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Relation between chronic urticaria and quality of life

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1. Abstract

Introduction: Chronic urticaria is a complex multifactorial dermatological disease. It is highly prevalent throughout the world and contributes to lower patients' quality of life. The purpose of this study is to evaluate the impact of chronic urticaria on the quality of life (QoL) and mental status in Portuguese patients.

Methods: This observational study included the evaluation of Portuguese patients from the consultation of chronic urticaria in the Coimbra University Hospital Centre, using several questionnaires including: weekly urticaria activity score (UAS7), Urticaria Control Test (UCT), Dermatology Life Quality Index (DLQI), Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) and the Hospital Anxiety and Depression Scale (HADS). The results of the questionnaires were posteriorly analysed, and the quality of life and mental status assessed in these patients were correlated with sociodemographic parameters and clinical aspects of chronic urticaria.

Results: We studied 112 patients, mainly female (80%), with an average age of 46 years, mostly classified with mild urticaria activity, according to UAS7, and the majority (85%) were poorly controlled, regarding the UCT classification. Using both CU-Q2oL and DLQI we obtained mean values of 48.98 (± 19.53) and 7.23 (± 7.67), respectively, that show a high impact on the QoL. CU also interferes with mental status values in HADS concordant with anxiety (in a total of 45 patients) and depression (in 22 patients). A strong and positive correlation was found between both instruments used to measure quality of life, with pruritus, number of papules, quality of sleep and the embarrassment caused by cutaneous lesions as the mostly affected parameters in our sample. QoL varies significantly with gender, degree of instruction, clinical severity of symptoms and level of disease control. Although not always directly related, clinical activity of the disease remains the most significant factor of patients' QoL. Anxiety and depression show a significantly relationship with quality of life, however it was not found a significant correlation with the urticaria clinical activity.

Discussion: Patient-Reported Outcomes (PRO) proved to be a practical and effective tool in daily clinic assessment of Portuguese patients suffering from chronic urticaria. The variation of quality of life according to sociodemographic characteristics is in conformity with literature. Moreover, new results were achieved regarding the level of instruction. The mostly impaired domains in our sample's QoL are not totally identical to previous studies, which suggests a meaningful effect of the geographic location. This investigation supported the significant influence of clinical activity of the urticaria and psychological well-being in QoL as previously published.

Conclusion: In Portuguese patients with urticaria, it is essential to establish an integrated approach that encompasses the clinical control of urticaria, but also the control of the associated psychological symptomatology.

Keywords: Quality of life; Chronic urticaria; Chronic spontaneous urticaria; Patient-reported outcomes; Clinical activity; Depression; Anxiety; Portuguese, DLQI, CU-Q2oL.

2. Resumo

Introdução: A urticária crónica é uma doença dermatológica complexa de natureza multifatorial. Apresenta uma alta prevalência em todo o mundo e dela decorre um impacto significativamente negativo na vida dos doentes. O objetivo deste estudo é avaliar o impacto da urticária crónica na qualidade de vida dos doentes portugueses, assim como no seu bem-estar mental.

Métodos: Este estudo observacional consistiu na avaliação de doentes portugueses, seguidos em consulta externa de urticária no Centro Hospital Universitário de Coimbra, tendo como instrumento de estudo os seguintes questionários: avaliação da atividade clínica da doença (UAS7), controlo da urticária (UCT), questionário de qualidade de vida em dermatologia (DLQI), questionário de qualidade de vida na urticária (CU-Q2oL) e escala hospitalar de depressão e ansiedade (HADS). Estes resultados foram analisados e os dados relativos à qualidade de vida e ao estado de ansiedade e depressão foram relacionados com os parâmetros sociodemográficos da amostra assim como com os aspetos clínicos da urticária.

Resultados Foram estudados 112 doentes, maioritariamente do sexo feminino (80%) com idade média de aproximadamente 46 anos, sofrendo a maioria de urticária crónica leve (de acordo com UAS7) e mal controlada (85%), segundo a classificação da UCT. Usando ambas as escalas CU-Q2oL e DLQI, obtivemos valores médios para cada, respetivamente 48.98 (± 19.53), e 7.23 (± 7.67), que demonstraram um alto impacto da qualidade de vida destes doentes, assim como uma relação significativa como os valores de HADS, encontrados nos doentes ansiosos (45 doentes) e deprimidos (22 doentes). Encontrou-se uma forte correlação positiva entre as escalas DLQI e CU-Q2oL e, de acordo a sua análise, o prurido, número de pápulas, qualidade de sono e vergonha causada pelas lesões cutâneas são os parâmetros de qualidade de vida mais afetados na amostra em estudo. A qualidade de vida destes doentes varia significativamente com o género, grau de instrução, severidade clínica e grau de controlo da doença. Apesar de nem sempre relacionada diretamente, a atividade clínica da doença permanece como o fator mais significativo na qualidade de vida. Ansiedade e depressão

apresentaram uma relação considerável com a qualidade de vida, no entanto não foi encontrada relação significativa entre o estado psicológico e a severidade da doença.

Discussão Os questionários de autopreenchimento incluídos neste estudo revelaram-se bastante práticos e eficazes na avaliação clínica de doentes com urticária cónica. As características sociodemográficas dos participantes assim como a sua influência nos níveis de qualidade de vida está de acordo com a literatura consultada. Novos resultados foram encontrados relativamente ao grau de instrução. Os parâmetros de qualidade de vida mais afetados na nossa amostra são em parte discordantes com estudos realizados em outras populações, o que destaca a importância do ambiente em que o doente se insere. Esta investigação vem ainda corroborar estudos anteriores no concerne ao impacto significativo da atividade clínica da urticária e do estado emocional na sua qualidade de vida da pessoa.

Conclusão: Nos doentes portugueses com urticária crónica, é essencial estabelecer-se uma abordagem integrada que englobe tanto o controlo clínico da urticária, como o controlo da sintomatologia psicológica a ela associada.

Palavras-chave: Qualidade de vida; Urticária crónica; Questionários; Atividade clínica; Depressão; Ansiedade; Portugueses; DLQI; CU-Q2oL.

3. Acronyms and Abbreviations

CIU – Chronic Inducible Urticaria

CSU – Chronic Spontaneous Urticaria

CU – Chronic Urticaria

CU-Q2oL – Chronic Urticaria Quality of Life Questionnaire

DLQI – Dermatology Life Quality Index

HADS – Hospital Anxiety and Depression Scale

IgE – Immunoglobulin E

IgG – Immunoglobulin G

Max – Maximum

Min – Minimum

p – significance value

PRO – Patient-reported outcomes

QoL – Quality of life

Sd – Standard deviation

UAS – Urticaria Activity Score

UAS7 – Urticaria Activity Score Over 7 Days

UCT – Urticaria Control Test

4. Introduction

Chronic Urticaria (CU) is a skin disorder defined by the presence of recurrent erythematous wheals and pruritus, with or without angioedema, for at least 6 weeks. Wheals can occur in any part of the body, last individually for less than 24 hours and blanch with pressure due to vasodilation and superficial dermal oedema in their pathogenesis basis.^{1,2}

This disease has a complex pathogenesis, mostly dependent on the discharge of pro-inflammatory molecules from mast cells present in the superficial dermis.¹ Mast cell activation occurs in response to auto-allergens recognized by immunoglobulin E (IgE) bound to mast cells, to Immunoglobulin G (IgG) antibodies that recognize IgE or its high affinity receptor on the surface of mast cells or in response to other stimulus.³ The most well-known pruritogen is histamine, which causes an inflammatory skin reaction and pruritis. When mast cell mediators act in the deep dermis, subcutaneous tissue and in the submucosa, patients experience swelling, known as angioedema.^{4,5}

When the symptoms of urticaria are induced by a stimuli, such as exercise, pressure, water or cold, it is classified as Chronic Induced Urticaria (CIU), however, in most cases no trigger is found as the cause of the urticaria lesions, which is defined as Chronic Spontaneous Urticaria (CSU). In this subgroup, some patients present autoantibodies, suggesting an autoimmune basis²

Despite lack of data found, *Costa et al 2016* reported a Portuguese incidence of 1% of CU and the same study highlighted the economic burden of this disease, with an average cost of over 6000€ per 5 years to treat a single patient with severe CU.⁶

Treatment of CU is based on an integrated approach of several factors, including eviction of triggers, dermatological care and pharmacological therapy. It is currently recommended the use of second-generation H1 antihistamines, also known as non-sedative antihistamines, as the first therapeutic option and it can be necessary to adjust the dose in the absence of efficacy. In case of resistance, more aggressive options can be tried such as systemic corticosteroids in very short regimens, or the anti-IgE monoclonal antibody Omalizumab and immunosuppression with cyclosporine.⁶⁻¹⁰

However, to treat urticaria can be very challenging and often insufficient to control the symptoms and patients suffer a considerably negative impact on their quality of life (QoL). Patients with CU experience transitory lesions frequently underestimated by physicians.¹¹ The assessment of their “silent suffering” is essential to understand the patients’ view of their disease and its consequences. Guidelines recommend the regular use of patient-reported

outcomes (PRO) for this purpose.^{12,13} Currently, there are three disease-specific instruments validated for CU: Urticaria Activity Score Over 7 Days (UAS7), Urticaria Control Test (UCT) and Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL). In addition to these scales, there are others also used in daily practice.^{9,13-15}

Moreover, the impact of disease on quality of life may not be directly related to its clinical severity, but to the stigma and discomfort caused, which reinforces the importance of the individuals' perception of their condition.^{16,17} Urticaria has been associated with a negative emotional impact, with patients experiencing somatization, depression, anxiety, insomnia, stressful life events, and others.¹⁷ A medical databases search^{11,18} revealed a high prevalence of psychosocial factors in patients with chronic spontaneous urticaria.^{17,19-21}

According to the latest guidelines for urticaria, further research is needed in order to assess CU disease activity and its impact in patient's QoL and both psychiatric and psychosomatic conditions. It has been pointed out the main need for future application of CU-Q2oL in different populations to obtain patients' views of their disease, aid treatment decision-making and to help allocating resources.^{9,15}

The aim of the present study is to estimate the impact of chronic urticaria on the quality of life of Portuguese patients and clarify in which domains they feel more affected. It is also our goal to identify how variables, such as age, gender, association with angioedema, CU severity and control, influence patients' QoL and emotional state of depression and anxiety.

