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Psychological impact of the COVID-19 pandemic on patients with allergic diseases

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ABSTRACT

Background: On March 2020, World Health Organization (WHO) declared COVID-19 to be a pandemic disease. Interactions between allergy-related inflammatory and psychiatric disorders including depression, anxiety, and post-traumatic stress disorder (PTSD) have been documented. Therefore, those who have pre-existing allergic conditions may have an increased psychiatric reaction to the stresses of the COVID-19 pandemic.

Objective: Identify the psychological impact of COVID-19 in patients with allergic diseases and determine if these individuals have a greater risk of presenting with post-traumatic stress disorder (PTSD).

Methods: It is a cross-sectional, survey-based study designed to assess the degree of symptoms of depression and the risk of PTSD using the Patient Health Questionnaire (PHQ-9) and the Impact of Event Scale-Revised (IES-R), respectively, in allergic patients.

Results: A total of 4106 surveys were evaluated; 1656 (40.3%) were patients with allergic disease, and 2450 (59.7%) were non-allergic (control) individuals. Of those with allergies, 76.6% had respiratory allergic disease including asthma and allergic rhinitis. Individuals with allergic disease reported higher scores regarding symptoms of PTSD on the IES-R scale (p = 0.052, OR 1.24 Cl 0.99-1.55) as well as a higher depression risk score in the PHQ-9 questionnaire (mean 6.82 vs. 5.28) p = 0.000 z = -8.76.

The allergy group presented a higher score in the IES-R questionnaire (mean 25.42 vs. 20.59), being more susceptible to presenting PTSD (p = 0.000, z = -7.774).

The individuals with allergic conditions were further divided into subgroups of those with respiratory allergies such as allergic rhinitis and asthma vs those with non-respiratory allergies such as drug and food allergy, urticaria and atopic dermatitis. This subgroup analysis compares respiratory versus non-respiratory allergic patients, with similar results on the IES-R (mean 25.87 vs 23.9) p = 0.0124, z = -1.539. There was no significant difference on intrusion (p = 0.061, z = -1.873) and avoidance (p = 0.767, z = -0.297), but in the hyperarousal subscale, patients with respiratory allergy had higher scores (mean 1.15 vs. 0.99) p = 0.013 z = -2.486.

Conclusions: Psychological consequences such as depression and reported PTSD are present during the COVID-19 pandemic causing an impact particularly in individuals with allergic diseases.

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Received 15 July 2020; Received in revised from 5 January 2021; Accepted 7 January 2021

Online publication date xxx

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Keywords: Allergic, COVID-19, Psychologic, Impact

BACKGROUND

2

In January 2020, World Health Organization (WHO) declared the outbreak of a new coronavirus disease, COVID-19, to be a Public Health Emergency of International Concern, and in March 2020, WHO made the assessment that COVID-19 was a pandemic disease. WHO and public health authorities around the world are acting to contain the COVID-19 outbreak.¹ Across the world, reactions to this unforeseen pandemic have impacted lives in a number of ways, to include lockdown and shelter in place orders which have led to job loss and economic devastation for some. The health and economic uncertainty, coupled with the sheer numbers of countries and people involved, have made the COVID-19 crisis the largest global disruption since World War II. This has been overwhelming for some, creating difficulty in coping with life during the pandemic.

SARS-CoV-2, the virus that causes COVID-19, is highly contagious, capable of causing severe pneumonia, acute respiratory distress syndrome, and death, particularly invulnerable populations such as those with respiratory diseases.^{2,3} In patients with allergic diseases it is recommended to monitor their allergy and asthma symptoms, as there may be overlapping symptoms which may lead to a misdiagnosis of COVID-19. The relationship betweenviralinfections, immuneresponse, and allergic diseases has been widely discussed, and it has been established that allergy can increase the risk of exacerbation of virus-induced symptoms.^{4,5} Respiratory allergiessuchasasthmaandallergicrhinitishavenot been shown to be risk factors for severe SARS-CoV-2 infection;⁶ however, the data are not yet conclusive, and allergic patients may experience a misperception of their allergic disease against COVID-19 leading to additional psychological changes.⁷

