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# Eosinophilic Esophagitis Patients Are Not at Increased Risk of Severe COVID-19: A Report From a Global Registry



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**What is already known about this topic?** No data has been published on the outcome of coronavirus disease 2019 (COVID-19) in eosinophilic esophagitis (EoE)/eosinophilic gastrointestinal disease (EGID) patients.

**What does this article add to our knowledge?** COVID-19 severity in EoE patients appears to be comparable to that of the general population.

**How does this study impact current management guidelines?** EoE/EGID patients with COVID-19 may be managed following guidelines for the general population.

**BACKGROUND:** The impact of coronavirus disease 2019 (COVID-19) on eosinophilic esophagitis (EoE) and eosinophilic gastrointestinal diseases (EGIDs) is unknown.

**OBJECTIVE:** We aimed to characterize patients with EoE and EGIDs who had COVID-19, assess severity of COVID-19 in the EoE/EGID population, and evaluate for COVID-19-induced EoE/EGID flares.

**METHODS:** We established an online global registry collecting physician entered, deidentified data related to patient demographics, EoE/EGID disease features, comorbidities, and treatments, COVID-19 source of exposure, symptoms, illness severity, hospitalizations, and deaths.

**RESULTS:** Ninety-four cases were reported between March 2020 and April 2021 (median age, 21 years; range, 1.5-53 years; 73% male). Most had atopy (73%), and 80% had isolated EoE. Before COVID-19, the EoE/EGID activity was reported as clinical remission in 51 (54%) and moderate in 20 (21%). EoE/EGID treatments at the time of COVID-19 included proton pump inhibitors 49 (52%), swallowed/topical steroids 48 (51%), and

dietary elimination 34 (36%). COVID-19 symptoms included cough (56%), fever (49%), anosmia (21%), and ageusia (22%). Most patients with COVID-19 had a mild course (70%), with 15% asymptomatic, 12% moderate, and 2% severe. Three patients were hospitalized, and no intensive care unit admissions or deaths were reported. Mean time from first symptoms to resolution in symptomatic patients was 10 days (range, 1-90 days). A single EGID flare was reported during COVID-19.

**CONCLUSIONS:** In a global EoE/EGID registry, relatively few COVID-19 cases have been reported. COVID-19 severity was comparable to the general population. Based on this registry, it does not appear that patients with EoE are at increased risk for severe COVID-19 infection or that COVID-19 leads to EGID flares. © 2021 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2022;10:143-9)

**Key words:** Corona virus; COVID-19; Eosinophilic oesophagitis; EGID; Eosinophilic GI disease; Epidemiology; Outcome; Risk factor

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*Abbreviations used**ACE2- Angiotensin converting enzyme-2**BMI- Body mass index**COPD- Chronic obstructive pulmonary disease**COVID-19- Coronavirus disease 2019**EGID- Eosinophilic gastrointestinal disease**EoE- Eosinophilic esophagitis**GI- Gastrointestinal**IQR- Interquartile range**PPI- Proton pump inhibitor**SARS-CoV-2- Severe acute respiratory syndrome coronavirus 2**SECURE EoE/EGID- Surveillance Epidemiology of Coronavirus Under Research Exclusion for EoE/EGID**TH2- T helper 2*

Since December 2019, more than 231 million people have been infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and over 4.7 million have died of the resultant coronavirus disease 2019 (COVID-19).<sup>1</sup> Throughout the first year and a half of the pandemic, much has been learned about the virus pathogenicity and risk factors for severe disease. The human receptor for SARS-CoV-2, angiotensin converting enzyme-2 (ACE2), is expressed in multiple human tissues, including the esophagus<sup>2</sup> and intestines.<sup>3</sup> Binding of the SARS-CoV-2 spike protein to ACE2 and proteolytic cleavage by TMPRSS2, a cellular serine protease, facilitate viral entry into cells.<sup>4</sup> Although the infection remains asymptomatic or mild in most patients, a minority may progress to moderate and/or severe disease or death. Risk factors for severe outcomes in COVID-19 include older age, obesity, chronic lung and cardiovascular disease, diabetes, immune suppression, and others.<sup>5,6</sup>

Early attempts to assess the COVID-19 burden in patients with eosinophilic esophagitis (EoE) and eosinophilic gastrointestinal diseases (EGIDs), whose main disease pathology is concentrated in tissues expressing the proteins necessary for viral invasion, failed to identify SARS-CoV-2 infected EoE/EGID patients.<sup>7-9</sup> Not only do EoE/EGIDs involve organs involved in SARS-CoV-2 infection, but they are also a form of immune dysregulation, and their mainstay treatments involve medications (proton pump inhibitors [PPIs] and steroids) that have been implicated in the risk for more severe COVID-19.<sup>10-13</sup> Furthermore, although normal and elevated peripheral eosinophil counts have been found to be associated with better outcomes in COVID-19,<sup>14,15</sup> it is theoretically possible that eosinophil depleting drugs, which are sometimes used for treatment of EoE/EGIDs, may induce more severe disease.<sup>16</sup>

To date, there have been no published series of COVID-19 or SARS-COV-2 infection in patients with either EoE or EGIDs distal to the esophagus, and only a single case report has been published.<sup>17</sup> A clear understanding of the impact that pre-existing EoE/EGIDs may have on COVID-19 severity, and conversely, how COVID-19 may impact EoE/EGID disease activity, is essential for guidance to both patients and practitioners. Using an international registry of EoE and EGID patients with COVID-19, we aimed to determine the characteristics of patients with EoE/EGIDs who were diagnosed with COVID-19, assess the severity of disease in this cohort, and evaluate for COVID-19-induced EoE/EGID flares.

