ORIGINAL ARTICLE
Iran J Allergy Asthma Immunol
August 2021; 20(4):423-431.
Doi: 10.18502/ijaai.v20i4.6952

Evaluation of the Reliability and Validity of the Persian Version of Urticaria Control Test (UCT)

Maryam Khoshkhui[1], Karsten Weller[2], Javad Fadaee[3], Marcus Maurer[2], Farahzad Jabbari Azad[1], and Maryam Emadzadeh[4]

[1] Allergy Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
[2] Dermatological Allergology, Department of Dermatology and Allergy, Allergie-Centrum-Charité, Charité – Universitätsmedizin Berlin, Berlin, Germany
[3] Department of Pediatrics, Faculty of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran
[4] Clinical Research Development Unit, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

Received: 11 October 2020; Received in revised form: 7 May 2021; Accepted: 16 May 2021

ABSTRACT

The urticaria control test (UCT) is a patient-reported outcome measure (PROM) for chronic urticaria (CU) patients. As a Persian version of the UCT was not available, the present research aimed to develop such a version, to test its reliability and validity as well as to evaluate urticaria control among Persian-speaking patients.

This research was conducted at the Urticaria Centre of Reference and Excellence (UCARE) of Ghaem Hospital, Mashhad, Iran. In a first step, a linguistically validated Persian version of the UCT was developed through a structured forward and backward translation process and subsequent cognitive debriefing interviews. In a second step, the Persian version of the UCT was completed by 100 well-characterized CU patients together with two anchor instruments, the Chronic Urticaria Quality of life Questionnaire (CU-Q2oL) and the urticaria activity score (UAS), to obtain information on its internal consistency reliability and convergent validity.

The Persian version of the UCT was found to have acceptable internal consistency reliability with a Cronbach's alpha coefficient of 0.68. In addition, the results obtained with the Persian UCT correlated with the CU-Q2oL total score (-0.48, $p<0.001$) and the UAS (-0.404, $p<0.001$), suggesting convergent validity. Virtually all patients had poorly controlled CU (UCT<12).

A Persian version of the UCT is now available and may help to improve the assessment and monitoring of disease control in Persian-speaking CU patients and to optimize treatment decisions.

Keywords: Chronic urticaria; Patient reported outcome measures; Quality of life; Reproducibility of results

INTRODUCTION

Urticaria presents as a red, itchy rash consisting of wheals, angioedema, or both. If urticaria lasts for more than 6 weeks, it is regarded as chronic urticaria (CU). CU affects about one percent of the total population.[1,2]

Corresponding Author: Maryam Emadzadeh, MD;
Clinical Research Development Unit, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran. Tel: (+98 51) 3841 7403, Email: ma.emadzadeh@gmail.com, emadzadehm@mums.ac.ir

Copyright © 2021 Khoshkhui et al. Published by Tehran University of Medical Sciences.

This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International license (https://creativecommons.org/licenses/by-nc/4.0/). Non-commercial uses of the work are permitted, provided the original work is properly cited.

Treatment of CU is still challenging despite the availability of very effective and non-sedating antihistamines, omalizumab, treatment guidelines, and tools for monitoring treatment responses.[3]

The signs and symptoms of CU are usually short-lived and vary considerably from day to day. This unpredictable nature of CU makes it difficult for treating physicians to get a reliable picture of the patient's current disease status and to decide about the best treatment approach. Accordingly, there is a need for instruments to reliably evaluate the patient's disease status and to monitor disease control over time, e.g. before and after treatment adjustments. Within the past years, different patient-reported outcome measures (PROMs) were developed to assess disease activity, quality of life impairment, and disease control. They are useful clinical instruments to monitor CU patients.[4,5] Among them are the Urticaria Activity Score (UAS),[2] the Chronic Urticaria Quality of Life Questionnaire (CU-Q_2oL),[5] the urticaria severity score (USS),[6,7] and the urticaria control test (UCT).[8]

The current international guideline for urticaria suggests the use of the UAS and CU-Q_2oL as PROMs to evaluate CU.[9] However, both PROMs suffer several limitations, including the fact that they can be used only for patients with chronic spontaneous urticaria but not for patients with chronic inducible urticaria. Moreover, the UAS only works prospectively, and the scoring of the CU-Q_2oL is often too complicated in routine patient care.

