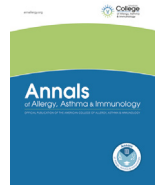




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Letters

Perceived stress links income loss and urticaria activity during the coronavirus disease 2019 pandemic



The pandemic of coronavirus disease 2019 (COVID-19) has caused substantially adverse effects on health and economy at both individual and societal levels. It was estimated that the worldwide unemployment rate might increase from 4.9% to 5.6% owing to the pandemic.¹ Decades of research have accumulated evidence on the adverse impacts of unemployment on poverty-related health outcomes and mental illness, such as stress and anxiety.² Interestingly, it has been well established that allergic diseases are associated with higher socioeconomic status (SES).³ However, it is less known whether adverse life events, such as loss of income, would trigger or enhance the activity of allergies. Few epidemiologic studies have addressed this question, but a recent review summarized the neuro-immuno-cutaneous crosstalk as a mechanism that links psychological stress and urticaria.⁴ The outbreak of COVID-19 uniquely creates a quasi-experiment and provides an opportunity to study this association. We assumed that the income loss could increase urticaria activity through mental stress; hence, we conducted a social media-based investigation in adult Chinese patients between February 27, 2020, and March 11, 2020. This was done by distributing a link to 2 WeChat groups consisting of 980 patients who were diagnosed as having urticaria in the Department of Dermatology, Xiangya Hospital, Changsha, People's Republic of China.

Loss of income was inquired by a question, "Since the epidemic of COVID-19, is there any change in your monthly income?" and categorized as complete loss, reduced, and unaffected. The primary outcome was the activity of chronic urticaria, determined by the urticaria activity score (UAS). The severities and frequencies of wheals and itch during the past 7 days were analyzed separately, and moderate-to-intense wheals or itch or frequencies of wheals or itch for more than 1 day per week were defined as the outcomes (binary). The secondary outcomes included perceived stress (visual analogue scale), symptoms of anxiety (2-item generalized anxiety disorder), and depression (Patient Health Questionnaire-2). The cutoffs were 7, 3, and 3 for stress in the visual analogue scale, 2-item generalized anxiety disorder, and Patient Health Questionnaire-2, respectively.^{5,6} Covariates for adjustments included sex, age, education, income, history of disease, and

outdoor activity restriction during the pandemic. Multivariable logistic regression was used to estimate the associations with adjustments. The effect size was presented as adjusted odds ratio (aOR) and 95% confidence interval. The mediation effect of stress was tested and estimated using the bootstrapping method. A *P* value of less than .05 was considered statistically significant. The data were analyzed with R version 3.5.2.

A total of 234 valid questionnaires were collected, and 182 of them were adult patients with chronic urticaria. The mean age of the patients was 33.7 plus or minus 10.9, and 55.5% were women. Only 68 (37.3%) reported unaffected income, whereas 54 (29.7%) reported reduced income, and 60 (33.0%) reported complete loss of income. By comparing the participants' characteristics, income loss was significantly associated with sex, educational level, income, and outdoor activity (all *P* values < .05), which were further adjusted in multivariable models. In general, loss of income was dose-dependently associated with urticaria activity with respect to the severities and frequencies of wheals and itch (Table 1). However, after adjustments for covariates, significant associations were only observed in the frequency of wheals (aOR = 2.45 for reduced income and aOR = 2.13 for loss of income) and intensity of itch (aOR = 2.19 for loss of income). Unexpectedly, income loss was not significantly correlated with the sum of the UAS.

Income loss was not significantly correlated with anxiety in the multivariable model, although a higher proportion of anxiety could be observed in patients who reported income loss. Income loss was associated with perceived stress with the largest effect size (aOR = 4.56, *P* = .029). According to the bootstrapping estimates for mediation effect, perceived stress significantly contributed to 19.3% of the total effect of income loss on urticaria activity (*P* = .040). The estimate for indirect effect was 0.03 (95% confidence interval, 0.01-0.06; *P* = .040). More importantly, income loss was no longer significantly correlated with urticaria activity after modeling stress (*P* = .080).

Our study examined the association of income loss with urticaria activity, in terms of the frequency of wheals and the intensity of itch, and this association is partly mediated or modified by perceived stress. The study has implications for the management of patients with chronic urticaria and further studies on the neuro-immuno-cutaneous interactions. The study has limitations, including selection bias owing to the nonprobability sampling method, limited generalizability to non-Chinese and non-urticaria population, lack of longitudinal observations, incapability to infer a causal relationship owing to the observational study design, and recall bias related to the self-reported measurements. Nevertheless, to the best of our knowledge, this is the first study that established an association of the pandemic-related impacts with adverse outcomes of chronic urticaria and proposed a hypothesis for the black box of association.