**METHODS**

We created the Surveillance Epidemiology of Coronavirus Under Research Exclusion for EoE/EGID (SECURE EoE/EGID) database to monitor SARS-CoV-2 infection outcomes in pediatric and adult patients with a diagnosis of EoE or EGID. SECURE EoE/EGID was established as a broad collaborative international effort due to the rarity of EGIDs and was based on similar work in inflammatory bowel disease.<sup>13</sup> The project was endorsed and promoted by Gastroenterology Societies in Europe, North America, and Latin America, Allergy and Immunology societies, and patient advocacy groups (Table E1, available in this article's Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org)). After the initial announcement of the database, several reminders were sent throughout 2020 and early 2021 and the link to the website was added to other disease-specific COVID-19 websites.

Medical providers were encouraged to report all EoE/EGID patients diagnosed with COVID-19 by a laboratory test (or when testing was unavailable, suspected based on a close contact with a test-confirmed patient and typical symptoms) regardless of the disease severity. To enable practitioners to easily access data entry, a dedicated website was established ([covidoeegid.org](http://covidoeegid.org)). Practitioners were instructed to enter data after the patient had COVID-19 for a long enough duration to experience complete or partial recovery, hospitalization, or death. For cases reported while patient was still symptomatic, the physician was contacted to assess for the final outcome before data analysis. We used REDCap (Research Electronic Data Capture), a secure, Web-based electronic data capture tool hosted at the Rabin Medical Center—Clalit Health Services to collect and manage study data.

Deidentified data were collected pertaining to patient demographics (age, gender, ethnicity, smoking status, concomitant atopic, and comorbid conditions), EoE/EGID disease features (type of EGID or EoE, year of diagnosis, disease activity [on both a 5-point scale and a continuous physician global assessment slide at the time of the last physician encounter before COVID-19], laboratory test values before COVID-19, current and past treatments), and COVID-19 disease features (method of diagnosis, year of infection, symptoms, illness severity [as determined by the reporting physician], length, need for hospitalization, COVID-19-related treatment, and deaths) (Figure E1, available in this article's Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org)).

We removed erroneous or duplicate reports by manually reviewing country and state (for US patients), year of birth, gender, and EGID type. A Google search of reporting physician and medical centers was performed to ascertain legitimacy of reports.

Statistical analysis was performed using IBM SPSS statistics 27 (IBM Corp, Armonk NY). We used descriptive statistics to summarize the basic demographic and clinical characteristics of the study population. We expressed categorical variables as proportions. Variables without normal distributions were expressed as median (interquartile range [IQR]; range). Associations of nonparametric variables with 2 independent samples were calculated with the Mann-Whitney test. Binary variables were analyzed by the Pearson  $\chi^2$  test. A *P* value of <.05 was considered significant.

The study was approved by the ethics committee of Rabin Medical Center.

**RESULTS**

During the 12-month period from April 2020 to March 2021, 94 patients were entered into the database from 8 countries.

**TABLE I.** Patient characteristics

Patient characteristics (n = 94)	n (%) or median (IQR)
<b>Age</b>	
At EoE/EGID diagnosis	17 (10-31)
At the time of COVID-19	21 (16-35)
<b>Male</b>	
	69 (73%)
<b>Race</b>	
	82% White
<b>GI region involved in EoE/EGID</b>	
Esophagus	90 (96%)
Stomach	11 (12%)
Small bowel	11 (12%)
Colon	5 (5%)
<b>EoE/EGID activity at the time of COVID-19</b>	
Complete remission	32 (34%)
Clinical remission but histologic activity	19 (20%)
Mild activity	17 (18%)
Moderate activity	20 (21%)
Severe activity	6 (6%)
<b>Treatment at the time of COVID-19</b>	
Proton pump inhibitors	49 (52%)
Topical steroids	48 (51%)
Dietary elimination	34 (36%)
Systemic steroids	2 (2%)
Enteric budesonide	2 (2%)
Biologics*	4(4%)
Azathioprine/6-mercaptopurine	1 (1%)

COVID-19, Coronavirus disease 2019; EoE/EGID, eosinophilic esophagitis/eosinophilic gastrointestinal diseases; GI, gastrointestinal; IQR, interquartile range.

\*Anti-IL5, anti-IL5r, dupilumab, vedolizumab.