Though, quality of life is the main outcome measure of this study, while emotional state of depression and anxiety are secondary outcome measures.

5. Materials and methods

We present an observational study conducted at the consultation of Urticaria of the Dermatology Department of the Coimbra University Hospital Centre, between December 2016 and December 2018. This work, included within a more extended study conducted at the Consultation of Urticaria, received the approval of the Ethics Committee of the Coimbra University Hospital Centre, and the “Comissão Nacional de Proteção de Dados”.

The study sample comprised a total of 112 patients, both male and female, aged above 16 years, with a clinical diagnosis of CU, who after detailed explanation of the objectives of the study signed the informed consent, and voluntarily participated after their regular consultation of urticaria.

An anonymous questionnaire was made including: individuals' characteristics (gender, age, duration of disease, education level, professional status and familiar situation), a score of clinical activity of urticaria over the last week (UAS7), a test to evaluate the control of urticaria (UCT), general and urticaria specific aspects on quality of life (respectively DLQI and CU-Q2oL), and questions related to the anxiety and depression state (Hospitalar Anxiety and Depression Scale – HADS), which will be furtherly detailed. Only patients able to understand the terms and sign the Term of Free and Informed Consent were admitted to the study.

Patients read and answered the questionnaires alone, but the researcher remained available to clarify any possible questions. For patients unable to read, the researcher read out loud the questions and explained the possible answers to the participants in the questionnaires.

The UAS7 was previously given to patients in order to be regularly registered by them during the week and brought to the consultation. The UAS7 questions were included in the questionnaire in order to be answered in case patients did not bring it along.

Our study was conducted using two different groups of questionnaires, as during the investigation we wanted to extend the aim of the study to comprise other parameters, UCT and DLQI, in a subsample of patients. In addition to this, the questionnaire was delivered after the consultant and, this way, its filling was limited by the time availability of patients. Thus, all patients answered the CU-Q2oL, but not all filled the other questions. An amount of 110 patients filled the HADS and 108 the UAS7 questionnaire. A subsample of 40 patients additionally filled the UCT and DLQI scale. Not all patients filled the totality of sociodemographic data.

The analysis was preformed respecting each subsample of patients.

5.1 Instruments used

5.1.1 Urticaria Activity Score Over 7 days (UAS7)

The UAS7 is a simple, validated, scoring system based on the assessment of itch intensity and number of hives. It is documented by the patient, once-daily, for seven days, allowing doctors to access disease activity during the previous week (Table 1).^{6,22}

Table 1: Categories of UAS according to the daily score.

Score	Number of hives (24h)	Itch severity (once every 24h)
0	0 (none)	None
1	<20 (few)	Mild (present but not annoying or troublesome)
2	20-50 (moderate)	Moderate (troublesome but does not interfere with normal daily activity or sleep)
3	>50 (many)	Intense (interferes with normal daily activity or sleep)

The summed scores create a daily Urticaria Activity Score (UAS) which, over a week, creates the weekly UAS (UAS7) with a score ranging from 0 to a maximum of 42. UAS7 scores are then categorized into five ranges describing 'CSU health states' (Table2).²³

Table 2: Categories of UAS7 according to the weekly summed score.

UAS7 score	Category
0	Asymptomatic
1-6	Well controlled urticaria
7-15	Mild activity
16-27	Moderate activity
28-42	Severe activity

5.1.2 Urticaria Control Test (UCT)

The UCT is a validated instrument designed to assess the level of disease control in CU patients and thereby help guiding treatment decisions. It consists in four simple questions related with the preceding four weeks, including signs and symptoms of the disease, QoL impairment, efficacy of treatment and overall disease control.^{6,14} Each question is graded from 0 to 4 and the total score is calculated by summing the individual scores. The lowest possible score is 0 (no control) and the highest score possible is 16 (complete control). A score ≥ 12 indicates well-controlled urticaria, while a score of ≤ 11 represents poor disease control.²⁴

5.1.3 Dermatology Life Quality Index (DLQI)

The DLQI is a questionnaire designed for the assessment of patients over the age of 16 suffering from any dermatological disease. Its aim is to estimate the impact of disease and its treatment on their lives, in the last seven days. It is a useful tool since it is simple to use and interpret, requiring an average of one or two minutes to be completed. The score of each question is as follows: Very much (3); A lot (2); A little (1); Not at all / Not relevant (0). One of the questions (“prevented work or studying”) has a bigger score (3 if yes is the answer). The DLQI is calculated by summing the score of each question resulting in a minimum of 0 and a maximum of 30. Higher scores correspond to a lower QoL.^{23,25}

Table 3: Categories of DLQI according to the final summed score.

Score	Effect in patient's life
0 – 1	No effect at all on patient's life
2 – 5	Small effect on patient's life
6 – 10	Moderate effect on patient's life
11 – 20	Very large effect on patient's life
21 – 30	Extremely large effect on patient's life

5.1.4 Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL)

The CU-Q2oL is a validated instrument for the assessment of quality of life impairment in patients with CU, over the last two weeks. It was created by Baiardine *et al* 2005²⁶ and recently its Portuguese version has been created.²⁷ It includes the evaluation of the physical, psychosocial and practical aspects of CU with a total of 23 questions that cover six key CU-specific domains: pruritus, swelling, impact on life activities, sleep problems, limits, and looks (table 4).

Table 4: Concepts and dimensions measured by CU-Q2oL

<p>Pruritus</p> <p>1 pruritus</p> <p>2 wheals</p> <p>Swelling</p> <p>3 eyes swelling</p> <p>4 lips swelling</p> <p>Impact on life activities</p> <p>5 work</p> <p>6 physical activities</p> <p>7 quality of sleep</p> <p>8 free time</p> <p>9 social relations</p> <p>10 eating</p>	<p>Sleep problems</p> <p>11 ease of falling asleep</p> <p>12 walking up during the night</p> <p>13 daytime tiredness</p> <p>14 ability to concentrate</p> <p>15 nervousness</p> <p>Limits</p> <p>16 bad mood</p> <p>17 limits in choosing food</p> <p>18 sport</p>	<p>Looks</p> <p>19 medication adverse effects</p> <p>20 bothersome</p> <p>21 embarrassing in public</p> <p>22 use of cosmetics</p> <p>23 choice of clothes</p>
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Within each dimension, items are scored on a 5-point scale, from 0 (not at all) to 4 (extremely), according to the patients' perception of the disturbance caused. These items are then summed to obtain an overall score, which is usually converted to a scale from 0 to 100. In this study, we used final scores and did not convert to percentage, as it would not change the results found. Higher values always correspond to higher QoL impairment, which means worse quality of life.²⁸

5.1.5 Hospital Anxiety and Depression Scale (HADS)

The aim of this scale is to measure symptoms of anxiety and depression during the last week and consists of 14 items, of which seven are for the anxiety subscale, and the other seven for the depression subscale. HADS-Anxiety (HADS-A) evaluates symptoms of generalized anxiety disorder, while HADS Depression (HADS-D) is focused on negative emotions. Each item has four alternatives, ranging between 0 and 3, not all in the same order of impairment. After adjusting the six items that are in a reserved order, all responses are summed to obtain the two subscales. Recommended cut-off scores are the following: scores 8 to 10 for doubtful cases and scores ≥ 11 for definite cases. However, as an optimal balance between sensitivity and specificity was found using a cut-off score of 8 or above for both HADS-A and HADS-D, and this value was used in the study for an easier interpretation.²⁹

5.2 Statistical methods

The variables were described according to their level of measurement. For the qualitative variables, absolute and relative frequencies were presented as for the quantitative variables we used mean and standard deviation, as well as median with quartiles, and amplitude of variation (minimum and maximum) for their description.

The comparison of the main outcome measure, QoL, whether assessed specifically for urticaria through the CU-Q2oL scale or generally related to a dermatologic condition, by the DLQI scale, was performed through the Mann-Whitney U Test whenever the factor comprised only two categories. The Kruskal-Wallis Test was used in case three or more categories were involved. Adjusted multiple comparisons were applied *a posteriori* when justified. Nonparametric tests were applied due to the lack of normality in quality of life distribution, according to factors involved. The adjustment to a Gaussian distribution was evaluated using the Shapiro-Wilk Test. Due to this fact, whenever there was the need to evaluate correlation between variables, Spearman's Rank-Order correlation was applied.

After this step, it was possible to select all variables which proved to contribute, somehow, to a distinct level of quality of life in patients with urticaria. Therefore, all those who presented

$p < 0.100$ in the previous step were selected for a regression analysis. The stepwise method was applied in order to assess variables according to their burden in prediction, and include only those that were predictive of quality of life. The assumptions of the regression models were evaluated, particularly the normality of the residuals, assessed by the Shapiro-Wilk Test, as well as residuals' independency and absence of autocorrelation, through the Durbin-Watson statistic (CU-Q2oL: DW = 1,559; DLQI: DW = 1,577). The robustness of the models was evaluated by the adjusted R^2 and the resulting p-value of the ANOVA result for the model. Statistical analysis was conducted in the SPSS³⁰, version 25, and evaluated at a significance level of 5%.

6. Results

6.1 Characterization of the sample

6.1.1 Sociodemographic features

The study enrolled 112 patients with a clinical diagnosis of chronic urticaria followed at the Dermatology Department of the Coimbra University Hospital Centre. Of these, 90 patients were female (80.35%) and 22 male (19.65%) aged between 16 and 82 years (figure 1).

