Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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.
[a]Adjusted 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 H_1 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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References

1. Kawohl W, Nordt C. COVID-19, unemployment, and suicide. *Lancet Psychiatry*. 2020;7(5):389–390.
2. Dooley D, Fielding J, Levi L. Health and unemployment. *Annu Rev Public Health*. 1996;17:449–465.
3. Silverberg JI, Hanifin JM. Adult eczema prevalence and associations with asthma and other health and demographic factors: a US population-based study. *J Allergy Clin Immunol*. 2013;132(5):1132–1138.
4. Konstantinou GN, Konstantinou GN. Psychological stress and chronic urticaria: a neuro-immuno-cutaneous crosstalk. A systematic review of the existing evidence. *Clin Ther*. 2020;42(5):771–782.
5. Lesage FX, Berjot S. Validity of occupational stress assessment using a visual analogue scale. *Occup Med (Lond)*. 2011;61(6):434–436.
6. Plummer F, Manea L, Trepel D, McMillan D. Screening for anxiety disorders with the GAD-7 and GAD-2: a systematic review and diagnostic metaanalysis. *Gen Hosp Psychiatry*. 2016;39:24–31.
7. Maurer M, Weller K, Bindslev-Jensen C, et al. Unmet clinical needs in chronic spontaneous urticaria. A GA^2LEN task force report. *Allergy*. 2011;66(3):317–330.
8. Jiang Y, Zilioli S, Rodriguez-Stanley J, Peek KM, Cutchin MP. Socioeconomic status and differential psychological and immune responses to a human-caused disaster. *Brain Behav Immun*. 2020;88:935–939.

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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The patient was a 42-year-old man with a longstanding history of asthma, morbid obesity, and CVID characterized by recurrent sinopulmonary infections. He was previously on regular monthly IVIG and was reportedly stable. However, he had not received any IVIG within the previous 6 months because of insurance issues. He experienced COVID-19 symptoms in May 2020 with a positive result of the nasopharyngeal polymerase chain reaction (PCR) swab for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). He was initially quarantined at home for 4 days. However, he developed fevers with worsening dyspnea and was, thus, admitted to a community hospital. Chest computed tomography revealed multifocal pneumonia. On hospital day 4, he was intubated because of worsening hypoxemia. On hospital day 5, he received convalescent plasma and started remdesivir. On hospital day 6, vancomycin was started for methicillin-resistant *Staphylococcus aureus* cultured from his sputum. He was subsequently transferred to our facility for a higher level of care.

On transfer, his presentation was consistent with acute respiratory distress syndrome. Notable laboratory results included IgG of 117 mg/dL, IgA of 10 mg/dL, undetectable IgM, erythrocyte sedimentation rate greater than 130 mm/h, and C-reactive protein greater than 300.0 mg/L. He had a white blood cell count of $8.27 \times 10^3/\mu L$ (76% neutrophils, 8% lymphocytes, 5% monocytes, 1% eosinophils, 2% atypical lymphocytes, and 8% bands). Ceftazidime was started for bacterial pneumonia. Furthermore, meropenem was started for sinusitis after the culture of purulent nasal secretions grew extended-spectrum beta-lactamase–producing *Escherichia coli* and sinus computed tomography revealed sinus mucosal thickening. He completed 10 days of remdesivir.

He received a 40 g (400 mg/kg) dose of IVIG on hospital day 9 with an increase in serum IgG to 442 mg/mL on hospital day 12 but with no considerable changes in his clinical status. On hospital days 14 and 15, he received high-dose IVIG of 1 g/kg divided into 2 equal doses. His serum IgG elevated to 1396 mg/dL on hospital day 17. He had modest clinical improvement in the subsequent days, including a reduction in fevers and slightly decreased oxygen requirement. Repeat IgG serum concentrations were 615 mg/dL on hospital day 22 and 472 mg/dL on hospital day 26.

The results of multiple nasopharyngeal PCR swab tests for SARS-CoV-2 remained positive during the hospitalization. The results of IgM and IgG serologies for SARS-CoV-2 obtained on hospital days 12 and 16 were both negative.

After hospital day 20, he again had fevers, required increased ventilatory support, and developed methicillin-resistant *S aureus* bacteremia. On hospital day 30, he had a cardiac arrest in the setting of hypoxemia and hypotension and, unfortunately, expired. The autopsy established the final pathologic diagnosis of COVID-19 pneumonia and bacteremia in the setting of CVID.

This case presents several considerations in the care of patients with CVID with COVID-19. The patient's body mass index was 39 kg/m^2, and obesity is a known risk factor for severe disease.[4] Furthermore, the patient was not receiving regular immunoglobulin replacement therapy in the months leading up to his COVID-19 diagnosis. Although it is unlikely that IVIG products available during that time would have contained specific antibodies against SARS-CoV-2, they may have contained cross-reactive antibodies for SARS-CoV, Middle East respiratory syndrome coronavirus, or other human coronaviruses that could potentially provide some protection.[5,6] In addition, regular IVIG therapy may have provided additional protection against the sinopulmonary and other bacterial superinfections that complicated the patient's illness.