Most patients were from the United States (70) and Spain (9) (Figure E2, available in this article's Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org)). Within the United States, patients resided in 17 different states (Figure E2, available in this article's Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org)), the majority from the Northeastern and Southwestern United States. The median age was 21 years (IQR: 16-31; range: 1.5-53), 73% were male, and 82% reported as White. Atopy was present in 71% of patients; 39% had asthma, of whom 43% had active disease based on either the use of  $\beta$ -agonists twice weekly, prophylactic inhaler use, or an asthma-related hospitalization in the previous year. The vast majority (98%) were nonsmokers (Table I). The median (IQR) body mass index (BMI) of patients over 16 years of age was 23.5 (21.8-26.9).

Insofar as the segment of the gastrointestinal (GI) tract involved in the eosinophilic disease, whereas the majority 90 (96%) had esophageal involvement, only 75 (79.8%) had isolated EoE, 2 (2.1%) had isolated eosinophilic colitis, and 1 had combined eosinophilic enteritis and colitis (1.0%). The remainder had eosinophilic esophageal involvement (EoE) of their EGID combined with other segments of the GI tract, including eosinophilic gastritis in 6 (6.4%), eosinophilic enteritis in 5 (5.3%), eosinophilic gastroenteritis in 3 (3.2%), and pan-GI involvement in 2 (2.1%) (Table I). The majority were in clinical remission (54%) at the time of the last assessment before COVID-19, though only 34% reported combined clinical and histological remission at the time of the last gastroenterologist follow-up before COVID-19. Seventeen patients (18%) had mild and 20 (21%) had moderate disease activity, whereas only 6

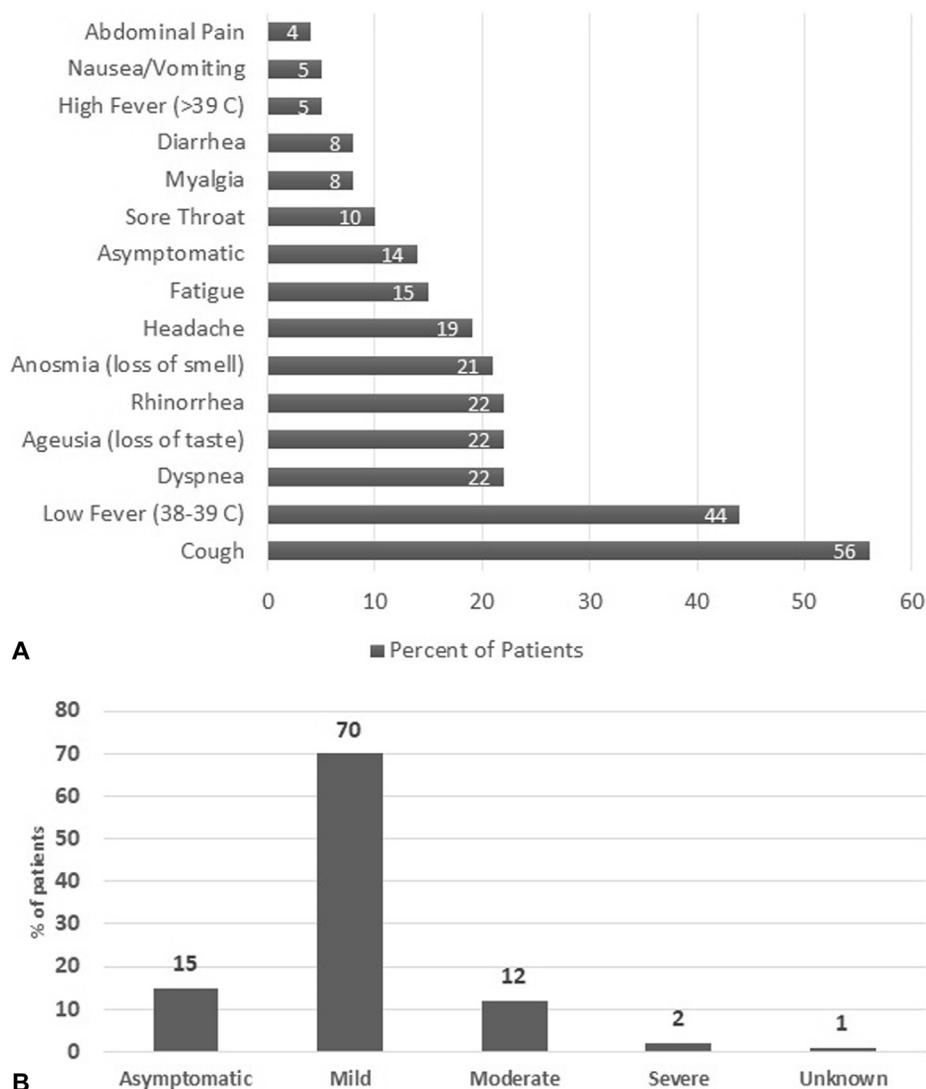
(6%) were assessed to have severe EoE/EGID activity. Other than atopic conditions, there were 22 comorbidities reported in 24 patients including anxiety disorder (4), attention deficit and hyperactivity disorder (3), celiac disease (2), inflammatory bowel disease (2), mast cell activation syndrome (2), and others (Table E2, available in this article's Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org)). Treatment for EoE/EGID at the time of SARS-COV-2 infection included PPIs 49 (52%), topical steroids (budesonide or fluticasone) 48 (51%), and elimination diet 34 (36%). Twenty patients (21%) were treated concomitantly with topical steroids and PPIs. Of patients receiving topical steroids, 48% received budesonide and 52% fluticasone. The topical steroid doses were  $1 \pm 1$  mg. Two patients each were receiving systemic steroids or enteric budesonide, 1 received azathioprine/6-mercaptopurine, and 4 patients were receiving a biologic treatment (Table I). Feeding tubes were reported by 3 patients; 5 patients had undergone esophageal dilation in the 3 months before COVID-19.