Asthma and other chronic respiratory diseases appear to be underrepresented in the

comorbidities reported for patients with COVID-19, observing a similar pattern as that reported in patients with SARS (2.4%); with this in mind, changes in the treatment of chronic respiratory diseases should not be considered, including chronic obstructive pulmonary disease (COPD) and asthma.⁸ With a great part of the world in quarantine, levels of anxiety have begun to surge, leading patients to identify, and in some cases, seek medical attention for symptoms that otherwise might not have caused concern.⁹

Other psychological reactions that appear in pandemics include emotional distress, maladaptive behaviors, and defensive responses. People who have greater susceptibility to psychological problems are particularly vulnerable.¹⁰

Interactions between allergy-related inflammatory and psychiatric disorders, such as depression,¹¹ anxiety, bipolar disorder, and schizophrenia have been previously documented.¹² More specifically, asthma, rhinitis, or atopic dermatitis and the combination of all 3 of these allergic diseases, have been associated with a higher risk of psychiatric disorders.¹³ A higher incidence of allergic diseases has been seen in patients with post-traumatic stress disorder (PTSD), and it has been suggested that immune activation is a contributor to clinical status.¹⁴ The prevalence of PTSD among direct victims of disasters such as natural, technological, or human-made (terrorism) ranges between 30% and 40%, while the range of PTSD rates in the general population is the lowest and expected to be between 5% and 10%.¹⁵ Immunologic morbidity has been reported in patients with history of PTSD including a lower number of lymphocytes, T cells, NK cell activity, and total amounts of IFN-g and IL-4.¹⁶ Other immune alterations such increased as levels of inflammatory cytokines including IL-1, IL-6, and TNF- α have also been studied.¹⁴ This time of pandemic crisis is generating stress throughout the population; therefore, the aim of this study was to identify the psychological impact of COVID-19 in patients with allergic diseases and determine if these individuals have a greater risk of presenting with PTSD.

METHODS

Surveys were sent out by allergists, to adults over 18 years old, via a Google Forms link, and shared through different social media platforms as well as by telephone in the case of patients who attended the allergy and immunology clinic. There were no other limitations regarding the population surveyed. Digital informed consent was provided by all survey participants prior to their enrollment. A copy of the survey will be available as an online supplement. Participants were allowed to deny the survey if they did not accept digital informed consent. The survey was anonymous, and confidentiality of the information was assured.

The study is a cross-sectional, survey-based, stratified study with demographic data and mental health measurements from 4106 participants collected from April 1 to 15, 2020 during a period in which our country, Mexico, was entering the uncertainty of phase 3 of the pandemic response due to COVID-19 and most of America was under quarantine.

The survey contained 2 questionnaires that assessed the degree of symptoms of depression, anxiety, and the risk of post-traumatic stress disorder (PTSD), using the 9-item Patient Health Questionnaire (PHQ-9) and the 22-item Impact of Event Scale-Revised (IES-R), respectively. Multivariable logistic regression analysis was performed to identify factors associated with mental health outcomes.

The 9-item PHQ test has a range of responses from 0 to 27 and is used to assess the severity of symptoms of depression. Scores are interpreted as follows: none-minimal (0-4), mild (5-9), moderate (10-14), moderately severe (15-20), and severe (20-27) depression. The 22 item IES-S test has a range of 0-88 and tests the severity of symptoms of distress. Scores are interpreted as follows: significant clinical concern (24-32), probable diagnosis of PTSD, and reflecting long-term suppression of immune system functioning (39 and above).^{16,19} With the introduction of the DSM-IV, the IES was updated to include 3 subscales: intrusion, avoidance, and hyperarousal.¹⁹ These categories were based on values established in the literature. The cutoff score for detecting symptoms of major depression and distress were 10 and 24, respectively. In the DSM-5, PTSD is included in a new category, Trauma- and Stressor-Related Disorders. The scales were used based on the DSM-IV. Participants who had scores greater than the cutoff threshold were characterized as having severe symptoms.¹⁷⁻¹⁹