The UCT is a retrospective PROM that consists of only 4 questions. Accordingly, it is easy to administer, easy to complete, and easy to score. It determines the current level of disease control and provides information on whether the current treatment is sufficient or not.[8] Treatment of CU is aimed to achieve the absence of signs and symptoms, i.e. complete disease control, and to minimize disease burden with a well-tolerated therapy.[2,8] The UCT may help to achieve this treatment goal if applied continuously over time.

The UCT was originally developed and published in 2014 in German. It can be used in all adult patients with any type of CU and has a recall period of 4 weeks. Its 4 questions have 5 answer options each that are scored from 0 to 4. Accordingly, the UCT score can reach between 0 and 16 points with higher scores indicative of a higher level of disease control. In the original publication of the UCT, a cut-off value of 12 points was identified with ≥12 points indicating well-controlled CU and<12 points indicating poorly controlled disease.

The present research aimed to develop a validated Persian version of the UCT. Also, it aimed to investigate the level of disease control in Persian CU patients as well as to identify and characterize subjects with poorly-controlled disease.

MATERIALS AND METHODS

Translation and Linguistic Validation of the Persian Version of the UCT

Two independent forward translations of the German version of the UCT were performed by two native Persian-speakers bilingual in German. Some minor differences between the two forward translations were resolved with the translators with the result of a consolidated Persian version of the UCT. Then, backward translations to Persian were performed by two independent German native bilingual speakers. The backward translations were checked against the original German version by the original author of the UCT, and inconsistencies were discussed and resolved with the Iranian team with the result of a final Persian translation of the UCT.

As a last step of the linguistic validation process, a cognitive debriefing was performed. To this end, the final Persian translation of the UCT was provided to 10 CU patients. The purpose of this step was to evaluate the clarity of the instructions, all questions and answer options as perceived by the patients as well as to make sure that the patient's perception of the items is equal to the intended content.

Validity and Reliability Analyses

To further test the validity and reliability of the Persian version of the UCT, it was handed out to 100 consecutive CU patients of the Urticaria Center of Reference and Excellence[10] at the Ghaem Hospital in Mashhad, Iran, from November 2017 to April 2018, together with the CU-Q_2oL and the UAS as anchor instruments.

Before participation, all subjects were asked to provide informed consent. All procedures of the study were explained and patients' demographic information was collected including age, gender, duration of the disease, and the presence or absence of angioedema. Furthermore, the autologous serum skin test (ASST) was performed.

Internal Consistency Reliability

To test the internal consistency reliability of the Persian version of the UCT, Cronbach's alpha coefficient was computed. A coefficient between 0.6 and 0.7 is commonly interpreted as acceptable; a coefficient between 0.7 and 0.9 is interpreted as good, and a coefficient≥0.9 is interpreted as excellent.[11,12]

Convergent Validity

To test the convergent validity of the UCT, its results were correlated with the results of the two anchor instruments, the CU-Q_2oL as well as the UAS. Pearson correlation coefficients of<0.3, 0.3-0.6, and>0.6 were interpreted as indicative of a weak, moderate, and strong correlation.[11,13]

The CU-Q_2ol is a disease-specific quality of life questionnaire for CU patients and consists of 23 items with a recall period of 2 weeks. Here, the Persian version of the CU-Q_2oL was used.[14] The achievable minimum and maximum total score of the CU-Q_2oL was 23 and 115, respectively. The higher the score of the CU-Q_2oL was, the higher the CU-related quality of life impairment was obtained.