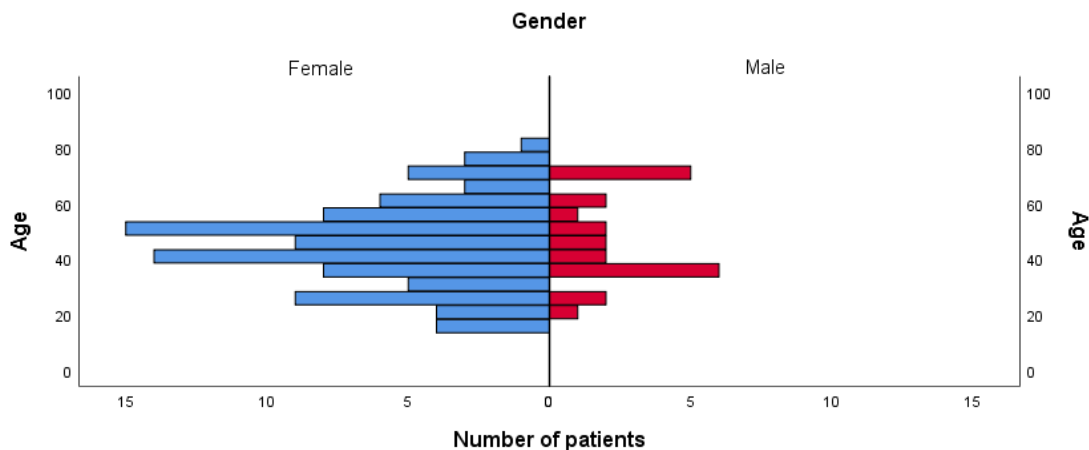


Figure 1: Bar graph showing age and gender distribution of the sample.

Table 4: Sociodemographic characteristics in the total of 112 patients.

Age (mean ± sd, years)	45.70 ± 15.79	Duration of CU (mean ± sd, years)	3.64 ± 6.21
	Patients n (%)		Patients n (%)
Gender		Professional status	
Female	90 (80.35)	Active	37 (71.2)
Male	22 (19.65)	Retired	6 (11.5)
Literacy		Unemployed	7 (13.5)
Illiteracy	2 (2.1)	Student	2 (3.8)
Able to read and write	3 (3.2)	No answer	60
Primary school	15 (15.8)	Familiar status	
Elementary school	11 (11.6)	Married	56 (62.2)
Middle school	18 (18.9)	Single	21 (23.3)
High school	20 (21.1)	Widower	4 (4.4)
Professional degree	5 (5.3)	Divorced	9 (10)
Graduated	21(22.1)	No answer	22
No answer	17		

Concerning the sociodemographic characteristics (represented in table 4), almost half of the patients have completed high school (48.5%) and more than half are married (62.2%) or professionally active (71.2%). A mean age of around 46 years was found in the sample, with an average of 4-year period since the diagnosis of chronic urticaria.

6.1.2 Clinical aspects of urticaria

All patients inquired suffer from chronic urticaria, most of them CSU, eventually associated with inducible urticaria. All patients with CIU experienced physical urticaria.

In a subsample of 40 patients, it was possible to extend the analysis of the urticaria behaviour (table 5). Angioedema was experienced, at any moment of the disease evolution, in 27 patients (67.5%). The most frequent comorbidity was depression, followed by allergic rhinitis and asthma.

Table 5: Clinical aspects of urticaria in the subsample of 40 patients.

	Patients (%)		Patients (%)
Angioedema		Classification of CU (%)	
Present	67.5	Spontaneous	86.8
Absent	32.5	Inducible urticaria	
Comorbidity		Physical urticaria	55.2
None	3.7	Undetermined form	5.3
Allergic rhinitis	18.5		
Asthma	11.1	Treatment	
Allergy to medications	3.7	None	2.5
Contact dermatitis	7.4	Antihistamines (1x/d)	32.5
Atopic dermatitis	0	Antihistamines (>1x/d)	47.5
Diabetis	3.7	Omalizumab	5
Thyroid pathology	11.1	Other	12.5
Depression	22.2		
Another one	3.7		

By analysing the distributing of scores from UAS7 questionnaires we identified a median value of 9 [3.5; 17] and mean value of 11.61 (\pm 9.98). Both values found allow us to insert our sample in the “Mild Activity” category.

Regarding the level of control, measured by UCT, a greater part was “poorly” controlled (85%), and only a minor part is “well” controlled (15%).

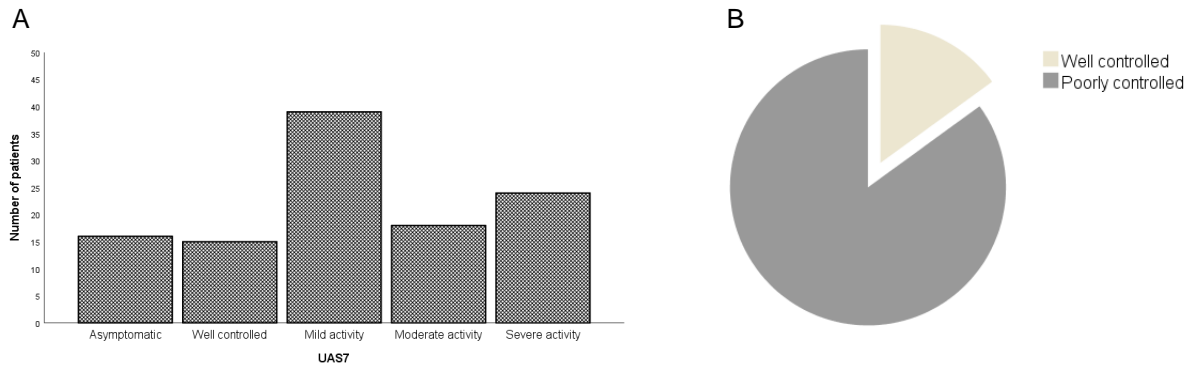


Figure 2: A - Histogram showing frequency of UAS7 categories in the sample (n=108). B - Pie graph showing distribution of patients according to UCT (n= 40).

6.2 Results of the Questionnaires

6.2.1 Quality of Life Assessment

The quality of life was measured using CU-Q2oL and DLQI scales, filled respectively by 112 and 40 patients, and distribution is shown in figure 3. Both scales will be presented in comparison for each variable studied and their values will be shown in their absolute final score.

The mean value found in the sample for CU-Q2oL was 49.13 ± 19.28 in a maximum possible of 115, while DLQI varied from 0 to 25 scoring a mean value of 7.23 ± 7.67 . Therefore, the sample was included in the category “Moderate effect on patient’s life”.

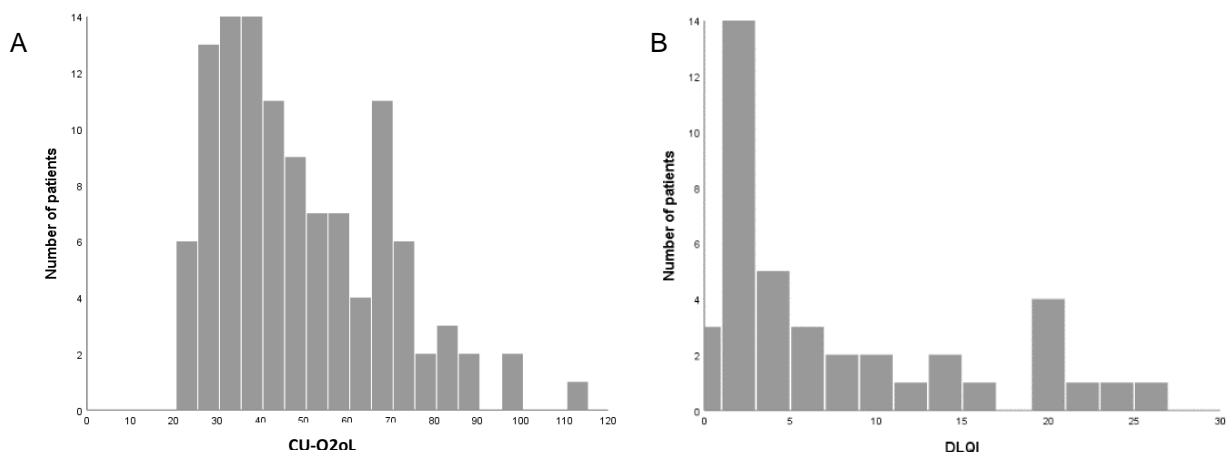


Figure 3: A - Histogram representing CU-Q2oL scores; B - DLQI scores.

Table 6: Description of CU-Q2oL and DLQI values.

Quality of Life	n	Min - Max	Mean (sd)	median [Q1 - Q3]
CU-Q2oL	112	9 - 113	48.98 (19.53)	43 [33.25; 64.75]
DLQI	40	0 - 25	7.23 (7.67)	3 [1.25; 13.25]

To further study patients' quality of life, we calculated the sum for each one of the 23 parameters evaluated in the Cu-Q2OI, in order to find out which areas are mostly affected in patients' daily life.

Table 7: Sum of scores for each parameter of CU-Q2oL evaluated in all the 112 patients. (Higher scores represented in bold.)

Pruritus	Score	Sleep problems	Score
Pruritus	330	Difficulties in falling asleep	250
Wheals	299	Wake up during the night	296
Swelling		Difficulties in keeping concentration	278
Eyes swelling	196	Feel nervous	242
Lip swelling	181	Limits	
Impact on life activities		Feel in a bad mood	224
Work	242	Have to put some limit in choosing your food	195
Physical activities	228	Sport practice	174
Sleep	259	Looks	
Spare time	238	Embarrassed due to urticaria symptoms	256
Social relationships	232	Embarrassed in going to public places	206
Eating behavior	189	Problems in using cosmetics	197
		Limits in choosing clothes material	221
		Limit your sport activities	188
		Troubled by drugs' side effects	204

By consulting the table (table 7), it is evident that pruritus and wheals are the parameters reflecting the biggest impact in patients' wellness. Awakenings during night, difficulties in keeping concentration and decreased quality of sleep are the following higher scores found.

A similar analysis was made using DLQI (table 8), in which skin conditions (itch and pain) scored the higher values, followed by embarrassment caused by skin condition.

Table 8: Sum of scores for each parameter of DLQI in the subsample of 40 patients. (Higher scores represented in bold.)