The IVIG can have immunomodulatory effects that have been postulated to be helpful in the inflammatory milieu of COVID-19.[7] The initial increase in the patient's IgG levels after high-dose IVIG waned rapidly, likely because of brisk consumption in the setting of infection. Any transient immunomodulatory effect was insufficient to significantly alter his clinical trajectory.

Notably, in the other reports of patients with CVID recovering from COVID-19, all of them had been receiving regular immunoglobulin replacement therapy preceding the COVID-19 diagnosis. The 2 patients who received IVIG did so early in their COVID-19 course,[1,2] suggesting that IVIG is more efficacious if administered early and in the setting of replete IgG levels. The single reported case of fatality was not noted to have received any antibody-containing products.[3]

This patient had minimal antibody response to SARS-CoV-2, as would be expected given his history of CVID. In contrast, most patients with COVID-19 develop detectable IgG antibody levels for SARS-CoV-2 within 2 weeks of symptom onset.[8] In addition, critically ill patients have been found to develop high levels of antibodies for SARS-CoV-2.[8] We hypothesize that a limited antibody response contributed to impaired nasopharyngeal viral clearance, given the multiple positive results of the PCR tests for SARS-CoV-2 during the patient's hospitalization. However, defects in antibody production are unlikely to be the sole or primary reason for this finding, because persistently positive PCR results for SARS-CoV-2 can be found even in mild cases and among immunocompetent hosts.[9] It is unclear whether additional convalescent plasma would have been helpful once his condition had become critical or whether it is primarily efficacious early in the illness. One study suggests that convalescent plasma did not reduce mortality among critically ill patients with COVID-19.[10] However, patients with a limited antibody response were not specifically examined.

To the best of our knowledge, this is the first report of a fatality from COVID-19 in a patient with CVID who had not been receiving regular infusions of immunoglobulin at the time of his infection. Patients with CVID may be at a unique risk for COVID-19–related morbidity and mortality, particularly those with comorbidities or inadequate immunoglobulin levels. It is important that patients with CVID have close follow-up and continuity of care during this pandemic. Convalescent plasma and IVIG can be considered, although their efficacy has not been defined. Further studies are needed to elucidate the immunologic mechanisms of COVID-19 in CVID and determine the optimal approach to care.

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References

1. Aljaberi R, Wishah K. Positive outcome in a COVID-19 patient with common variable immunodeficiency after IVIG. *Ann Allergy Asthma Immunol*. 2020;125:349–350.
2. Fill L, Hadney L, Graven K, Persaud R, Hostoffer R. The clinical observation of a patient with common variable immunodeficiency diagnosed as having coronavirus disease 2019. *Ann Allergy Asthma Immunol*. 2020;125(1):112–114.
3. Quinti I, Lougaris V, Milito C, et al. A possible role for B cells in COVID-19? Lesson from patients with agammaglobulinemia. *J Allergy Clin Immunol*. 2020;146(1):211–213.e4.
4. Docherty AB, Harrison EM, Green CA, et al. Features of 20133 UK patients in hospital with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ*. 2020;369:m1985.
5. Díez JM, Romero C, Gajardo R. Currently available intravenous immunoglobulin contains antibodies reacting against severe acute respiratory syndrome coronavirus 2 antigens. *Immunotherapy*. 2020;12(8):571–576.
6. Gao X, Zhou H, Wu C, et al. Antibody against nucleocapsid protein predicts susceptibility to human coronavirus infection. *J Infectol*. 2015;71(5):599–602.

7. Cao W, Liu X, Bai T, et al. High-dose intravenous immunoglobulin as a therapeutic option for deteriorating patients with coronavirus disease 2019. *Open Forum Infect Dis*. 2020;7(3):ofaa102.
8. Qu J, Wu C, Li X, et al. Profile of immunoglobulin G and IgM antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [e-pub ahead of print]. *Clin Infect Dis*. https://doi.org/10.1093/cid/ciaa489. Accessed June 24, 2020.
9. Gombar S, Chang M, Hogan CA, et al. Persistent detection of SARS-CoV-2 RNA in patients and healthcare workers with COVID-19. *J Clin Virol*. 2020;129:104477.
10. Zeng QL, Yu ZJ, Gou JJ, et al. Effect of convalescent plasma therapy on viral shedding and survival in patients with coronavirus disease 2019. *J Infect Dis*. 2020;222(1):38–43.

Differentiating characteristics of patients with asthma in the severe acute respiratory syndrome coronavirus 2 infection

The pandemic due to the infection by the betacoronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which began in Wuhan, People's Republic of China, in December 2019, causing the infectious coronavirus disease 2019 (COVID-19),[1] surpassed 21 million infections and more than 700,000 deaths globally,[2] with numbers that continue to rise. The prognosis of SARS-CoV-2 infection worsens when comorbidities such as high blood pressure (HBP), chronic obstructive pulmonary disease, diabetes mellitus (DM), cardiovascular disease, and obesity are associated.[3,4] There are communications that suggest that asthma may be a factor that determines the severity of COVID-19, compared with others, indicating it does not imply an increased risk.[5] The prevalence of asthma in Spain is estimated at 6.3% of the population[6] and in a cohort of hospitalized patients in Spain with SARS-CoV-2 infection was 8.4%.[7] The main objective of our study was to analyze how the SARS-CoV-2 infection has affected patients with asthma in terms of prevalence, morbidity, hospitalization, and mortality.