The UAS was used as an in-clinic assessment.[15] To this end, the treating physician retrospectively rated, together with the patients, the daily intensity of wheals from 0 to 3 as well as the daily intensity of pruritus from 0 to 3 over 7 days. Also, the extent of itching is rated between 0 and 3. Accordingly, the achievable minimum and maximum UAS were 0 and 42, respectively.

Autologous Serum Skin Test (ASST)

To perform the ASST, under aseptic conditions, a sample of 5 cc blood was taken from the brachial vein and stored in a closed falcon test tube without any anticoagulant at room temperature for 30 minutes. Once full coagulation occurred, full segregation was done in a lab centrifuge at the speed of 2000 rpm for 10 minutes. Insulin syringes were used for intradermal injection of 0.05 cc of the patient's serum to the volar aspect of the forearm as well as to inject histamine and saline as positive and negative controls. After 30 minutes, the test result was obtained. The ASST was regarded as positive when the wheal at the serum injected site was at least 1.5 mm larger than the wheal of the negative control.[16]

Statistical Analyses

All the statistical analyses were done in the Statistical Package for the Social Sciences software (SPSS.23), IBM Corporation, Armonk, NY, USA. Confirmatory factor analyses (CFA) were done by IBM SPSS AMOS 23.0.0. In the present research, a p<0.05 was regarded as significant.

Ethical Issues

In advance of the conduction of this research, all subjects were instructed on how to fill out the questionnaires and their informed consent to participate was obtained. They were ensured of the confidentiality of the information they provided, and that their participation had no interference with the medical staff care provision. The present research received the ethical code of IR.MUMS.fm.REC.1396.610 from the ethics committee of Mashhad University of medical sciences.

RESULTS

Patient Characteristics

In the present research, 100 consecutive CU patients were included. The patient characteristics are summarized in Table 1.

Internal Consistency of the Persian Version of the UCT

All 100 CU patients fully completed the UCT. When interviewed subsequently, they were all found to have a similar conception and understanding of the items as originally indented and faced no problem filling out the questionnaire.

The internal consistency reliability of the Persian version of the UCT was found to be acceptable with a Cronbach's alpha coefficient of 0.68.

Convergent Validity of the Persian Version of the UCT

The UCT score showed a moderate correlation with the CU-Q_2oL total score (-0.48, p<0.001) and a weak to moderate correlation with the UAS (-0.404, p<0.001), suggesting moderate levels of convergent validity for the Persian version of the UCT. The correlation coefficients of the UCT and its subgroups with CU-Q_2oL total score are shown in Table 2.

Table 1. Chronic spontaneous urticaria (CSU) patients characteristics

Subject characteristic		%
Gender	Female	66
Age	≤ 20 years	7
	21-40 years	61
	41-60 years	28
	>60 years	4
Disease duration	≤ 2 years	65
	2-10 years	31
	>10 years	4
Angioedema		43
ASST*	Positive	58

*ASST: Autologous Serum Skin Test; n = 100

Table 2. Correlation between Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) total score and urticaria control test (UCT) scores; using Pearson correlation test

Variable	Correlation coefficient	*p*
First question	-0.47	<0.001
Second question	-0.48	<0.001
Third question	-0.28	<0.005
Fourth question	-0.2	<0.048
UCT total score	-0.48	<0.001

CFA was also run to test whether or not the 4 questions of UCT identified cohered together into a single construct. The single-factor model [$\chi 2$/df ratio=0.169; CFI=1.00, TLI=1.00, SRMR=0.008, RMSE<0.0001] yielded excellent fit (Figure 1, Table 3).

CU Control in Persian-speaking Patients

The mean UCT score±SD of all included patients was 5.3±2.0 (median: 5), indicating poorly controlled CU in most patients. Table 4 shows the frequency of the patient's responses to the four UCT items. Only one patient achieved a UCT score of 12 points, indicative of a well-controlled CU. Figure 2 shows the proportion of patients achieving different possible UCT scores.