Parameter	Score
Level of itchy, sore, painful or stinging skin	56
Embarrassment/ self-consciousness caused by skin condition	46
Influence in shopping/ looking after your home/ little garden	28
Influence in the choose of clothes	34
Influence in social/leisure activities	25
Difficulty to practice of sport	18
Prevention from studying/working	12
Influence in studying/working	17
Influence in relationship with partner/close friends/relatives	10
Effect in sexual activity	9
Impact of treatment in daily activities	10

As previously mentioned, only a total of 40 patients filled both questionnaires related to quality of life. These values were analysed using the Pearson Correlation (Figure 4) and, according to the coefficient, ($r^*=0.883$, $p<0.001$), we can conclude that both scales have a “high positive correlation”.³¹

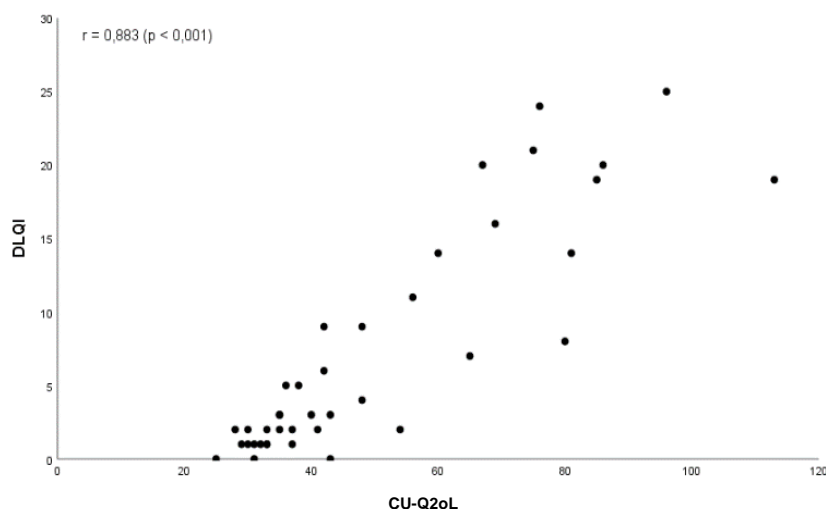


Figure 4: Scatter plot showing the correlation between quality of life measured by CU-Q2oL and DLQI.

6.2.2 Anxiety and depression status

Among the 110 patients who filled the HADS questionnaire, only a minority were found to be in a state of depression or anxiety. For the category depression, 22 were “depressed” (18.8%) and 88 were mentally healthy (81.2%). In terms of anxiety, 45 were categorised as “anxious” (40.9%) whereas 65 (59.1%) did not report these symptoms.

6.3 Correlation between sociodemographic and clinical characteristics of CU and quality of life and mental status

6.3.1 Quality of life and gender

The results of the questionnaires evaluating the quality of life was statistically different between genders. Regarding Cu-Q2oL, Mann-Whitney U Test showed significant difference between male and female ($p=0.007$), with higher values seen in females, representing decreased quality of life (figure 6). No statistically difference among genders was found by DLQI ($p = 0.092$).

The level of QoL did not show any relevant pattern neither according to the age of the patients nor to the time evolution of the disease.

Table 9: Differences of CU-Q2oL scores between genders.

CU-Q2oL	Min - Max	Mean (sd)	Median [Q1 - Q3]
Female	23 - 113	51.62 (19.92)	48 [35; 68.50]
Male	9 - 66	38.78 (14.14)	37 [28; 50]

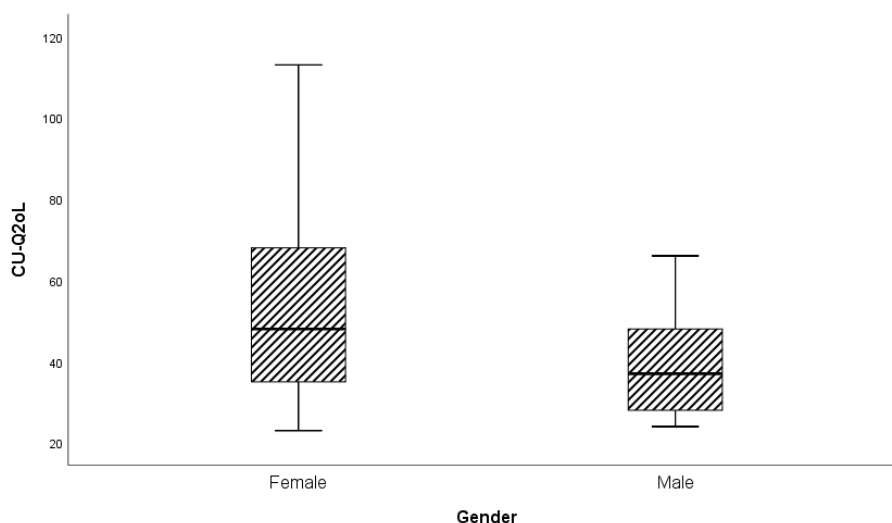


Figure 6: Box plot showing different values of CU-Q2oL score in female and male groups of patients.

6.3.2 Quality of life and degree of instruction

Concerning the level of education and analysing CU-Q2oL data, a statistically significant relationship was found between the degree of patients' instruction and their quality of life. The group with highest level of education (graduated degree) has the lowest mean and median value of CU-Q2oL, which represents a better QoL. However, there is no direct correlation between the other categories of the level of instruction and the interference of urticaria on the QoL, since the second lowest score for CU-Q2oL occurs in patients who just completed "Elementary school" (table 10). Statistically significant differences were found between the "Graduated" group and the remaining literacy levels, except for two.

Table 10: CU-Q2oL values' distribution according to the degree of instruction.

	Degree of instruction	n	Cu2-QoL		
			Min-Max	Mean (sd)	Median [Q1; Q3]
	Illiteracy	1	55-55	55	55 [55; 55]
$p=0.013$	Able to read and write	2	63-113	88 (35.36)	88 [63; 113]
$p=0.051^*$	Primary school	14	26-96	52.36 (20.75)	46.5 [37; 59]
	Elementary school	11	29-66	45.82 (12.39)	43 [37; 54.]
$p=0.005$	Middle school	18	25-82	55.72 (18.68)	60 [42; 72]
$p=0.049$	High school	20	23-97	51.50 (21.43)	49.5 [34.5; 66.]
$p=0.010$	Professional degree	5	38-74	61.80 (15.56)	70 [54; 73]
	Graduated	21	25-86	40 (14.25)	37 [32; 42]

A similar relation between literacy and QoL can be seen with the DLQI scale.

QoL measured by Cu-Q2oL and DLQI is not statistically related ($p > 0.05$) to the professional status and familiar situation of these patients.

6.3.3 Quality of life and clinical activity of CU

Mean and median QoL values calculated with CU-Q2oL for each category of UAS7 are presented below, as well as categories of UAS7 for which a statistically significant difference was found (table 11). The range values of quality of life scores are significantly higher as the disease increases its severity (figure 7). For DLQI, significance ($p= 0.003$) was found between the categories mild/severe activity.

Therefore, the clinical activity of urticaria is highly correlated with QoL measured both by CU-Q2oL and DLQI, which were found to be statistically associated with UAS7 ($p<0.001$ for CU-Q2oL and $p= 0.002$ for DLQI).

Table 11: CU-Q2oL values in different categories of USA7. The arrows (→) represent the statically significant related groups. p values: 1- $p < 0.001$; 2- $p = 0.031$; 3- $p = 0.008$; 4- $p = 0.004$.

UAS7 category	n	Min - Max	Mean (sd)	Median [Q1 - Q3]
Asymptomatic	15	9 - 56	33.6 (12.11)	35 [25; 41]
Well controlled	14	24 - 67	42.14 (15.04)	42 [27; 51]
Mild activity	37	25 - 86	43.97 (15.92)	37 [33; 50]
Moderate activity	18	31 - 97	56.33 (17.06)	53 [45; 69]
Severe activity	24	26 - 113	63.38 (22.38)	66 [41.5; 78]

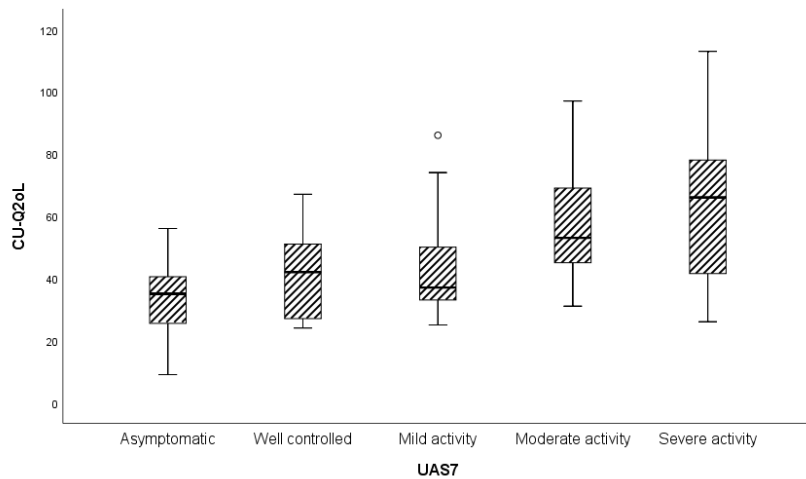


Figure 7: Box plot representing CU-Q2oL values according to UAS7 categories.

In the two parameters evaluated by the UAS7 (severity of the itch and number of papules) a significant difference can be seen in patients' QoL using both scales (table 12). A higher number of papules and a more intense pruritus contributes to deteriorate one's psychological and physical state, contributing to a lower QoL.

Table 12: CU-Q2oL and DLQI values for each parameter comprised in UAS7 scale.

	CU-Q2oL			DLQI	
	Level	Median [Q1 - Q3]	p	Median [Q1 - Q3]	p
Itch severity	None	39 [35; 43]	0,002	1.5 [0; 3]	0,005
	Slight	35 [30.5; 40]		2 [1; 5]	
	Moderate	48 [40; 65]		4 [2; 11]	
	Intense	75 [60; 81]		16 [14; 19]	
Number of papules	None	32.5 [30; 39]	0,004	1.5 [0,5; 2,5]	0,002
	Few	36 [31.5; 45.5]		2 [1; 4.5]	
	Moderate	60 [41; 69]		11 [3; 20]	
	Many	80 [76; 81]		14 [8; 19]	

6.3.4 Quality of life and disease control

Regarding UCT score, the four parameters related to the degree of control of urticaria allow us to divide patients in “well” and “poorly” controlled (figure8).