The diagnosis of COVID-19 was made by nasopharyngeal swab polymerase chain reaction in 79%, an antigen-based test in 7%, and serology in 3%. There were 9% of patients who were diagnosed as "suspected" cases on the basis of a close contact with a confirmed case and typical symptoms. These were all from the first months of the pandemic when diagnostic testing was very limited in many countries. The most common sources of exposure were a household contact in 28%, a work contact in 10%, travel in 3%, and unknown in 30%. The mean time from the diagnosis of EoE/EGID to COVID-19 was  $5.0 \pm 4.2$  years.

Symptomatic patients (n = 80) most often presented with cough, low-grade fever, dyspnea, ageusia, rhinorrhea, and anosmia (Figure 1). Only a minority of patients reported GI complaints during the duration of their COVID-19. These included diarrhea (8%), nausea/vomiting (5%), and abdominal pain (4%), with only 3 patients having an overlap between different GI complaints. COVID-19 severity (Figure 1) was reported as mild (70%) or asymptomatic (15%) in most. Only 12% reported moderate and 2% severe disease.

There was no significant association between COVID-19 severity (asymptomatic/mild vs moderate/severe) and any of the standard EoE/EGID medications used by the patient (Table II). Similarly, for other treatments (systemic steroids, immunomodulators, anti-IL5, anti-IL5r, dupilumab, enteric budesonide, vedolizumab, cromolyn, systemic steroids), no statistically significant differences were found; however, there were too few cases to make clinically meaningful comparisons. No significant association was found between EoE/EGID disease activity (clinical remission vs any clinical activity) and COVID-19 severity, although a trend was present to associate any EoE activity and mild COVID-19 ( $P = .07$ ). There was a single, mild flare of EoE during mildly symptomatic COVID-19 reported in a 34-year-old, nonatopic, man with EoE. He had previously undergone esophageal dilation and was treated with a combination of dietary elimination, topical steroids, and PPIs, under which he had been in full endoscopic and histological remission before COVID-19. There were 2 patients reported withholding their EoE meds of their own accord during COVID-19. The median time from first symptoms to resolution (excluding asymptomatic patients) was 10 days (IQR: 5-18.5; range: 1-90).

Three patients had been hospitalized for COVID-19. All 3 were over 40 years old, and none needed mechanical ventilation or extracorporeal membrane oxygenation. The first was a



**FIGURE 1. (A)** Symptoms (n = 80) and **(B)** severity (n = 94) of eosinophilic esophagitis/eosinophilic gastrointestinal disease patients with coronavirus disease 2019.

40-year-old nonatopic, nonobese female eosinophilic colitis patient who was hospitalized with fever, cough, dyspnea, headaches, and myalgia. She received lopinavir and hydroxychloroquine, and was discharged after 7 days. Symptoms resolved after a total of 17 days. The second patient was a 41-year-old, nonasthmatic, overweight (BMI: 26) man with EoE treated with topical fluticasone (0.8 mg/day). He was hospitalized with a low fever, cough, dyspnea, and diarrhea, and then developed a pulmonary thromboembolism. The patient received lopinavir and ritonavir. His symptoms resolved after 28 days. The final hospitalization was of an obese (BMI: 32) 43-year-old man with mild intermittent asthma, food allergy, and EoE. He was treated with an elimination diet and PPIs, and had prior esophageal dilation. He was hospitalized for 3 days with high fever, cough, dyspnea, rhinorrhea, and diarrhea. It is unknown if he received antiviral treatment. His symptoms fully resolved after 60 days.

To make an estimate of the minimal value for the year-long incidence of COVID-19 in EoE/EGID, centers including patients were asked the number of EoE/EGID patients they follow. Of 7 US centers that responded, there were 39 COVID-19 cases out of 4391 patients giving an incidence of 1:113 (8850/1 million). On a worldwide basis, there were 57 COVID-19 cases out of 5549 patients, giving an incidence of 1:97 (10,309/1 million). This is compared with the total US incidence since the beginning of the pandemic of 104,050 cases/1 million population, or a worldwide incidence of 23,848 cases/1 million population.<sup>18</sup>

**DISCUSSION**

We investigated the natural history of COVID-19 in pediatric and adult EoE/EGID patients using a web-based, international, collaborative, physician-driven reporting system. Such



**TABLE II.** COVID-19 severity stratified by eosinophilic esophagitis/eosinophilic gastrointestinal disease treatment at the time of infection