Demographic data was self-reported by the participants, including gender (male or female), age, geographic location (Mexico, United States, and Latin American countries), marital status (single, married, divorced, living with a couple, widow), educational level (elementary school, middle school, high school, undergraduate, postgraduate and others), place of residence (house or apartment with or without patio), and patient's reported allergic disease (allergic rhinitis, asthma, atopic dermatitis, urticaria, food allergy, drug allergy). Medication intake specifically regarding allergy and psychopharmacologic agents was not inquired.

Data analysis was performed using SPSS statistical software version 25.0 (IBM Corp). The significance level was set at $\alpha = 0.05$, and all tests were 2-tailed. The ranked data, which were derived from the counts of each level for symptoms of depression, and distress, are presented as numbers and percentages. The nonparametric Mann-Whitney U test and Kruskal-Wallis test were applied to compare the severity of each symptom between 2 or more groups. To determine potential risk factors for symptoms of depression, and distress in participants, multivariable logistic regression analysis was performed, and the associations between risk factors and outcomes are presented as odds ratios (ORs) and 95% Cls, after adjustment for confounders, including gender, age, geographic location, marital status, educational level, place of residence, and presence of allergic disease.

RESULTS

A total of 4106 surveys were evaluated; the majority were female 2991 (72.9%). Patients were divided into those with allergic disease 1656

4 Gonzalez-Diaz et al. World Allergy Organization Journal (2021) 14:100510 http://doi.org/10.1016/j.waojou.2021.100510

(40.3%) and the control group, those who were non-allergic 2450 (59.7%). The average ages were 35.2 and 36.7, respectively.

48.6% were married, Mexican nationality 96.2% (3949), 79.9% live in a house with a patio and 55.8% had an undergraduate education. (Table 1).

A total of 1656 patients with allergic disease were included in the study: 76.6% (1268 respondents) had respiratory allergic disease (asthma and allergic rhinitis) and 23.4% (388 respondents) had non-respiratory allergic disease (atopic dermatitis, urticaria, food allergy and drug allergy).

Characteristics	Allergy group n = 1656 (40.3%)	Control group n = 2450 (59.7%)
Age (year) Mean Range 18-59 years >60 years	35.2 18-82 1557 99	36.7 18-80 2275 175
Sex Male Female Others	404 (24.4%) 1249 (75.4) 3 (0.2%)	705 (28.8%) 1742 (71.1%) 3 (0.1%)
Geographic location Mexico Others	1597 (96.4%) 59 (3.6%)	2352 (96%) 98 (4%)
Marital status Single Married Divorced Living with a couple Widow	698 (42.1%) 760 (45.9%) 70 (4.2%) 113 (6.8%) 15 (1%)	880 (36%) 1235 (50.4%) 118 (4.8%) 185 (7.5%) 32 (1.3%)
Educational level Elementary school Middle school High school Undergraduate Postgraduate Others	10 (0.6%) 31 (1.9%) 132 (8%) 907 (54.7%) 546 (33%) 30 (1.8%)	10 (0.4%) 89 (3.6%) 312 (12.7%) 1384 (56.5%) 592 (24.2%) 63 (2.6%)
Place of residence Apartment without balcony Apartment with balcony House with backyard House without backyard Country House	122 (7.4%) 124 (7.5%) 1280 (77.3%) 111 (6.7%) 19 (1.1%)	133 (5.4%) 180 (7.3%) 2001 (81.7%) 114 (4.7%) 22 (0.9%)
Atopic disease Allergic rhinitis: Allergic Rhinitis and asthma: Allergic Rhinitis, asthma and atopic dermatitis: Allergic rhinitis, asthma, atopic dermatitis and food allergy: Other:	660 (39.8%) 90 (5.4%) 23 (1.3%) 24 (1.4%) 859 (51.8%)	

Table 1. Characteristics of allergy and control group

Of these patients, 64% (1055 individuals) presented 1 allergic condition (AC) and 23% (386 individuals) had 2 reported allergic conditions (Fig. 1).