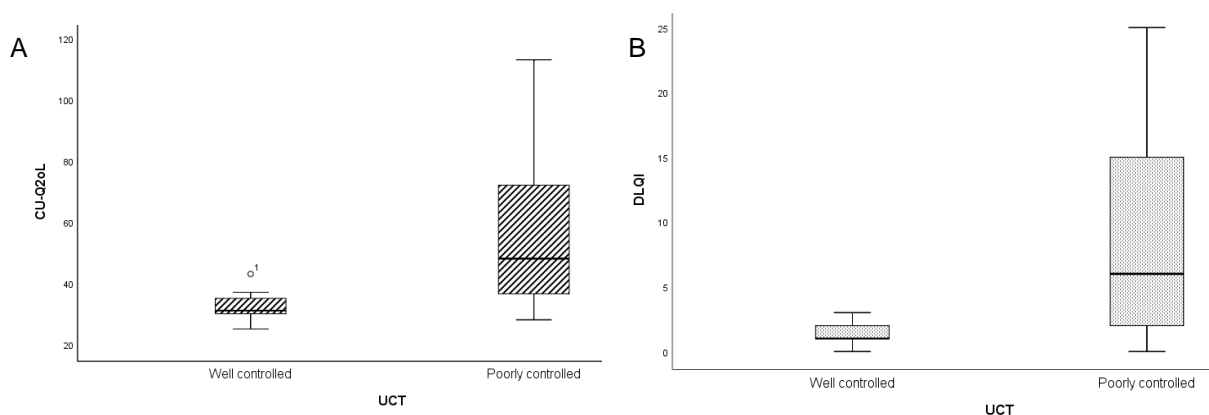


Figure 8: A- Box plot showing CU-Q2oL values according to UCT categories. B- Box plot showing DLQI values according to UCT categories

The Mann-Whitney U Test confirmed the existence of a statistically significant difference between QoL in these two groups, since patients with a good control of the disease reveal a much better quality of life than those with poor control (table14).

Table 14: A- CU-Q2oL and DLQI values in different categories of UCT.

UCT	n	CU-Q2oL		DLQI	
		Min - Max	Median [Q1 -Q3]	Min - Max	Median [Q1 - Q3]
Well controlled	9	25- 43	31 [29.5; 36]	0 – 3	1 [0.5; 2.5]
Poorly controlled	31	28 - 113	48 [36; 75]	0 – 25	6 [2; 16]

In the four parameters evaluated by the UCT, statistically significant differences were found in quality of life among the various categories, particularly between “slight” and “severe”. This means the control of urticaria is strongly related to the patients’ QoL, with higher levels of physical symptoms, the perception of a higher impact in quality of life and the insufficiency of treatment leading to a poor control of the disease, and contributing to a higher score in both scales.

Table 15: Significance values (*p*) for each parameter of UCT.

	CU-Q2oL	DLQI
UCT global	<0.001	0.002
Physical symptoms	<0.001	<0.001
Affected QoL	<0.001	<0.001
Insufficiency of treatment	<0.001	0.001
Control of disease	0.007	0.020

6.3.5 Quality of life and treatment used for CU

No statistically significant relation was found between the different drugs used for the treatment of CU and QoL measurements ($p=0.079$ for CU-Q2oL and 0.116 for DLQI), but the range and mean values of CU-Q2oL differ depending on the current treatment. Clinical severity of the disease was also evaluated according to treatment (table 13). Omalizumab revealed to be effective in diminishing the clinical severity of disease and in increasing patients' QoL.

Table 13: Clinical activity of urticaria (by UAS7) and quality of life (by CU-Q2oL and DLQI) according to treatment on course.

Treatment	n	Mean UAS7	Mean (sd) CU-Q2oL	Mean (sd) DLQI
None	1	28 (Severe activity)	67 (0)	20 (0)
Antihistamines (1x/d)	13	17.77 (Moderate activity)	42,85 (19,15)	4,15 (5,29)
Antihistamines (>1x/d)	19	25.55 (Moderate activity)	54,21 (22,2)	7,89 (7,23)
Omalizumab	2	7 (Mild control)	30 (0)	1,5 (0,71)
Other	5	19.6 (Moderate activity)	56,8 (28,42)	12,4 (11,44)

6.3.6 Quality of life and mental status

The quality of life of this sample revealed to be significantly related to anxiety and depression status, measured by the HADS scale (table 16).

Table 16: CU-Q2oL values according to psychological state measured by HADS.

	n	CU-Q2oL		p
		Min -Max	Median [Q1 - Q3]	
Depressed	22	32-113	64 [41; 74]	<0.001
Normal	88	23-97	41.5 [33; 56]	
Anxious	45	23-113	56 [38,5; 70,5]	<0.001
Normal	65	23-97	38 [31; 51]	

Regarding anxiety (HADS-A), data evidenced its contribution to lower patients' quality of life when comparing to patients mentally healthy (figure 9-A). Concerning the depression status (HADS-D), results showed a statistically significant difference between CU-Q2oL scores depending if the patient is classified as depressed or not, with depression contributing to a lower quality of life (figure 9-B). These patients evidence worse levels of QoL than anxious patients.

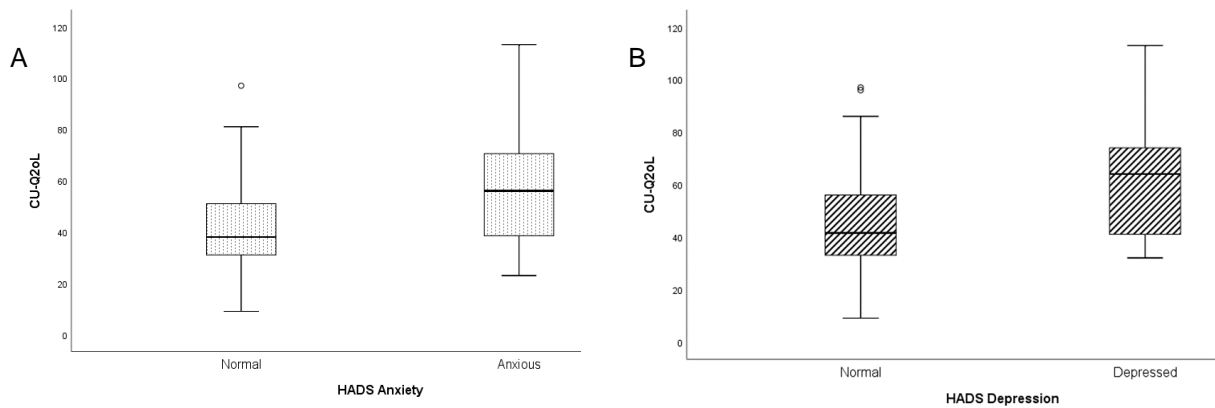


Figure 9: A- Box plot representing CU-Q2oL values according to HADS-A. B- Box plot representing CU-Q2oL values according to HADS-D categories.

No statistically significant difference in the state of anxiety or depression was found when QoL was measured by DLQI.

No correlation was found between the activity of urticaria evaluated by the UAS7 and HADS anxiety ($r = 0.249$) or depression HADS ($r=0.205$).

6.3.7 Other parameters of chronic urticaria and their influence on QoL and mental status

The presence of angioedema showed no statistically significant difference neither in CU-Q2oL nor HADS score values ($p=0.527$ for Cu-Q2oL; $p=0.826$ for HADS-A and $p= 0.691$ for HADS-D). Furthermore, QoL measured by both CU-Q2oL and DLQI did not present a statistically significant difference between both classifications of urticaria (CSU and CIU) nor between the different comorbidities referred by the patients.

6.4 Predictors of Quality of Life

The variables that proved to have an influence on patients' QoL were selected, which means those that significantly ($p<0.05$) or approximately ($p<0.10$) influence QoL, measured by both DLQI and CU-Q2oL. The variables assumed as potential predictors of quality of life in urticaria were: gender, grade of education completed, UAS7, UCT, HADS-A, HADS-D, intensity of pruritus in the last week, number of papules in the last week, treatment made for urticaria, self-perception of quality of life, intensity of the physical symptoms, and insufficiency of treatment in the control of symptoms.

For CU-Q2oL, the regression analysis identified as predictors of better quality of life the good control of CU symptoms, measured by UCT ($\beta = -0,407$; $p = 0,003$), and being male ($\beta = -0,192$; $p = 0,029$). The insufficiency of treatment to control the symptoms ($\beta = 0,378$; $p = 0,012$), the intensity of physical symptoms ($\beta = 0,386$; $p = 0,016$) and the self-perception of a negative impact in QoL ($\beta = 0,433$; $p = 0,007$) contributed to decrease quality of life, increasing CU-Q2oL final score. These factors explain 73% of the variability found in the quality of life, ($R^2_{adj} = 0,730$; $p = 0,029$) thus, the quality of life of the patient with urticaria, measured through the Cu2QoL scale, can be reliably predicted by the following equation:

$$CU - Q2oL = 37,616 + 7,315 \times QoL_p + 6,113 \times Insuf_{T_t} - 21,120 \times UCT + 7,845 \times PSI - 13,909 \times Gender$$

Here, QoL_p (quality of life self-perception), $Insuf_{T_t}$ (insufficiency of treatment) and PSI (physical symptoms intensity), correspond to the questions "How is your quality of life affected by urticaria?", "How insufficiency is your treatment to the control of symptoms?" and "How intense are your physical symptoms of urticaria?" included in UCT. This way, each parameter varies between 0 (nothing) and 4 (very much). UCT represents the result of the UCT scale, taking the value 0 for a good control and 1 for poor control. $Gender$ admits the value 1 for female and 2 for male.