Treatment	Moderate/severe COVID-19 (n = 13)	Asymptomatic COVID-19 (n = 80)	P value
Diet	4	30	.45
Oral topical steroids	6	41	.77
Systemic steroids	0	2	>.99
PPI	8	40	.44
AZA-6MP	0	1	>.99
Enteric budesonide	0	2	>.99
Anti-IL5	0	1	>.99
Benralizumab	1	0	.14
Dupilumab	1	0	.14
Vedolizumab	0	1	>.99
Cromolyn sodium	1	1	.26

AZA-6MP, Azathioprine 6-mercaptopurine; COVID-19, coronavirus disease 2019; PPI, proton pump inhibitor.

collaborative efforts are necessary to assess outcomes of rare diseases such as EoE/EGIDs. Although non-EoE/EGID cases were only rarely reported, we demonstrated that COVID-19 in EoE patients generally follows a mild course with full recuperation, regardless of EoE/EGID severity or treatment at the time of the viral infection, and that there may be fewer COVID-19 cases in the overall EoE/EGID population than in the overall US and worldwide populations. In our cohort, no cases of long COVID-19 were reported because patients may have been entered into the database soon after primary recuperation. To date there have been no patient series (and only a single case report)<sup>7</sup> reporting COVID-19 outcomes in EoE/EGID patients. Both Savarino et al<sup>8</sup> and Franceschini et al<sup>9</sup> did not find any cases of COVID-19 in their Italian cohorts of EoE/EGID patients (n = 135 and n = 36, respectively) at a time when Italy was a hotspot for COVID-19, highlighting the advantages of broad collaborative research.

In lieu of a control group, disease severity of our EoE/EGID cohort may be compared with large population-based cohorts. In our cohort, 85% of patients had an asymptomatic or mild course, with only 2% severe disease regardless of EoE directed treatment type or EoE/EGID disease activity at the time of COVID-19. These values are comparable to the natural history of COVID-19 in the general population. In a review of over 72,000 COVID-19 cases in China, Wu and McGoogan<sup>19</sup> reported 81% mild disease and 19% severe/critical. In contrast to their cohort in which only 2% of patients were under the age of 18 years, in our EoE/EGID cohort, 29 of 94 (31%) patients were in this age group who generally had mild COVID-19. A recent review of systematic reviews stated that the mean age of reported COVID-19 cases in the published literature was 58 years,<sup>6</sup> whereas in our cohort, the oldest patient was 53 years old. Furthermore, our patients had relatively few significant comorbidities that are known risk factors for severe COVID-19 disease. It is unclear if the low frequency of COVID-associated comorbidities is representative of the broader EoE/EGID patient population. In addition, a recent systematic review and meta-analysis<sup>20</sup> found that the rates of true asymptomatic COVID-19 cases were approximately 35% of tested populations (screening of contacts of index cases or population-based screening). Our cohort reported 15% asymptomatic cases that may be

comparable in light of the fact that most EoE/EGID patients were not tested for the presence of infection over time; thus many such cases were likely not identified. Identification of additional asymptomatic cases would likely lead to a higher frequency of asymptomatic/mild spectrum of disease.

Recently, Chiang et al<sup>21</sup> demonstrated that adult patients with EoE as well as children with or without EoE have lower levels of the ACE2 gene expression in the esophagus than non-EoE adult controls. Furthermore, atopic EoE patients trended toward lower TMPRSS2 expression than nonatopic EoE patients, suggesting that younger age and an EoE-associated T helper 2 (TH2) profile may be protective of GI infection rates of SARS-CoV-2. Lower expression of ACE2 and/or TMPRSS2 in the esophagus in EoE patients may explain the curious finding of low rates of GI symptoms reported by our patients. Furthermore, several studies have reported that normal or elevated eosinophil counts are associated with better outcomes in COVID-19 patients.<sup>14,15,22</sup> These studies further support the notion that individuals who harbor a TH2 predominant milieu have better outcomes, possibly because this profile protects from the damaging effects of a TH1-associated cytokine storm.<sup>9,21</sup> This theory, however, has been challenged by others who note the decreased lymphocyte counts in severe COVID-19 and that Th17 hyper-response may actually be responsible for the cytokine storm, suggesting that augmenting a TH1 response in severe patients may actually be beneficial to them.<sup>23,24</sup> Because only few of the patients in our cohort had blood tests performed soon before or during their COVID-19 (none of which included T-cell subtyping), and because the vast majority had relatively mild disease, we could not assess for this association in EoE/EGID patients.

In our study, neither the use of PPI nor of swallowed topical steroids was associated with moderate or severe COVID-19. Chronic PPI use, one of the main EoE/EGID-associated treatments, has been implicated in risk of SARS-CoV-2 infection<sup>10</sup> as well as poorer COVID-19 outcomes,<sup>10-12</sup> though recent data have challenged this.<sup>25</sup> Similarly, patients using chronic systemic steroids in inflammatory bowel diseases<sup>13</sup> and rheumatic disease<sup>26,27</sup> have had more severe COVID-19 outcomes. However, inhaled steroids used for asthma and chronic obstructive pulmonary disease (COPD) maintenance treatment appear to be safe.<sup>28,29</sup> It is possible that the general health and relatively young

age of our patients mitigated the effects of PPI. As to swallowed topical steroids, debate exists as to the systemic exposure of patients using these formulations of budesonide or fluticasone.<sup>30-32</sup> If systemic exposure exists, it is minor in most cases—presenting a situation akin to that of inhaled corticosteroids for asthma or COPD, which may explain the lack of an association with deleterious effects in EoE patients.