Potential Patient Characteristics Influencing CU Control in Persian-speaking Patients

The UCT results in patients with different characteristics are shown in Table 5. No major differences were found between patients of different gender, ages, disease duration, presence or absence of angioedema, and a negative or positive ASST result.

Table 3. Urticaria control test (UCT) single factor confirmatory factor analyses (CFA) model fit measures

Measure	Estimate	Threshold	Interpretation
CFI	1.000	>0.95	Excellent
TLI	1.000	>0.95	Excellent
RMSEA	0.000	<0.06	Excellent

CFI: comparative fit index; TLI: Tucker-Lewis index; RMSEA: Root mean square error of approximation

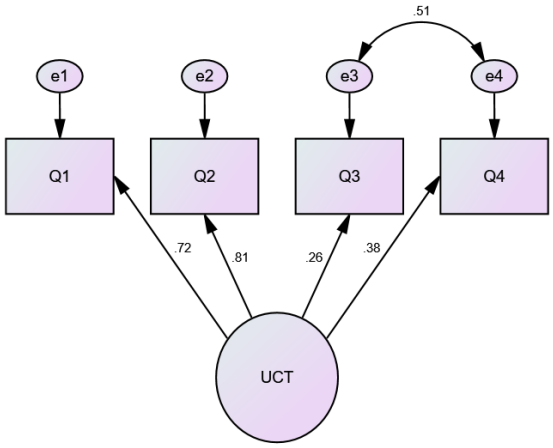

Figure 1. Single-factor confirmatory factor analyses (CFA) model.
Note: Model-based on maximum likelihood (ML) estimations. All of the standardized coefficients are significant at the 0.05 level.

Table 4. Frequency of the Iranian patient's responses to the four urticaria control test (UCT) items

UCT items	N (%)
UCT item 1 - Physical discomfort due to CU*	
Very much	27
Much	41
Somewhat	28
A little	4
Not at all	0
UCT item 2 – Quality of life impairment due to CU	
Very much	17
Much	38
Somewhat	34
A little	11
Not at all	0
UCT item 3 – Treatment failure related to CU	
Always	27
Very frequently	22
Occasionally	30
Rarely	17
Very rarely	4
UCT item 4 – Overall CU control	
Not at all	24
A little	33
Somewhat	31
Much	12
Very much	0

*CU - chronic urticaria

Table 5. Urticaria control test (UCT) results in patients with different characteristics

	Mean UCT score ± SD	Median UCT score	*p*
Gender			
Female	5.03±2.74	5	0.215*
Male	5.76±2.86	5.5	
Age			
≤ 20 years	7.14±2.41	7	0.197**
21-40 years	4.98±2.93	5	
41-60 years	5.28±2.27	5	
61-80 years	6.50±3.87	6.5	
Disease duration			
0- 2 years	5.52±2.73	6	0.362**
2-10 years	4.8±2.62	4	
>10 years	5.00±4.96	4.5	
Angioedema			0.516*
Yes	5.06±2.76	5	
No	5.43±2.82	5	
ASST			0.438*
Positive	5.46±2.65	5	
Negative	5.02±2.99	4.5	

ASST: Autologous Serum Skin Test, *Independent sample t-test, **Kruskal-Wall test