For the DLQI scale, the regression analysis identified as predictors of a worse quality of life factors as the intensity of physical symptoms of CU, ($\beta = 0,706$; $p < 0,001$); with a particular emphasis on pruritus severity ($\beta = 0,283$; $p = 0,044$). This way, a good quality of life, according to DLQI, will be found in a patient with low intensity physical symptoms, particularly pruritus. For this scale, these factors are able to explain 52.8% of the variability found in quality of life, ($R^2_{aj} = 0,528$; $p < 0,001$) which can be reliably predicted by the following equation:

$$DLQI = -5,925 + 3,843 \times PSI + 2,417 \times UAS7_{itch}$$

PSI varies discreetly between 0 (nothing) and 4 (very much) as it corresponds to the answer for the question "How intense are your physical symptoms of urticaria?", and $UAS7_{itch}$ (intensity of itch over the last 7 days) is the result of the patient's classification of pruritus over the last week, reported using UAS7, and varying discreetly between 0 (none) and 3 (intense).

7. Discussion and Conclusion

The aim of this study was to estimate the impact of CU in Portuguese patients' quality of life, understanding which parameters are mostly affected so that physicians can improve the management of these patients. Currently, a variety of tools and questionnaires are available to assist medical doctors in the diagnosis and assessment of patients with CU.¹⁴ Their correct use contributes to establish the patient outcome, essential to optimize the management of this disease, which can be really challenging.¹⁵ Both literature and guidelines recommend PRO (Patient-reported outcomes) in the daily clinic in order to facilitate disease monitoring and management. The UAS7, for evaluating severity, and the CU-Q2oL, for evaluating QoL impairment specifically related to urticaria, are the two validated and disease-specific instruments for assessing PRO and their use may contribute to increase the involvement of patients in their disease, enhancing the satisfaction with care and improving patient-physician communication.¹³

With this study, we were able to verify the applicability of these tools in Portuguese patients with chronic urticaria. In fact, by delivering the questionnaires that access aspects not previously enquired in the consultation, we noticed that patients were much more comfortable with talking and discussing minor aspects of their disease as they filled the questions, than before. A great satisfaction was evident, for noticing physicians' interest not only on their illness, but also on their psychological state and impact of disease in their daily lives.

The compliance of patients in filling the questionnaire, its simplicity and easiness to apply (takes an average of 10 minutes to fill), proves how convenient it is to use PRO in clinical routine practice for the evaluation of chronic urticaria in our patients and as well as in the primary outcome of future clinical trials, as proposed by *GA2LEN consensus report*.⁹

Skin diseases, including chronic urticaria, were shown to affect significantly patient's quality of life, which may not be directly related with the clinical activity of the disease.¹⁶ Our study is particularly useful since it is based in scales that access the patients' perception of their quality of life rather than an external measurement, which could underestimate the real impact in the life of the patient. Based on these data, it is important to evidence that the aim of the dermatologist should not only be the control of clinical aspects of urticaria but also the development, aside with the patient, of strategies to cope with stress, embarrassment, physical discomfort, emotional imbalance and negative impact in work productivity and sleep quality.

Currently, there are no concrete epidemiological data concerning chronic urticaria in Portugal, but it is estimated that 1% of the population suffers from this condition, with a higher prevalence in female, and 2/3 suffering from CSU.^{6,23,32,33}

In the present study, about 80% of patients were female, supporting previous data concerning the high prevalence of female in CU. In international studies, CSU has a higher prevalence than the other types of chronic urticaria and the present study corroborated this data, with an incidence of 86.6% reported for this type of urticaria.^{28,34–37}

The mean age of our patients was 45.7 years, similar to values previously reported, and the duration of urticaria was 3.64 years, reflecting a population with a long-standing urticaria, as found in many studies.^{28,34–37} The percentage of patients with angioedema (2/3) is higher than values found in other studies (a mean of 1/3 of UC have been reported), reflecting the clinical severity of patients studied in our consultation and included in the study.^{32,33}

There is lack of information from previous studies regarding the association of urticaria with sociodemographic factors, such as level of instruction and professional status, however, in our study we found a considerably high percentage of patients who have completed high school and who are professionally active.³⁸

As for comorbidities, presented by the majority of patients, depression, allergic rhinitis and asthma are the most prevalent. The strong association between dermatological diseases, highlighting urticaria, and psychological/psychiatric had already proven.^{16,17,21} As for allergic rhinitis and asthma, it has also previously been shown and the explanation consists in the immune-mediated mechanism of urticaria.^{5,39}

To study patients' QoL, a disease specific and a generic scale, respectively the CU-Q2oL and DLQI, were used, in which a higher score reflects a worse condition. The parameters that showed the greatest impact on quality of life were, for CU-Q2oL, skin condition (pruritus and wheals) and sleep problems (night awakening, difficulties in keeping concentration, impact in sleep), followed by the embarrassment due to urticaria symptoms. For DLQI, the domains skin condition (itch and pain) and embarrassment caused by cutaneous lesions scored the highest counts.

The symptoms of CU have, consequently, been shown to be the most important factor in patients' perception of QoL, emphasizing the importance of clinical control of urticaria as the first approach to improve patients' quality of life. These results are consistent with studies performed in Spanish patients, in which “sleep” was markedly impaired.³⁷ Likewise our results, studies in German, Polish and Brazilian population show “itch” and “embarrassment” as the most affected areas, as well as a noticeable impact specially in Brazilians in items such as “tiredness” and “concentration”.^{28,34,36} A Turkish study showed “pruritus” and “sleep” to be the most affected scales, whereas “swelling” was the least affected.³⁵

“Eating behavior/ Impact on life activities” and “Limits in choosing food” scored a low count in the present study, contributing slightly to quality of life impairment, which is consistent with the results found.^{34,36} It is also concordant with studies which evidenced that IgE-mediated food allergy was not a cause of the disease in CU.^{2,32}

Regarding the following parameters, sleep problems and low concentration can be deeply related with each other, since urticaria can lead to a difficulty in falling asleep, due to the severity of symptoms and stress caused, which decreases quality of sleep. Awakening several times during night therefore result in sleep deprivation during the day, which results in difficulties maintaining concentration in routine activities and work. As for the embarrassment caused by urticaria symptoms, it reflects the importance of esthetical aspects or perceived changes in body appearance in a patient’s daily life and contact with others at work or in leisure activities. This may be correlated with the item “choice of clothes”, that was relatively high rated in both questionnaires, as clothes can be chosen in order to cover and help disguising the signs of hives.

Both QoL scales assess different periods of time, as CU-Q2oL is related to the last two weeks, whereas DLQI relates only to the last week, which could be a cause of significant differences found between their scores. However, this was not the case, as both scales revealed to be strongly and positively correlated, which indicating compatibility within the measures used. By using these two scales it is possible to have a perception if both of them reflect the impact of urticaria on quality of life in the same way, in other words, if the variables with statistically significant different effect in quality of life are the same. This was not always the case but it should be borne in mind that the sample used for the DLQI scale contained only 40 patients, compared to a total of 112 that filled the CU-Q2oL. This fact is an important limitation of the study. Also, the reduced number of patients filling the DLQI can justify the lack of significant differences found when using this scale. However, the high correlation between the two scales can support the use of DLQI alone in a quick assessment of patients’ QoL or for comparison of items serially tested. Despite being a more generic scale, DLQI was found to be effective in detecting some variables with significant influences in QoL, although not as much as CU-Q2oL.

For the variable "gender", females revealed to feel a greater impact of the disease in comparison to male, which is in agreement with the literature.^{28,32,34–37,40} This can be explained by their high susceptibility in having certain domains affected (embarrassment due to urticaria symptoms; problems in using cosmetics and sleep problems). In addition, female present greater emotional fragility, being the gender with higher prevalence of depression, anxiety and nervousness.^{17,18,41} Also, female have proved to be more affected than male in specific parameters, such as “sleep problems”.³⁵

Higher scores of UAS7, indicating stronger disease activity, were associated with lower levels of QoL as demonstrated in other studies.¹¹ CU-Q2oL allowed us to find statistically different levels of quality of life between four groups of urticaria severity, whereas the DLQI only detected differences between two groups (mild/severe activity), showing the higher capacity of CU-Q2oL to detect minor differences in QoL.

Both in CU-Q2oL and DLQI, the parameter "itch and wheals symptoms" scored the highest count but, although the final score for QoL does not always correlate directly with the clinical severity of the disease, we can conclude that both are closely related.

An effective (pharmacological or non-pharmacological) control of the clinical symptoms contributes to a healthier emotional state and consequently increase in patients' quality of life.⁴² This is not surprising since it is known that pruritus is the main and more debilitating symptom in CU, which was confirmed by the correlation with the UCT³⁶. In this analysis, a significantly higher CU-Q2oL value was found in the group of poorly controlled patients. Similar results were obtained for each parameter included in UCT, in which the worse control leads to higher values in CU-Q2oL, and consequently decreased QoL. The one's perception of his physical symptoms as well as of the insufficiency of treatment in controlling the disease are, thereby, areas to be taken in consideration for an integrated approach. Patients' own view of their condition is being increasingly valued as there are no reliable biomarkers to identify and measure disease activity and control.^{5,13,43}

Additionally, we achieved a reliable equation able to explain 73% of the variability found in the quality of life measured by CU-Q2oL including the patient's gender, disease control and three UCT parameters (self-perception of quality of life, insufficiency of treatment and physical symptoms). Therefore, the profile of a patient with good quality of life would be a man with the perception of a small impact of the disease in his quality of life, who considers his current treatment sufficient to have a satisfactory control of physical symptoms. As for DLQI, physical symptoms and severity of itch over the last week are the main predictors of a better quality of life, explaining 52.8% of the variability found in QoL, according to the equation formulated.

With respect to psychiatric pathology, by using the DLQI scale it was not possible to detect significant differences between the "normal" and "depressed" / "anxious" groups, but CU-Q2oL allowed to find in the pathological groups a significantly lower quality of life. Depression appears to have a major impact on our study, both because it is present as the most frequent comorbidity and since it contributes to deteriorate patients' quality of life, more than the state of anxiety.