This study has limitations that must be acknowledged. First, although this is the first and largest series of patients with EoE/EGIDs and COVID-19, there were still too few patients with EGID distal to the esophagus to fully assess the effect of either the EGID or its treatments on the natural history of COVID-19 in such patients. Furthermore, even for EoE, the size of the cohort still makes conclusive statements difficult. To increase the numbers of patients entered, we contacted physicians several times throughout the year to promote the database including the addition of the URL on society dedicated COVID-19 sites, emails to dedicated EoE/EGID research groups and list-serves, and added requests through patient advocacy groups to notify their physicians in the event that they, as patients, were infected with SARS-CoV-2 regardless of severity. In contrast to other chronic diseases, such as inflammatory bowel disease or chronic liver disease, patients with EoE/EGID may not be in a close contact with their treating physician, and clinic visits are less frequent, especially during clinical remission. However, it is not implausible that there were simply few COVID-19 cases in this patient group as reflected by the minimal incidence rates calculated from our cases. However, because patients were neither actively contacted nor universally tested for COVID-19, actual or maximal incidence rates are unknown, and these values are minimum rates. The study was not intended as a formal epidemiological study, and as most SARS-CoV-2 infections are asymptomatic or mild, it may be that many cases were not reported to the treating physicians or that visibility of the database was not high enough, introducing a reporting bias or recruitment bias from highly motivated centers. In addition, severe cases, including either death or disability, may not have been reported because patients were not in contact with their gastroenterologist/immunologist and were thus regarded as lost to follow-up. Another limitation is that we relied on physician reports that were sometimes secondhand reports of data passed on from the patients who had been treated elsewhere. Disease severity was recorded as assessed by the physician entering the data. Because formal guidelines on the nomenclature of disease severity were only developed as the pandemic advanced, and differ between time periods, reporting countries, and guidelines,<sup>33</sup> these were not specifically queried nor reported. Furthermore, we do not have data on the need for supplemental oxygen or COVID-19-associated imaging that are used by some guidelines to assess severity. Other disease-specific databases similarly did not assess severity by specific metrics during the initial data collections.<sup>34,35</sup> Because of the rarity of COVID-19 in our population, we chose to include the few cases that were not confirmed by testing but rather diagnosed epidemiologically based on a close contact with a testing-confirmed patient and having disease appropriate symptoms. These cases were all from high-prevalence areas at times when confirmatory testing was not yet available. These may also have introduced bias into the data. The main strength of this study is the robust, worldwide collaboration that enabled us to collect data on a rare incidence taking place in rare diseases. The prevalence of EoE has been assessed as 34.4/100,000<sup>36</sup> and

of other EGIDs between 3.3 and 8.4/100,000,<sup>37</sup> making collaborative studies essential to reach meaningful conclusions.

In summary, in a global EoE/EGID registry, relatively few COVID-19 cases have been reported. The reported cases of EoE/EGID with COVID-19 are generally mild, with only 3 hospitalizations, no deaths, and none having reported nonresolving symptoms or long COVID. Based on this registry, it does not appear that EoE patients are at increased risk for severe COVID-19 infection or that COVID-19 leads to EoE/EGID flares.

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## ONLINE REPOSITORY

COVID-19 and EOE/EGID		AAA +   -	Returning?
<p>This form is to be completed by a health care professional caring for a patient with EOE/EGID and documented coronavirus (COVID 19). The form should be completed after the patient has had COVID 19 for a long enough duration to experience partial or complete recovery, hospitalization, or death.</p> <p>Thank you!</p>			
<b>Reporting center information</b>			
Name of reporting center	<input type="text"/>		
Name of treating physician	<input type="text"/>		
email address of treating physician	<input type="text"/>		
<b>Patient Demographics</b>			
Is patient older than 89 years old?	<input type="radio"/> Yes <input type="radio"/> No	<a href="#">↻</a>	
Gender	<input type="radio"/> Male <input type="radio"/> Female <input type="radio"/> Other	<a href="#">↻</a>	
Race/Ethnicity *mark as many as apply	<input type="checkbox"/> Native American/Canadian/Alaska Native <input type="checkbox"/> Black/ African American <input type="checkbox"/> Arab <input type="checkbox"/> Western European <input type="checkbox"/> Native Australian <input type="checkbox"/> Hispanic/Latino <input type="checkbox"/> Eastern European <input type="checkbox"/> South Asian (Indian) <input type="checkbox"/> Asian <input type="checkbox"/> White <input type="checkbox"/> Other		
Country of residence	<input type="text"/>		

**FIGURE E1.** COVID-EoE/EGID base questionnaire. *COVID*, Coronavirus disease; *EGID*, eosinophilic gastrointestinal disease; *EoE*, eosinophilic esophagitis.