In total, 1656 patients declared to suffer from 2535 allergic diseases, of which 57.2% (1449) were respiratory allergic diseases, and 42.8% (1086) were non respiratory allergies (Fig. 2).

The allergy group presented a higher score in the IES-R questionnaire (mean 25.42 vs. 20.59), being more susceptible to presenting PTSD (p = 0.000, z = -7.774). They also presented higher scores on the IES-R subscales: intrusion (mean 1.2 vs. 0.96), avoidance (mean 1.15 vs. 0.99) and hyperarousal (mean 1.12 vs. 0.84), being statistically significant p = 0.000 z = -7.856, p = 0.000 z = -6.027, and p = 0.000 z = -8.563 respectively.

This group also had a higher depression risk score in the PHQ-9 questionnaire (mean 6.82 vs. 5.28) p = 0.000 z = -8.76. Even so, both groups presented data suggesting mild depression symptoms (Table 2).

The group with respiratory allergy also had higher IES-R scores (mean 25.87 vs 21.05) p = 0.000 z = -7.176. In the IES-R subscales, respiratory allergic patients were at higher risk: intrusion (mean 1.22 vs 0.98) p = 0.000z = -7.481, avoidance (mean 1.15 vs 1.01) p = 0.000 z = -5.045, and hyperarousal (mean 1.15 vs 0.86) p = 0.000 z = -8.379.

In addition, in the respiratory allergy group a higher score on the PHQ-9 depression scale (mean 7.14 vs. 5.35) p = 0.000, z = -9.43 was evidenced (Table 3).

Finally, respiratory versus non-respiratory allergic patients were compared, with similar results (mean 25.87 vs 23.9) p = 0.0124, z = -1.539. There was no significant difference on intrusion (p = 0.061, z = -1.873) and avoidance (p = 0.767, z = -0.297), but in the hyperarousal subscale, patients with respiratory allergy had higher scores (mean 1.15 vs. 0.99) p = 0.013 z = -2.486.

Patients in the respiratory allergy group also had a higher risk of depression symptoms in the PHQ-9 questionnaire (mean 7.14 vs. 5.7) p = 0.000

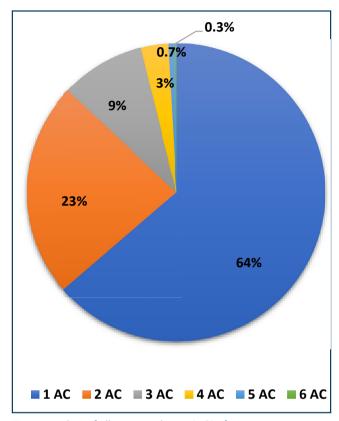


Fig. 1 Number of allergic conditions (AC) of atopic patients

z = -4.006 compared to allergic patients without respiratory pathologies (Table 4).

There is an increased risk of having an allergic disease and presenting symptoms of PTSD on the IES-R scale (p = 0.052, OR 1.24 Cl 0.99-1.55). Also being female and having PTSD symptoms on the IES-R scale (p = 0.000, OR 1.41, Cl 1.18-1.68), as well as being between 18 and 59 years old (p = 0.001, OR 1.87, Cl 1.27-2.76), although in our