The need for a therapeutic approach encompassing patients' psychopathological domains becomes very clear from this study. An anxious or depressed patient will tend to overvalue the physical symptoms of urticaria, feeling more affected by them, therefore, even if the disease is close to what would be a satisfactory clinical control for a patient free of comorbidity, this would not happen in this group of patients. Simple measures as an attempt to understand the underlying cause of psychological imbalance, a detailed approach to patient's personal life, or even the physician's request of an assessment by the specialist of this area could be enough to solve this type of situations.

Although it remains unclear if psychological imbalances are the cause or the result of dermatological problems, the cross-sectional design of this study does not allow conclusion regarding causal links between the high scores on these parameters and CU. Despite the attempt to establish a temporal relation between the diagnosis of urticaria and the diagnosis of depression, it was not possible to collect reliable data as patients reported that the beginning of symptoms and installation of both diseases did not correspond to the precise moment of the definite diagnosis. Several studies suggest that multifactorial origin of CU includes psychological and social factors which can lead to depression and decrease patients' QoL. Other hypothesis suggest that mental debility increases the probability of the onset of urticaria, which is this way more probable for depressed and anxious patients. Some investigators link vasodilation-induced by emotional status to urticaria lesions in the skin.^{17,18,21} and a previous study presented swelling (a very frequent symptom present) as cause of anxiety and mood disturbances in the patients, affecting also other domains.^{18,36}

Patients with higher education presented worse values of quality of life, which goes against data from the literature.^{28,40} This fact was verified when comparing the category of graduated patients with the others, but not in groups of categories not including "graduated". These results can be justified since patients with higher literacy are more knowledgeable and tend to work in jobs requiring greater intellectual effort. At work, they may feel a superior influence in domains such as "difficulties in falling asleep", "lack of sleep" and "difficulties in concentration", and thus have their quality of life worsened. These individuals will also be more critical with their illness and its treatment, revealing a more integrated perception of their condition. Also, the questionnaire itself will be better understood and therefore these patients will present a higher capacity to answer each question correctly.

In this study, our sample was comprised by patients followed in the Dermatological Service of Dermatology, at Coimbra University Hospital Centre. Therefore, a selection effect in every variable cannot be excluded as the sample was obtained in a specific service and not constituted by patients from different hospitals or clinics in other parts of the country.

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10. Supplement

10.1 Ethical Commission Approval

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CHUC - Conselho de Administração

Exmo Senhor
Dr. Martins Nunes
Presidente do Conselho de Administração
Centro Hospitalar e Universitário de Coimbra, EPE

10 Cel / 29.12.16

29.12.16

Artsch
29.12.2016

Prof. Doutor José Saraiva da Cunha
Prof. Doutor José Saraiva da Cunha - EPE

SUA REFERÊNCIA	SUA COMUNICAÇÃO DE	NOSSA REFERÊNCIA	DATA
		CHUC-116-16	21-12-2016

ASSUNTO: Aprovação do Projeto de Investigação CHUC-116-16

A pedido de *Prof. Doutor Pedro Ferreira*, recebeu esta Unidade um pedido de autorização de um Projecto de Investigação sobre **"VALIDAÇÃO DO INSTRUMENTO DE MEDIÇÃO Cu-Q2oL DE QUALIDADE DE VIDA EM PESSOAS COM URTICÁRIA CRÓNICA"**, ao qual não se aplicam as normas previstas na Lei n.º 21/2014 de 16 de Abril e colheu parecer favorável da Comissão de Ética deste Hospital.

Informa-se V. Ex.ª. que este projecto não acarreta qualquer encargo financeiro adicional para o CHUC.

Solicita-se assim a autorização do Conselho de Administração para este Projecto.

Com os mais respeitosos cumprimentos,

Pl' A Coordenadora da Unidade de Inovação e Desenvolvimento

S. Saraiva
(Prof. Doutor José Saraiva da Cunha)

CHUC - EPE	
CONSELHO DE ADMINISTRAÇÃO	
Reg. N.º	10264 PCS
Origem	
Data	22.12.2016

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Comissão de Ética para a Saúde


Visto/ À U.D.
para efeitos de
C.H.U.C. - EPE
Adjunto de 12/11/2016
Director Clínico

Ex.mo Senhor
Prof. Doutor José Pedro Figueiredo
Digmº Director Clínico do CHUC

Date: 12/11/2016

SUA REFERÊNCIA	SUA COMUNICAÇÃO DE	NOSSA REFERÊNCIA	DATA
		N.º 228/CES	28-11-2016

Proc. N.º **CHUC-116-16**

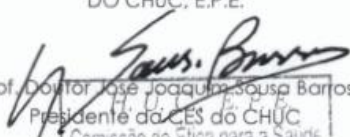
ASSUNTO: Estudo Observacional "Validação do instrumento de medição Cu-Q2oL de qualidade de vida em pessoas com urticária crónica" - Prof. Doutor Pedro Augusto de Melo Lopes Ferreira, Centro de Estudos e Investigação em Saúde da Universidade de Coimbra (estudo a ser realizado nos Serviços de Dermatologia e Imunoalergologia do CHUC).
(Entrada do processo na CES a 04.11.2016)

Cumprir informar Vossa Ex.ª de que a Comissão de Ética para a Saúde do Centro Hospitalar e Universitário de Coimbra, reunida em 25 de Novembro de 2016, com a presença da maioria dos seus membros, após análise do projeto mencionado em epígrafe e ouvido o relator, emitiu parecer favorável. Parecer aprovado por unanimidade.

Mais se informa que a CES do CHUC deve ser semestralmente actualizada em relação ao desenvolvimento dos estudos favoravelmente analisados e informada da data da conclusão dos mesmos, que deverá ser acompanhada de relatório final.

Com os melhores cumprimentos,

A COMISSÃO DE ÉTICA PARA A SAÚDE
DO CHUC, E.P.E.


Prof. Doutor José Joaquim Sousa Barros
Presidente da CES do CHUC
Comissão de Ética para a Saúde

LP/CES

A CES do CHUC: Prof. Doutor José Joaquim Sousa Barros; Prof.ª Doutora Maria Fátima Pinto Saraiva Martins; Dr. Mário Rui Almeida Branco; Enf.ª Adélia Tinoco Mendes; Prof. Doutor Carlos Alberto Fontes Ribeiro; Padre José António Afonso Paiz; Dr. José António Faiz; Dr. José Alves Gato Gonçalves; Enf.ª Fernando Matheus; Dr. José António Pinheiro; Dra. Cláudia Santos; Dr. Paulo Figueiredo.

10.2 Questionnaire

QUESTIONÁRIO DE QUALIDADE DE VIDA

Este questionário contém perguntas que nos ajudarão a compreender como é a qualidade de vida dos doentes com urticária crónica

Por favor, demore o tempo que entender por forma a responder completamente às perguntas colocadas. Sendo este questionário anónimo, garantimos a completa confidencialidade dos dados que nos fornecer.

Nunca ninguém poderá ser identificado a partir dos resultados deste inquérito.

Assim, muito agradecemos que responda às perguntas abaixo da forma que considerar a mais correta.

Agradecemos desde já a sua disponibilidade e participação.

Começemos por alguma informação relativa à sua situação clínica.

1. Há quanto tempo disseram-lhe que tem urticária? _____ anos _____ meses

2. Possui algum angioedema (inchaço)? Sim Não

3. Como classificaria a sua urticária? ₁ Espontânea
₂ Pressão
₃ Frio
₄ Dermografismo
₅ Outra

} Induzida/Física

4. Como avalia o nível de prurido (comichão), na última semana?

- ₁ Nenhum – não noto qualquer prurido, não me incomoda
- ₂ Ligeiro – quase não noto qualquer prurido, só de vez em quando
- ₃ Moderado – estou ciente do prurido quase todo o tempo, e incomoda bastante
- ₄ Intenso – este prurido é constante e passo o tempo a coçar-me. Não durmo bem há dias

5. Como avalia o número de pápulas (babas), na última semana?

- ₁ Nenhum – sem pápulas
- ₂ Ligeiro – menos de 20 pápulas em 24 horas
- ₃ Moderado – entre 20 e 50 pápulas em 24 horas
- ₄ Intenso – mais de 50 pápulas em 24 horas

6. Já algum médico ou outro profissional de saúde lhe disse que tinha alguma destas condições?

- | | |
|---|---|
| <input type="checkbox"/> ₁ Rinite alérgica | <input type="checkbox"/> ₇ Diabetes |
| <input type="checkbox"/> ₂ Asma | <input type="checkbox"/> ₈ Problema de tiroide |
| <input type="checkbox"/> ₃ Alergias a medicamentos | <input type="checkbox"/> ₉ Úlcera péptica (estômago) |
| <input type="checkbox"/> ₄ Alergias a alimentos | <input type="checkbox"/> ₁₀ Depressão |
| <input type="checkbox"/> ₅ Eczema atópico | <input type="checkbox"/> ₁₁ Outra, Qual? _____ |
| <input type="checkbox"/> ₆ Dermatite de contacto | |

7. Faz algum tratamento para a sua urticária?

- ₁ Nenhum
- ₂ Anti-histamínicos uma vez por dia
- ₃ Anti-histamínicos mais de uma vez por dia
- ₄ Omalizumab
- ₅ Outro

8. As seguintes perguntas destinam-se a avaliar a situação atual da sua doença.

Por favor, leia atentamente cada pergunta na totalidade e, das cinco respostas apresentadas, escolha a que melhor corresponde ao seu estado. Considere apenas **as últimas 4 semanas**. Não pense durante muito tempo e lembre-se de responder a todas as perguntas e escolher apenas uma resposta para cada uma delas.

A. Nas últimas 4 semanas, com que intensidade sofreu com os sintomas físicos da urticária (comichão, babas e/ou inchaços)?

- muitíssimo muito ligeiramente pouco nada

B. Nas últimas 4 semanas, em que medida a sua qualidade de vida foi afetada pela urticária?

- muitíssimo muito ligeiramente pouco nada

C. Nas últimas 4 semanas, com que frequência o tratamento da urticária foi insuficiente para controlar os sintomas de urticária?