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This study is reviewed and approved by the institutional research ethics board of Xiangya Hospital, Central South University, Changsha, People's Republic of China (approval number, 202002024).

The data are available on request to the corresponding author.

Minxue Shen and Yangjian Xiao contributed equally to this work.

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Table 1
Association of Income Loss With Urticaria Activity and Patient-Reported Outcomes

Characteristic	Unaffected		Reduced			Complete loss		
	n (%)	aOR	n (%)	aOR (95% CI) ^a	P value	n (%)	aOR (95% CI) ^a	P value
Primary outcomes								
Frequent wheals (>1 d/wk)	23 (33.8)	Reference	29 (53.7)	2.45 (1.15–5.25)	.020	32 (53.3)	2.13 (1.01–4.50)	.048
Frequent itch (>1 d/wk)	30 (44.1)	Reference	29 (53.7)	1.52 (0.72–3.22)	.271	35 (58.3)	1.90 (0.90–4.03)	.093
Moderate-to-intense wheals	8 (11.8)	Reference	9 (16.7)	1.67 (0.59–4.78)	.338	16 (26.7)	2.61 (0.97–6.99)	.057
Moderate-to-intense itch	20 (29.4)	Reference	22 (40.7)	1.57 (0.73–3.38)	.248	29 (48.3)	2.19 (1.02–4.68)	.044
Secondary outcomes								
Anxiety (GAD-2, ≥3)	17 (25.0)	Reference	18 (33.3)	1.80 (0.79–4.11)	.161	21 (35.0)	1.34 (0.60–3.00)	.483
Depression (PHQ-2, ≥3)	31 (45.6)	Reference	26 (48.2)	1.18 (0.57–2.47)	.657	26 (43.3)	0.83 (0.40–1.76)	.633
Perceived stress (VAS, ≥7)	3 (4.4)	Reference	6 (11.1)	2.56 (0.59–11.2)	.208	12 (20.0)	4.56 (1.17–17.8)	.029

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; GAD-2, 2-item generalized anxiety disorder; PHQ-2, Patient Health Questionnaire-2; VAS, visual analogue scale.

^aAdjusted for sex, annual income, and outdoor activity restriction.

Chronic urticaria has detrimental effects on the quality of life and mental health, whereas psychiatric comorbidities could aggravate urticaria activity, which, in turn, results in a vicious circle. More importantly, the needs for disease control remain largely unmet in chronic urticaria, because a substantial number of patients benefit little from H₁ antihistamines.⁷ Consequently, research for novel mechanisms involved in the neuroimmune inflammation in urticaria is needed, because it will enlighten the development of new therapeutic strategies for patients with unsatisfied disease control and impaired quality of life. Admittedly, we realized that a social stressor is not the Achilles' heel of urticaria, because it only contributed to approximately 20% of the total effect. In addition, we observed no significant correlation between income loss and the total score of the UAS partly because of the lack of associations of income loss with the frequency of itch and severity of wheals. This might introduce additional measurement errors and conceal the true effect toward null. Another possible explanation is the effect modification by SES. A study found that lower SES was associated with a larger increase in perceived stress and higher levels of interleukin-6 in survivors who experienced a disaster, indicating that individuals from different SES backgrounds respond differently to stressors both psychosocially and biologically.⁸ In conclusion, during this pandemic period, dermatologists and psychologists can work together and remotely to identify the patients who have experienced loss of income and social distancing and to provide personalized care to minimize the adverse outcomes of urticaria and many other allergic diseases.

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A fatal case of coronavirus disease 2019 in a patient with common variable immunodeficiency



Common variable immunodeficiency (CVID) is a heterogeneous group of primary immunodeficiency syndromes characterized by hypogammaglobulinemia and impaired vaccine responses. Although immunodeficiency is described as a risk factor for coronavirus disease 2019 (COVID-19), limited data are available

regarding CVID. Of note, 3 recent reports describe mostly positive outcomes in patients with CVID who were diagnosed as having COVID-19,^{1–3} with only 1 fatality.³ All these patients had adequate immunoglobulin G (IgG) levels at the time of COVID-19 diagnosis.^{1–3} We present a case of a patient with a history of CVID and severely low IgG levels owing to a lapse in immunoglobulin replacement therapy, who died of complications related to COVID-19 despite receiving convalescent plasma and high-dose intravenous immunoglobulin (IVIG).

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