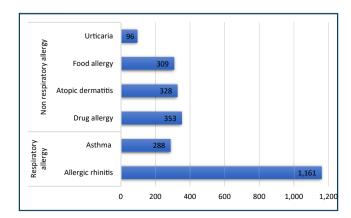


Fig. 2 Respiratory and non-respiratory allergy

6 Gonzalez-Diaz et al. World Allergy Organization Journal (2021) 14:100510 http://doi.org/10.1016/j.waojou.2021.100510

		Allergy Group IES-R		Control Group		Allergy Group PHQ-9		Control Group PHQ-9
n=		1656		2450		1656		2450
Mean		25.422		20.597		6.82	24	5.289
Median		21		16		5		4
IQR	28		3	23		8		7
Z		-7.774				-8.76		
<i>P</i> -value		0.000				0.00	00	
	Intr	usion	Avoidance	Hyperarousal	Intr	rusion	Avoidance	Hyperarousal
Mean		1.2	1.15	1.12	C).96	0.99	0.84
Median	1		1	0.83	0.75		0.88	0.5
IQR	1	.28	1.37	1.38		1	1.12	1.16
Z	-7	.856	-6.027	-8.563				
P-value	0.	000	0.000	0.000				

Table 2. Allergy vs. Control group

	Respiratory Allergy IES-R		Control Group IES-R	Respiratory Allergy PHQ-9		Control Group PHQ-9
N=	126	58	2838	126	58	2838
Mean	25.8	71	21.056	7.14	40	5.357
Median	21.	5	17	6		4
IQR	29)	24	8.2	5	7
Z	-7.1	96		-9.4	43	
P-value	0.00	00		0.00	00	
	Intrusion	Avoidance	Hyperarousal	Intrusion	Avoidance	Hyperarousal
Mean	1.22	1.15	1.15	0.98	1.01	0.86
Median	1	1	0.83	0.75	0.88	0.67
IQR	1.25	1.37	1.5	1.12	1.12	1.16
Z	-7.481	-5.045	-8.379			
P-value	0.000	0.000	0.000			

Table 3. Respiratory allergy group vs. Control group

	Respiratory Allergy IES-R	ALI	SPIRATORY LERGY ES-R	Respiratory Allergy PHQ-9	AL	NON-RESPIRATORY ALLEGY PHQ-9		
N=	1268		388			388		
Mean	25.871		23.9			5.7		
Median	21.5		20			4		
IQR	29		28			8		
Z	-1.539			-4.006				
P-value	0.124			0.000				
	Intrusion	Avoidance	Hyperarousal	Intrusion	Avoidance	Hyperarousal		
Mean	1.22	1.15	1.15	1.12	1.14	0.99		
Median	1	1	0.83	0.88	1.00	0.75		
IQR	1.37	1.25	1.33	1.25	1.37	1.50		
Z	-1.873	-0.297	-2.486					
P-value	0.061	0.767	0.013					

Table 4. Respiratory allergy vs. Non-respiratory allergy Group

population the majority is in this age range. The allergic group that presented an educational level of undergraduate presented higher scores in the IES-R questionnaire (p = 0.002, OR 1.00, Cl 1.00-1.01). There was no significant difference in the place of residence (p = 0.251, OR 0.995, IC 0.98-1.00), marital status (p = 0.971, OR 1.00, IC 0.91-1.09) and if they had their allergic disease under control (p = 0.821, OR 1.00, IC 0.97-1.00).

The group with allergic respiratory disease has an increased risk of developing PTSD (p = 0000, OR 1.38, CI 1.15-1.66), the female gender (p = 0.000, OR 1.66, CI 1.43-1.93), and being in the age group between 18 and 59 years (p = 0.000, OR 3.46, CI 2.46-4.85).

The undergraduate group has a higher score in the IES-R questionnaire (p = 0.001, OR 1.00, IC 1.00-1.01). There was no difference in the place of residence (p = 0.406, OR 0.99, IC 0.99-1.00), marital status (p = 0.157, OR 1.00, IC 0.99-1.00), and having control of allergic respiratory disease (p = 0.625, OR 1.00, CI 0.99-1.00).

The group with allergic disease had a higher risk of developing depression symptoms on the PHQ-9 scale (p = 0.001, OR 1.37, Cl 1.13-1.65), as well as the female population had a higher risk of depression (p = 0.000, OR 1.65, Cl 1.43-1.91), and

having an age of 18-59 years (p = 0.000, OR 3.97, Cl 2.86-5.51). It was also evidenced that the single marital status had a higher risk of depression in both men and women (p = 0.000, OR 1.2, Cl 1.11-1.29). There was no higher risk depending on the place of residence (p = 0.590, OR 1.00, Cl 0.99-1.00), educational level (p = 0.219, OR 1.00, Cl 0.99-1.00) and the control of their allergic disease (p = 0.309)., OR 1.00, Cl 0.99-1.00).

