diagnoses.^{6,7} In our sample three-quarters of the children (70%) with CIU had at least one life-time psychiatric disorder which was compared with 26% in the control group. The most frequent diagnoses were anxiety disorders. Taken together, these findings suggest that CIU and psychiatric disorders, especially anxiety disorders, are associated in children.

In this study, subjects with CIU had higher depression and trait anxiety scores. Moreover, CBCL scores revealed that the study group had more somatic complaints and were more anxious/depressed. These results are consistent with those of previous studies which were conducted with CIU adults. Sperber *et al.*²¹ demonstrated that subjects with CIU were significantly more depressed, quite anxious, experienced significant discomfort in interpersonal relationships and were somatically preoccupied. In another study,²² analysis of the MMPI (Minnesota Multiphasic Personality Inventory) profile showed that hypochondriasis, depression, hysteria and social introversion scores were higher in patients with CIU than the control group. Another report from Turkey²³ found that subjects with CIU had higher depression and anxiety scores. Finally, in a recent study⁵ patients with CIU reported significantly more

Table 4 The correlation coefficients related to Children's Depression Inventory (CDI), State-Trait Anxiety Inventory for Children (STAI-C) and Child Behavior Checklist (CBCL) scores in the study group

	Age		Gender		Disease duration		Disease severity	
	r	P	r	P	r	P	r	P
CDI	0.39	0.05	0.19	0.34	-0.20	0.32	0.31	0.12
STAI-C								
State anxiety	0.25	0.21	0.01	0.96	-0.06	0.78	0.36	0.06
Trait anxiety	-0.16	0.43	0.01	0.98	-0.10	0.63	0.30	0.12
CBCL								
Total score	-0.21	0.28	0.00	1.00	0.08	0.69	0.09	0.64
Internalizing score	-0.20	0.32	0.04	0.86	-0.26	0.20	0.01	0.96
Externalizing score	-0.20	0.31	0.14	0.48	-0.01	0.95	0.19	0.35
Withdrawn	0.35	0.08	-0.04	0.86	0.02	0.92	-0.09	0.66
Somatic complaints	-0.28	0.15	0.06	0.76	-0.06	0.76	0.19	0.34
Anxious/depressed	0.36	0.06	-0.11	0.58	-0.18	0.38	-0.05	0.80
Social problems	-0.21	0.30	0.28	0.16	0.13	0.53	0.19	0.33
Thought problems	0.12	0.57	0.15	0.46	-0.09	0.66	-0.31	0.12
Attention problems	-0.14	0.50	0.12	0.56	0.07	0.72	-0.02	0.93
Delinquent problems	-0.30	0.129	-0.068	0.735	0.077	0.704	0.169	0.401
Aggressive problems	-0.173	0.39	0.12	0.54	0.05	0.81	0.14	0.47

somatic problems, anxiety and depression than patients with allergy. The implication of these findings is that subjects with CIU are particularly prone to manifesting psychiatric symptoms such as anxiety and depression.⁵

In our sample, the CBCL revealed that children with CIU had significantly higher internalizing and lower, but not statistically significant, externalizing scores. Interestingly several studies found an association between childhood atopic disorders (e.g. asthma, atopic eczema) and internalizing but not externalizing behaviours.^{24–27} Children with CIU may be prone to develop certain specific psychiatric symptoms (e.g. internalizing rather than externalizing).

Patients with CIU have been shown to experience high levels of stress, in particular life event stress.⁵ In a study, 81% of patients with CIU believed that their illnesses were due to stress.⁷ Prior to the onset of CIU, subjects had significantly more stressful life events and more subjective feelings related to life events than the general population.²⁸ In our study group, two-thirds of subjects experienced a stressor event within the 6 months before the disease onset. The frequency of psychiatric disorders was higher in children who had stressful life events than in those who did not. The explanation of this finding is that children with CIU are particularly prone to stress and manifesting psychiatric disorders. Moreover, it was suggested that psychiatric symptoms secondary to stressful life events may precipitate the emergence of urticarial symptoms in susceptible subjects.²³

The severity of the underlying disease may play a role in psychological morbidity. However, in parallel with previous studies,^{7,22,23,29} we found no impact of disease activity and disease duration on psychiatric functioning. As was suggested by several authors, 'perceived' subjective disease severity might have more impact on psychological health status than did objective clinical severity.²⁹ Unfortunately, in this study, no data have been collected on the patients' perceived subjective severity of CIU. On the other hand, there was a positive relation between age and depression scores in the study group. This was an expected finding because depression scores increase with increasing age in the general population.³⁰

Psychiatric assessment of the children relied both on clinical interviews, and parental and self-reports. However the limitations of our results must be considered. The small sample size is its main limitation. Secondly, the study group consisted of cases from an outpatient setting (not based on the general population). As this is a first study on the psychological functioning of children with CIU, our results need to be considered as preliminary data that must be followed by further research.

In conclusion, this study shows that psychiatric morbidity is high among paediatric patients with CIU. Our results suggest that the psychological status of children with CIU should be screened by clinicians and that an interdisciplinary approach combining dermatological and psychiatric evaluation is necessary for the management of CIU. Further studies are required to determine the effects of appropriate psychiatric interventions including pharmacotherapy and/or psychotherapy on the course of CIU.

What's already known about this topic?

- Although there are several studies on psychiatric comorbidity and psychological problems in adults with chronic urticaria there are no data in the literature about children and adolescents with chronic urticaria.

What does this study add?

- Consistent with the adult studies we found a high frequency of psychiatric comorbidity which supports the claim that dermatological diseases and psychiatric disorders are associated. Clinicians need to be aware of psychological problems in this group of patients.

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