<b>Smoking status</b>	<input type="radio"/> No exposure <input type="radio"/> Active smoker <input type="radio"/> Passive exposure	↻
<b>Does patient have Asthma?</b>	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Unknown	↻
<b>Does the patient have Atopic dermatitis?</b>	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Unknown	↻
<b>Does the patient have Allergic rhinitis?</b>	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Unknown	↻
<b>Does the patient have food allergy?</b>	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Unknown	↻
<b>Does the patient suffer from any other chronic disease other than EOE/EGID?</b>	<input type="radio"/> Yes <input type="radio"/> No	↻
<b>EOE/EGID information</b>		
<b>Type of EOE/EGID *mark as many as apply</b>	<input type="checkbox"/> Eosinophilic Esophagitis (EOE) <input type="checkbox"/> Eosinophilic Gastritis (EG) <input type="checkbox"/> Eosinophilic Enteritis (EE) <input type="checkbox"/> Eosinophilic Colitis (EC)	
<b>Year of diagnosis</b>	<input type="text"/>	
<b>Age at diagnosis</b>	<input type="text"/>	
<b>Lab work performed in the 4 months prior to the COVID-19 infection:</b>		
<b>Eosinophils</b>	<input type="radio"/> $10^3/\mu\text{L}$ <input type="radio"/> Not Done	↻
<b>WBC</b>	<input type="radio"/> $10^3/\mu\text{L}$ <input type="radio"/> Not Done	↻
<b>Hemoglobin</b>	<input type="radio"/> (gr/L) <input type="radio"/> (gr/dL) <input type="radio"/> Not Done	↻

FIGURE E1. Continued.

<b>Albumin</b>	<input type="radio"/> gr/L <input type="radio"/> gr/dL <input type="radio"/> Not Done	↻
<b>ESR</b>	<input type="radio"/> mm/h <input type="radio"/> Not Done	↻
<b>CRP</b>	<input type="radio"/> mg/L <input type="radio"/> mg/dL <input type="radio"/> mg/% <input type="radio"/> Not Done	↻
<b>EOE/EGID-related disease activity</b>		
<b>Global assessment of disease activity prior to COVID-19 exposure</b>	<input type="radio"/> Complete remission (clinically and, as much as known, also histologically) <input type="radio"/> Clinical remission (but, as much as known, histologically active) <input type="radio"/> Mild disease activity <input type="radio"/> Moderate disease activity <input type="radio"/> Severe disease activity	↻
<b>Longitudinal physician global assessment - Make your global assessment of the patient's EoE/EGID disease severity in the year prior to infection.</b>	<div style="display: flex; justify-content: space-between;"> <span>Remission</span> <span>Severe disease activity</span> </div>	↻
<b>Imaging</b>		
<b>Type of last imaging prior to COVID-19 infection</b>	<input type="radio"/> US <input type="radio"/> MRE <input type="radio"/> CTE <input type="radio"/> Barium Swallow	↻
<b>Year of last imaging test</b>	<input type="text"/>	

FIGURE E1. Continued.

<b>Imaging results</b>	<div style="border: 1px solid black; height: 50px; width: 100%;"></div> <p style="text-align: right; font-size: small;">Expand</p>
<b>Endoscopic assessment (upper endoscopy or ileocolonoscopy or video endoscopy)</b>	
<b>Year of last endoscopic assessment</b>	<input type="text"/>
<b>Assessment of endoscopic severity</b>	<p><input type="radio"/> None</p> <p><input type="radio"/> Mild</p> <p><input type="radio"/> Moderate</p> <p><input type="radio"/> Severe</p> <p style="text-align: right; font-size: small;">↻</p>
<b>Please describe endoscopic results</b>	<input type="text"/>
<b>EOE/EGID-related treatments</b>	
<p><b>Please select current EOE/EGID medication (within 3 months of infection)</b> <b>*Mark as many as apply</b></p> <p><b>In this section, questions about stopping treatment refer to stopping PRIOR to the COVID-19 infection.</b></p>	<p><input type="checkbox"/> Dietary Elimination</p> <p><input type="checkbox"/> Swallowed Topical Steroids</p> <p><input type="checkbox"/> Systemic Steroids</p> <p><input type="checkbox"/> PPI</p> <p><input type="checkbox"/> Azathioprine/6mp</p> <p><input type="checkbox"/> Enteric Budesonide</p> <p><input type="checkbox"/> Anti IL-5 (Mepolizumab, Reslizumab)</p> <p><input type="checkbox"/> Anti IL-5 receptor (Benralizumab)</p> <p><input type="checkbox"/> Dupilumab</p> <p><input type="checkbox"/> Vedolizumab</p> <p><input type="checkbox"/> Omalizumab</p> <p><input type="checkbox"/> Anti Siglec-8 antibody</p> <p><input type="checkbox"/> Montelukast</p> <p><input type="checkbox"/> Cromolyn</p> <p><input type="checkbox"/> Ketotifen</p> <p><input type="checkbox"/> Other</p>

FIGURE E1. Continued.