Finally, patients with allergic respiratory disease have a higher risk of presenting depression symptoms (p = 0.000, OR 1.60, CI 1.34–1.92), also the female gender (p = 0.000, OR 1.58, CI 1.37– 1.83), and being under 60 years old is the risk factor with the highest association in presenting depression symptoms (p = 0.000, OR 4.37, CI 3.16-6.05). There is no statistically significant relationship depending on the place of residence (p = 0.764, OR 1.00, CI 0.99–1.00), the educational level (p = 0.153, OR 1.00, CI 0.99–1.00), marital status (p = 0.519, OR 1.00, CI 0.99–1.00), and the control of allergic respiratory disease (p = 0.843, OR 1.00, CI 0.99–1.00).

DISCUSSION

Prior research has reported a wide spectrum of psychological impact that outbreaks or worldwide

conflicts can cause on the population. At an individual level, it can trigger new psychiatric symptoms in people with no diagnosed mental illness, aggravate the condition of those with pre-existing mental illness, and cause stress for the caregivers that are affected. Regardless of exposure, people may present with fear and anxiety of becoming ill or dying, triggering a mental breakdown.²⁰ Psychiatric morbidities have been found including depression, anxiety, and posttraumatic stress disorder symptoms.^{21,22}

Our study revealed that during this period of guarantine due to COVID-19, the psychological impact in patients with allergic diseases was greater compared to individuals without allergy. Allergic patients had a higher risk of depression symptoms measured with the PHQ-9 scale and of reported PTSD evaluated with the IES-R scale which is measured within 2 weeks of exposure to event, impacting specifically in the intrusion, avoidance, and hyperarousal section. Individuals with respiratory allergy such as asthma and rhinitis were particularly vulnerable to a higher PHQ-9 and PTSD scale. Previous studies have demonstrated an association between PTSD and an increased incidence of allergic and autoimmune diseases.²³ Huang et al showed a significant link between PTSD and asthma,²⁴ where underlying alterations in psychophysiological, neuroendocrine, and neurobiological systems have been implicated.²⁵ Glenk et al reported that allergic individuals showed higher scores regarding emotion suppression, had increased pre-stress concentrations of plasma oxytocin, and demonstrated a stronger salivary cortisol response to stress than healthy people.²⁶

In the group of allergic patients from 18 to 59 years of age, there was a higher risk of depression and PTSD, being predominant in the female population surveyed. These results contrast with other studies that have reported older adults as a highrisk group of PTSDs due to several factors in adapting such as an increased sense of insecurity and vulnerability; a loss of sense of control and predictability; and a need to reaffirm familiar relationships, attachments, and routines.²⁷ Kelly et al reported that seasonal allergies were positively associated with odds of mild depression and PTSD. Asthma was not significantly associated with any psychiatric disorder.²⁸

Similar to our results, depression as well as anxiety and reported PTSD have been found to affect women more than men, peaking at the age of 20-40 years, possibly due to underlying biological predispositions such as hormonal fluctuation related to the menstrual cycle.²⁷ Also, depression was more prevalent in unmarried or widowed individuals, as previously reported.²⁹

In our results, the level of patient's allergic disease control did not influence the risk of developing depression or affect the scores in the PHQ-9 questionnaire. Depression may modify the degree of severity with which symptoms are perceived by patients and in consequence modify the level of asthma control, while poorly controlled asthma could lead to depression.^{30,31} According to Ferro et al, adolescents with asthma are associated with an increased risk of clinically relevant symptoms of depression; on the other hand food allergy is associated with an increased risk of clinically relevant symptoms of anxiety.³²