For the analysis of information contained in electronic health records, we used Savana, an artificial intelligence–enabled system based on natural language processing and neural networks, which combines computational skills with natural language processing by joining Big Data and artificial intelligence approaches, capable of reusing information expressed in natural language in clinical reports. It performs an immediate statistical analysis of patients found on the platform and provides relevant results for the input variables provided by the user.[8] To ensure the privacy of all patients, Savana anonymized the data. Savana carried out the search in the entire population of Castilla la Mancha community, extracting data from primary care, specialized care, hospitals, and emergency departments until July 2020, detecting COVID-19 diagnoses, and in this group, patients diagnosed as having asthma either by a pneumologist or an allergist with functional respiratory tests (spirometry with bronchodilation, methacholine test) or by a compatible clinic by the primary care physician. For this study, we included only patients who tested positive for SARS-CoV-2 with reverse transcriptase polymerase chain reaction and analyzed demographic characteristics, hospitalization data, comorbidities (HBP, dyslipidemia, DM, smoking), and mortality. For statistical analysis, Student t test was used for mean differences of independent variables and χ^2 for dichotomous variables with a 95% confidence interval.

A total of 6310 patients were diagnosed as having SARS-CoV-2 infection, confirming their positivity by reverse transcriptase polymerase chain reaction. From these, a total of 577 were diagnosed as having asthma, resulting in a prevalence of 9.14%. The mean age of the patients with SARS-CoV-2 (SC2) was 59 $\pm$ 19 years, and that of the patients with asthma with SARS-CoV-2 (SC2-A) was 55 $\pm$ 20 years. Among SC2, 2983 (41%) were men, whereas 3327 (59%) were women. Among SC2-A, 198 (31%) were men, whereas 379 (69%) were women. In the analysis of comorbidities, we found the following data when analyzing SC2 and SC2-A: HBP 3239 (51%) and 296 (51%), dyslipidemia 2283 (36%) and 216 (37%), DM 1641 (26%) and 142 (25%), smoking 873(14%) and 103(18%). Hospitalization was required for 2164 (34.2%) SC2 and 131 (22.7%) SC2-A, with a prevalence of 6.05% for the hospitalized patients with asthma. Deaths in the SC2 population were 250 (3.96%), and in the SC2-A population, there were 21 (3.64%) deaths (Table 1).

To our knowledge, this cohort is one of the first studies in Spain to describe the prevalence of infection, hospitalization, and morbidity/mortality of patients with asthma with SARS-CoV-2 infection.

The prevalence of infections in our population with asthma was 9.14%, similar to that obtained in a review of patients hospitalized with COVID-19 in Spain.[7] In the study by Chhiba et al,[3] the prevalence of SARS-CoV-2 infection in patients with asthma in the Chicago Illinois area, requiring hospitalization or not was 14.4%. These data suggest that the prevalence may vary by geographic area. In both groups (SC2/SC2-A), the average age was in the range of 50 to 60 years. In addition, there was a higher percentage of women among the infected patients with asthma, in those requiring hospitalization, and in deaths. In SC2, hospitalization and death occurred more frequently in men. Of the analyzed comorbidities, HBP was the most common in both groups, dyslipidemia and DM were similar in proportion, and smoking was more common in patients with asthma.

There is no consensus in the literature as to whether asthma is a comorbidity that increases the risk of a more severe form of SARS-CoV-2 infection.[5] The data from our study reveal that there is lower mortality in the population with asthma. A possible explanation is based on the fact that one of the targeted mechanisms of the entry of the virus into the host cell is through the angiotensin-converting enzyme 2 receptor, a process dependent on the TMPRSS2 protease, allowing the adhesion of the spike protein and performing fusion between the virus and the membrane cells.[9] The use of inhaled corticotherapy in asthma, which is very widespread in our environment, could have a protective effect by decreasing the expression of the angiotensin-converting enzyme 2 receptor and the TMPRSS2 protein, although more studies are needed to prove this.[10] To date, the recommendations for patients with asthma are to maintain their treatment, trying to achieve the best therapeutic adherence.

We consider the following limitations of our study: its retrospective nature and no consideration given to other variables that could influence the results. In addition, the basic treatment of each patient with asthma had not been assessed. The laboratory data that determine, to some extent, the evolution and severity of the SARS-CoV-2 infection had not been measured either. It is possible that there is a selection bias, as there is more surveillance of patients with asthma compared with the general population.

Our study reveals that the prevalence of asthma was 9.14% and the hospitalization rate was 6.05% in the total number of SARS-CoV-2 infections in the community of Castilla la Mancha. In addition, HBP was the most associated comorbidity analyzed in both groups (SC2 and SC2-A). We also found a difference in mortality, being lower in patients with asthma, although owing to the small number of patients in this group, it did not reach statistical significance.

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