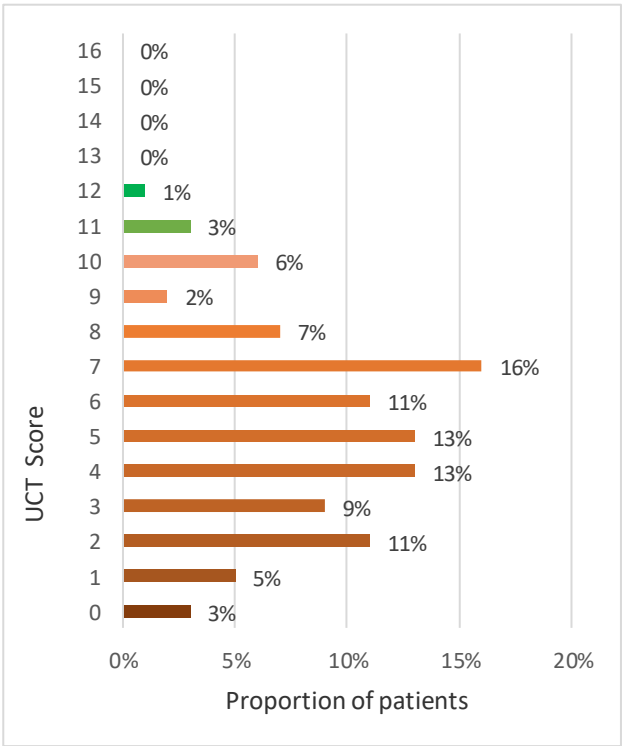

Figure 2. The proportion of chronic spontaneous urticaria (CSU) patients achieving different urticaria control test (UCT) scores

DISCUSSION

Here, we report the development of a validated Persian version of the UCT together with data on its internal consistency reliability and convergent validity as well as on potential factors that influence disease control. The use of the Persian UCT, for the first time, shows that virtually all patients with CU who were referred to UCARE of Ghaem Hospital, have poorly controlled disease.

In our study, like in previous ones, the majority of patients presented with chronic urticaria of fewer than 2 years duration,[16-19] Also, CU was more prevalent among women and in the age group of 20-40 years, which again corresponds well to previous reports.[13,16,20,21] Our finding that 43% of the patients presented with angioedema is consistent with the results of similar investigations. Other studies have also reported prevalence rates of about 40-50%.[16,22,23] In our study population, 58 patients (58%) had a positive ASST. In previous studies, this value has been estimated at 40-60 percent.[24,25]

Patients' UCT scores correlated with disease activity as assessed by the UAS as well as the quality of life impairment, measured with the CU-Q2oL. This correlation refers to the internal consistency of the Persian version of the UCT and the suitability of its use in clinical trials and routine clinical practice. Correlations and Cronbach's alpha were somewhat weaker than those reported in other studies.[11,19,26,27] This could be due to different reasons, including cultural ones, affecting items of the UCT and the CU-Q2oL. For example, people in Iran, especially women, usually cover all parts of their body in public and this may modify the patients' reply to questions about embarrassment in public due to CU and types of selected clothes because they should routinely cover the affected parts and it may reduce their embarrassment. Additionally, it needs to be kept in mind that the tools for assessing the quality of life were not the same in all studies, e.g Nakatani et al, used the Dermatology Life Quality Index (DLQI)[27] while we used CU-Q2oL. Another reason is that the UCT reflects a patient's judgment of disease control, which is linked to patients' expectations regarding the outcome of their medical treatment. Expectations on the efficacy of treatment and the onset of improvement may differ between countries. There may also be country differences in the rates of patients who exaggerate or understate their disease situation.

In this study, the mean UCT scores of virtually all patients showed poorly-controlled CU. The same result was found in previous studies in Iran.[28,29] This is remarkable, but not surprising, as rates of uncontrolled CU are high globally.[30,31] In the recent AWARE study, the proportion of patients with uncontrolled chronic spontaneous urticaria (UCT score <12) at baseline was 78%.[30] In the validation study of the UCT performed in Lebanon, the rate was 79%.[26] It is noteworthy that our Urticaria Center of Reference and Excellence (UCARE), where this study was performed, is the only tertiary referral center in the northeast of Iran. Patients referred to our UCARE are often refractory to standard treatment, and most of them had experienced various previous unsuccessful treatment attempts. Thus, it is not surprising that the proportion of patients with poorly controlled CU is very high.[2,8,11,19,26]

The strengths of this study include the use of the CU-Q2oL, which is designed specifically for patients with CU, and the fact that this study was performed by a single-center highly specialized in urticaria. The latter provides confidence that all patients included in this study had CU. Its limitations include the omission of analyses of test-retest reliability, responsiveness, and known-groups validity, all of which are well established and characterized, and that we did not include patients with chronic inducible urticaria.