Atopic dermatitis is associated with high levels of social withdrawal, stigmatization, anxiety, and depression among patients and their caregivers. Stress caused by atopic dermatitis can make the symptoms of the disease worse.³³ Individuals with chronic urticaria may develop PTSD symptoms which influence their psychological well-being through using different levels of emotional suppression, especially suppressing depression. The levels depend on the severity of PTSD symptoms and whether they experienced interpersonal traumas.³⁴

During pandemics such as the one being experienced all over the world, a worry for health, changes in everyday life, job loss, economic ordeal and family conflicts may occur and lead to depression disorders. Previous studies measured the impact of COVID-19 early on. Zhang et al used the Chinese version 9-item General Health Questionnaire (GHQ-9) and 7-item Generalized Anxiety Disorder (GAD-7) scale to evaluate the prevalence and severity of psychological distress in patients recovered from COVID-19 infection, individuals under guarantine, and the public in general. They found severe depression symptoms in the general population compared to our study in which individuals with allergic diseases showed mild symptoms.³⁵ Cultural differences and state of the pandemic, as well as public perception of the virus, may be some of the causes for the differences. Based on their results, they recommended prompt intervention measures that should be taken to alleviate the psychological issues faced.³⁵ Vanaken et al published, after the execution of this study, the use of IES-COVID19 which proved to be a reliable and valid measure for investigating stress symptoms related to trauma regarding intrusion and avoidance due to short- and long-term impact of the COVID-19 pandemic. The IES-COVID19 may be a resourceful instrument in assessing individual changes in traumatic stress symptoms over time.³⁶

To the best of our knowledge this is one of the first studies that evaluates the psychologic effect of COVID-19 in allergic patients. However, a limitation to this study is that there are no premeasurements: therefore, it may not be well defined if the reactivity to the environmental stressor is causal. As specialists in the allergy field, it is imperative that we recognize the psychological burden that the pandemic has on our patients which may be a limiting factor in overcoming the crisis. We conclude that psychological consequences such as depression, anxiety, and PTSD are present during the COVID-19 pandemic and cause an impact in individuals with allergic diseases that may persist even after the pandemic has ended. If we acknowledge this impact and how it affects people during the pandemic, we are better able to implement interventions, follow up, and contribute to the entire well-being of our patients. Due to a worldwide increase in allergic diseases, the mechanisms involved in stress experiences as well as best practice management strategies should be studied in-depth.

SUPPORTING INFORMATION LEGENDS

Survey: Psychological Impact of COVID-19 in Patients With Allergic Diseases.

Abbreviations

COVID 19: coronavirus disease 2019; CoV-2: coronavirus 2; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, fourth edition; IFN-g: interferon gamma; IL-1: interleukin 1; IL-4: interleukin 4; IL-6: interleukin 6; NK cells: natural killer cells; OR: odds ratio; SARS: severe acute respiratory syndrome; TNF- α : tumoral necrosis factor alfa

Funding

The authors declare that no funding was received for the present study.

This study was approved by the clinical research ethics committee of the University Hospital and Faculty of Medicine of the Autonomous University of Nuevo Leon in Mexico before the initiation of this study. Participants have signed written informed consent.

AUTHOR CONTRIBUTIONS

Sandra Nora Gonzalez-Diaz and Bryan Martin: Design of the study, manuscript elaboration, and revision. Rosalaura Villarreal Gonzalez and Cindy de Lira-Quezada contributed to design of the study, data collection, interpretation of the results, and manuscript writing. Alejandra Macias-Weinmann and Rosa Ivett Guzman-Avilan contributed to data collection and Carlos Macouzet-Sánchez manuscript writing and data collection as well. Mariano Garcia-Campa, Andres Noyola-Perez and David Garcia-Gonzalez performed statistical analysis and interpretation of results. All authors read and approved the final manuscript.

Additional data is available upon request.

Declaration of competing interest

The authors declare they have no conflicts of interest to disclose.

Appendix A Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.waojou.2021.100510.

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