- muitíssimo muito ligeiramente pouco nada

D. No geral, até que ponto conseguiu controlar a urticária nas últimas 4 semanas?

- muitíssimo muito ligeiramente pouco nada

9. As seguintes questões dizem respeito ao modo como se tem sentido na ÚLTIMA SEMANA. Pedimos que leia cada uma das afirmações e faça uma cruz (X) na alínea (a, b, c ou d) correspondente à resposta que considere que melhor descreve o seu caso. Não demore muito tempo a pensar nas respostas. A sua reação imediata será provavelmente a que melhor traduz o modo como se sente. Por favor, para cada afirmação, faça apenas uma cruz.

A) Sinto-me tenso(a) e/ou nervoso(a):

- i. Quase sempre
- ii. Muitas vezes
- iii. Por vezes
- iv. Nunca

B) Ainda sinto prazer nas coisas de que gostava gostar:

- i. Tanto como antes
- ii. Não tanto agora
- iii. Só um pouco
- iv. Quase nada

C) Tenho uma sensação de medo como se algo terrível estivesse para acontecer:

- i. Sim e muito forte
- ii. Sim, mas não muito forte
- iii. Um pouco, mas não me aflige
- iv. De modo algum

D) Sou capaz de ver o lado divertido das coisas:

- i. Tanto como dantes
- ii. Não tanto como dantes
- iii. Muito menos agora
- iv. Nunca

E) Tenho a cabeça cheia de preocupações:

- i. A maior parte do tempo
- ii. Muitas vezes
- iii. Por vezes
- iv. Quase nunca

F) Sinto-me animado(a):

- i. Nunca
- ii. Poucas vezes
- iii. De vez em quando
- iv. Quase sempre

G) Sou capaz de estar descontraidamente sentado(a) e sentir-me relaxado(a):

- i. Quase sempre
- ii. Muitas vezes
- iii. Por vezes
- iv. Nunca

H) Sinto-me mais lento(a) como se fizesse as coisas mais devagar:

- i. Quase sempre
- ii. Muitas vezes
- iii. Por vezes
- iv. Nunca

I) Fico de tal como preocupado(a) e com medo, que até parece que sinto um "aperto no estômago":

- i. Nunca
- ii. Por vezes
- iii. Muitas vezes
- iv. Quase sempre

J) Perdi o interesse em cuidar do meu aspeto físico:

- i. Completamente
- ii. Não dou a atenção que devia
- iii. Talvez cuide menos do que dantes
- iv. Tenho o mesmo interesse de sempre

L) Sinto-me de tal forma inquieto(a) que não consigo estar parado(a):

- i. Muito
- ii. Bastante
- iii. Não muito
- iv. Nada

M) Penso com prazer nas coisas que podem acontecer no futuro:

- i. Tanto como antes
- ii. Não tanto agora
- iii. Bastante menos agora
- iv. Quase nunca

N) De repente, tenho sensação de pânico:

- i. Muitas vezes
- ii. Bastantes vezes
- iii. Por vezes
- iv. Quase nunca

O) Sou capaz de apreciar um bom livro, um programa de radio ou de televisão:

- i. Muitas vezes
- ii. De vez em quando
- iii. Poucas vezes
- iv. Quase nunca

10. Pretendemos agora saber quanto o seu problema de pele o/a afetou DURANTE A ÚLTIMA SEMANA. Por favor marque (☒) UMA resposta a cada uma das 10 seguintes perguntas.

A. Na última semana sentiu a pele irritada e mais sensível, comichão ou sensação de picadas?

- ₃ Muito
- ₂ Bastante
- ₁ Um pouco
- ₀ Nada

B. Na última semana sentiu-se embaraçado/a ou incomodado/a por causa do estado da sua pele?

- ₃ Muito
- ₂ Bastante
- ₁ Um pouco
- ₀ Nada

C. Na última semana até que ponto o seu problema de pele prejudicou a sua vida normal (fazer compras, cuidar da casa, tratar das plantas, etc.)?

- ₃ Muito
- ₂ Bastante
- ₁ Um pouco
- ₀ Nada
- ₀ Não aplicável

D. Na última semana a escolha da roupa que usou teve que ver com o estado da sua pele?

- ₃ Muito ₀ Não aplicável
₂ Bastante
₁ Um pouco
₀ Nada

E. Na última semana até que ponto o seu problema de pele afetou o convívio com outras pessoas ou mesmo os seus tempos livres?

- ₃ Muito ₀ Não aplicável
₂ Bastante
₁ Um pouco
₀ Nada

F. Na última semana até que ponto o seu problema de pele o(a) impediu de praticar desporto?

- ₃ Muito ₀ Não aplicável
₂ Bastante
₁ Um pouco
₀ Nada

G. Na última semana o seu problema de pele impediu-o(a) de trabalhar ou estudar?

- ₃ Sim ₀ Não aplicável
₀ Não

Se a sua resposta foi NÃO, até que ponto a sua pele foi problema no trabalho ou na escola?

- ₂ Bastante
₁ Um pouco
₀ Nada

H. Na última semana o estado da sua pele criou-lhe problemas no relacionamento com colegas de trabalho, o/a seu/sua companheiro(a), alguns amigos próximos ou familiares?

- ₃ Muito ₀ Não aplicável
₂ Bastante
₁ Um pouco
₀ Nada

I. Na última semana até que ponto o seu problema de pele afetou a sua vida sexual?

- ₃ Muito ₀ Não aplicável
₂ Bastante
₁ Um pouco
₀ Nada

J. Na última semana até que ponto os tratamentos para a sua pele lhe criaram problemas, por exemplo de sujar a casa ou lhe tomarem demasiado tempo?

- ₃ Muito ₀ Não aplicável
₂ Bastante
₁ Um pouco
₀ Nada

11. Até que ponto se sentiu incomodado/a, durante os últimos 15 dias, pelos seguintes sintomas?

A. Prurido (comichão)

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

B. Pápulas ou erupções cutâneas (inchaços, babas)

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

C. Olhos inchados

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

D. Lábios inchados

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

12. Indique se a urticária, nos últimos 15 dias, o/a tem limitado nas seguintes áreas da vida diária

A. Trabalho

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

B. Atividade física

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

C. Sono

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

D. Tempos livres

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

E. Relações sociais

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

G. Alimentação

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

13. Com as perguntas que se seguem queremos conhecer melhor as dificuldades e os problemas que possam estar relacionados com a sua urticária (nos últimos 15 dias)

A. Tem problemas em adormecer?

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

B. Acorda durante a noite?

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

C. Durante o dia está cansado/a porque à noite não dormiu bem?

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

D. Tem dificuldade em concentrar-se?

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

E. Sente-se nervoso/a?

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

F. Sente-se deprimido/a?

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

G. Sente-se limitado/a na escolha dos alimentos?

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

H. Tem vergonha dos sinais que a urticária provoca no seu corpo?

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

I. Tem vergonha de frequentar lugares públicos?

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

J. É um problema para si usar cosméticos (ex. perfumes, cremes, loções e espuma de banho, maquilhagem)?

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

K. Sente-se limitado/a na escolha das roupas que usa?

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

L. Limita a sua atividade desportiva por causa da urticária?

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

M. Sente-se incomodado/a com os efeitos colaterais dos medicamentos para a urticária?

₁ Nada ₂ Pouco ₃ Moderado ₄ Muito ₅ MUITÍSSIMO

Por fim, agradecemos que nos fornecesse alguns dados, apenas para fins estatísticos.

14. Qual é o seu sexo? ₁ Feminino ₂ Masculino

15. Qual é a sua idade? _____ anos

16. Qual é a sua situação familiar?

- ₁ Casado/a com registo
- ₂ Casado/a sem registo – união de facto
- ₃ Solteiro/a
- ₄ Viúvo/a
- ₅ Divorciado/a
- ₆ Separado/a

17. Qual é a sua situação profissional?

- ₁ Ativo. Qual a profissão? _____
- ₂ Reformado/Aposentado
- ₃ Desempregado
- ₄ Estudante
- ₅ Outra. Qual? _____

18. Que grau de ensino é que completou?

- ₁ Não sabe ler nem escrever
- ₂ Só sabe ler e escrever
- ₃ 1º ciclo do Ensino Básico (1º - 4º ano) / Antiga 4ª classe
- ₄ 2º ciclo do Ensino Básico (5º - 6º ano) / Antiga 6ª classe / Ciclo Preparatório
- ₅ 3º ciclo do Ensino Básico (7º - 9º ano) / Curso Geral dos Liceus
- ₆ Ensino Secundário (10º - 12º ano) / Curso Complementar dos Liceus
- ₇ Ensino Médio
- ₈ Ensino Superior (Politécnico ou Universitário)

MUITO OBRIGADO

10.3 Informed Consent



Serviço de Dermatologia – Unidade de Alergologia

ESTUDO CLÍNICO: Caracterização da urticária crónica, suas comorbilidades, resposta aos tratamentos e avaliação do rebate desta patologia na qualidade de vida utilizando os seguintes questionários- UAS7 (Urticaria activity score), questionário de controlo da urticária (urticaria control test – UCT) e de qualidade de vida nos pacientes com urticária (Cu₂-QoL) e escalas de ansiedade e depressão hospitalar (HADS) em pacientes da Consulta de Urticária do Serviço de Dermatologia dos CHUC

CONSENTIMENTO INFORMADO

EU, _____, abaixo assinado(a), seguido(a) na Consulta de Dermatologia (Urticária) dos CHUC por URTICÁRIA e/ou ANGIOEDEMA fui informado dos objectivos do estudo e das vantagens que da minha participação podem advir para a melhor caracterização e controlo da minha patologia.

Tendo tomado conhecimento que os dados serão avaliados sem acesso à minha identificação, aceito, voluntariamente, na resposta aos questionários que se adequem à minha patologia, durante as minhas deslocações habituais à Consulta de Urticária.

Coimbra, __ de _____ de 2018

O paciente

O investigador principal
(Margarida Gonçalo, N^o mec. 7200)

Serviço de Dermatologia e Venereologia – CHUC
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