In conclusion, the UCT is a valuable tool that helps to assess the level of disease control and guide treatment decisions in CU patients. The Persian version of the UCT is now available and validated and may help to improve the assessment and monitoring of disease control in Persian-speaking CU patients as well as to optimize therapy.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ACKNOWLEDGEMENTS

The supervision of the vice chancellor for research (code: 960483) of Mashhad University of Medical Sciences is highly appreciated. Also, the authors would like to thank the Clinical Research Development Unit of Ghaem Hospital for its assistance in data analysis.

REFERENCES

1. Gonçalo M, Gimenéz-Arnau A, Al-Ahmad M, Ben-Shoshan M, Bernstein JA, Ensina LF, et al. The global burden of chronic urticaria for the patient and society. Br J Dermatol. 2021;184(2):226-36.
2. Zuberbier T, Aberer W, Asero R, Bindslev-Jensen C, Brzoza Z, Canonica GW, et al. The EAACI/GA 2 LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update. Allergy. 2014;69(7):868-87.
3. Greaves M. Chronic urticaria. J Allergy Clin Immunol. 2000;105(4):664-72.
4. Weller K, Siebenhaar F, Hawro T, Altrichter S, Schoepke N, Maurer M. Clinical measures of chronic urticaria. Immunol Allergy Clin North Am. 2017;37(1):35-49.
5. Weller K, Zuberbier T, Maurer M. Clinically relevant outcome measures for assessing disease activity, disease control and quality of life impairment in patients with chronic spontaneous urticaria and recurrent angioedema. Curr Opin Allergy Clin Immunol. 2015;15(3):220-6.
6. Jariwala SP, Moday H, De Asis ML, Fodeman J, Hudes G, De Vos G, et al. The Urticaria Severity Score: a sensitive questionnaire/index for monitoring response to therapy in patients with chronic urticaria. Ann Allergy. 2009;102(6):475-82.
7. Jáuregui I, Ortiz de Frutos F, Ferrer M, Giménez-Arnau A, Sastre J, Bartra J, et al. Assessment of severity and quality of life in chronic urticaria. J Investig Allergol Clin Immunol. 2014;24(2):80-6.
8. Weller K, Groffik A, Church MK, Hawro T, Krause K, Metz M, et al. Development and validation of the Urticaria Control Test: a patient-reported outcome instrument for assessing urticaria control. J Allergy Clin Immunol. 2014;133(5):1365-72.
9. Zuberbier T, Aberer W, Asero R, Abdul Latiff AH, Baker D, Ballmer-Weber B, et al. The EAACI/GA²LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. Allergy. 2018;73(7):1393-414.
10. Maurer M, Metz M, Bindslev-Jensen C, Bousquet J, Canonica GW, Church MK, et al. Definition, aims, and implementation of GA^{2}LEN urticaria centers of reference and excellence. Allergy. 2016;71(8):1210-8.
11. Kulthanan K, Chularojanamontri L, Tuchinda P, Rujitharanawong C, Maurer M, Weller K. Validity, reliability and interpretability of the Thai version of the urticaria control test (UCT). Health Qual Life Outcomes. 2016;14(1):61-6.
12. George D, Mallery M. Using SPSS for Windows step by step: a simple guide and reference. 2003.
13. Nunnally JC. Psychometric theory 3E: Tata Mc Graw-Hill Education; 1994.
14. Tavakol M, Mohammadinejad P, Baiardini I, Braido F, Gharagozlou M, Aghamohammadi A, et al. The persian version of the chronic urticaria quality of life questionnaire: factor analysis, validation, and initial clinical findings. Iran J Allergy Asthma Immunol. 2014; 13(4):278-85.
15. Hawro T, Ohanyan T, Schoepke N, Metz M, Peveling-Oberhag A, Staubach P, et al. The Urticaria Activity Score—validity, reliability, and responsiveness. J Allergy Clin Immunol Pract. 2018;6(4):1185-90.
16. Black K. The autologous serum skin test: a screening test for autoantibodies in chronic idiopathic urticaria. Br J Dermatol. 1999;140(3):446-52.
17. Baiardini I, Pasquali M, Braido F, Fumagalli F, Guerra L, Compalati E, et al. A new tool to evaluate the impact of chronic urticaria on quality of life: chronic urticaria quality of life questionnaire (CU-Q2oL). Allergy. 2005;60(8):1073-8.
18. Khan DA. Chronic urticaria: diagnosis and management. Allergy and asthma proceedings. 2008;29(5):439-46.
19. Ye Y-M, Kim S-C, Ban G-Y, Shin Y-S, Park H-S. Adaptation and Validation of the Korean Version of Urticaria Control Test. J Allergy Clin Immunol. 2017;139(2):AB245.
20. Maurer M, Weller K, Bindslev-Jensen C, Giménez-Arnau A, Bousquet P, Bousquet J, et al. Unmet clinical needs in chronic spontaneous urticaria. A GA2LEN task force report 1. Allergy. 2011;66(3):317-30.
21. Młynek A, Zalewska-Janowska A, Martus P, Staubach P, Zuberbier T, Maurer M. How to assess disease activity in patients with chronic urticaria? Allergy. 2008;63(6):777-80.
22. Axelrod S, Davis-Lorton M. Urticaria and angioedema. Mt Sinai J Med. 2011;78(5):784-802.
23. Kaplan AP. Chronic urticaria: pathogenesis and treatment. J Allergy Clin Immunol. 2004;114(3):465-74.
24. Grattan C, Wallington T, Warin R, Kennedy C, Lbradfield J. A serological mediator in chronic idiopathic urticaria—a clinical, immunological and histological evaluation. Br J Dermatol. 1986;114(5):583-90.
25. Guttman-Yassky E, Bergman R, Maor C, Mamorsky M, Pollack S, Shahar E. The autologous serum skin test in a cohort of chronic idiopathic urticaria patients compared to respiratory allergy patients and healthy individuals. J Eur Acad Dermatol Venereol. 2007;21(1):35-9.

26. Irani C, Hallit S, Weller K, Maurer M, El Haber C, Salameh P. Chronic urticaria in most patients is poorly controlled: results of the development, validation, and real life application of the Arabic urticaria control test. Saudi Med J. 2017;38(12):1230.
27. Nakatani S, Oda Y, Washio K, Fukunaga A, Nishigori C. The Urticaria Control Test and Urticaria Activity Score correlate with quality of life in adult Japanese patients with chronic spontaneous urticaria. Allergol Int. 2019;68(2):279-81.
28. Fadaee J, Khoshkhui M, Emadzadeh M, Hashemy SI, Hosseini RF, Azad FJ, et al. Evaluation of Serum Substance P Level in Chronic Urticaria and Correlation with Disease Severity. Iran J Allergy Asthma Immunol. 2019(4):1-9.
29. Zabolinejad N, Molkara S, Bakhshodeh B, Ghaffari-Nazari H, Khoshkhui M. The expression of serotonin transporter protein in the skin of patients with chronic spontaneous urticaria and its relation with depression and anxiety. ArcDermatol Res. 2019;311(10):825-31.
30. Maurer M, Costa C, Gimenez Arnau A, Guillet G, Labrador-Horrillo M, Lapeere H, et al. Antihistamine-resistant chronic spontaneous urticaria remains undertreated: 2-year data from the AWARE study. Clin Exp Allergy. 2020;50(10):1166-1175.
31. Maurer M, Giménez-Arnau A, Ensina LF, Chu C-Y, Jaumont X, Tassinari P. Chronic urticaria treatment patterns and changes in quality of life: AWARE study 2-year results. World Allergy Organ J. 2020;13(9):100460.