<p><b>Has the patient ever had an esophageal dilation?</b></p>	<p><input type="radio"/> Yes <input type="radio"/> No</p>	<p>↻</p>
<p><b>Does the patient currently have a feeding tube?</b></p>	<p><input type="radio"/> Yes <input type="radio"/> No</p>	<p>↻</p>
<p><b>Past EOE/EGID treatments (discontinued at least 3 months prior to infection)</b></p>	<p> <input type="checkbox"/> Dietary Elimination  <input type="checkbox"/> Swallowed Topical Steroids  <input type="checkbox"/> Systemic Steroids  <input type="checkbox"/> PPI  <input type="checkbox"/> Azathioprine/6mp  <input type="checkbox"/> Enteric Budesonide  <input type="checkbox"/> Anti IL-5 (Mepolizumab, Reslizumab)  <input type="checkbox"/> Anti IL-5 receptor (Benralizumab)  <input type="checkbox"/> Dupilumab  <input type="checkbox"/> Vedolizumab  <input type="checkbox"/> Omalizumab  <input type="checkbox"/> Anti Siglec-8 antibody  <input type="checkbox"/> Montelukast  <input type="checkbox"/> Cromolyn  <input type="checkbox"/> Ketotifen  <input type="checkbox"/> Other                 </p>	
<p><b>Was patient receiving any other medication not related to EOE/EGID</b></p>	<p><input type="radio"/> Yes <input type="radio"/> No</p>	<p>↻</p>
<p><b>COVID-19- related data</b></p>		
<p><b>The COVID-19 diagnosis was</b></p>	<p><input type="radio"/> Confirmed <input type="radio"/> Suspected</p>	<p>↻</p>
<p><b>Patient weight (kg) closest to COVID-19 infection</b></p>	<input type="text"/>	
<p><b>Patient height (cm) closest to COVID-19 infection</b></p>	<input type="text"/>	

FIGURE E1. Continued.

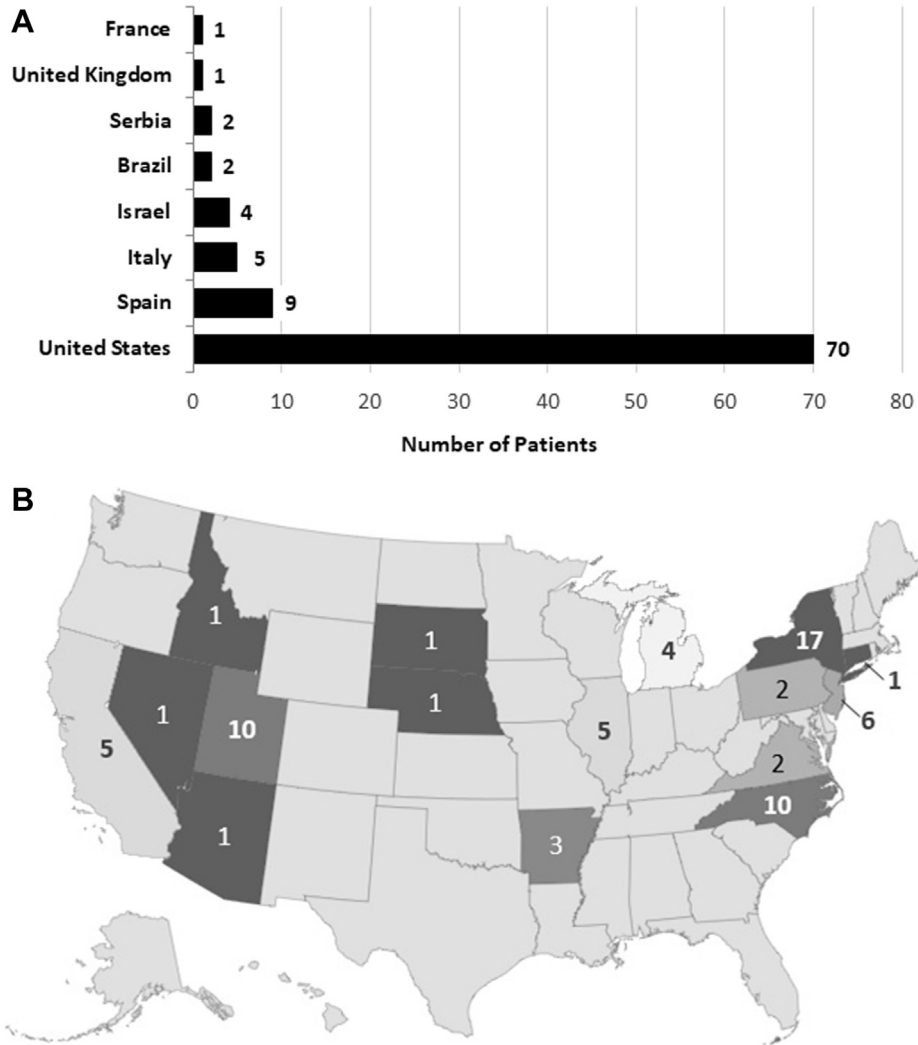


<b>Who was the index contagious case, if known</b>	<input type="checkbox"/> parent <input type="checkbox"/> spouse <input type="checkbox"/> child <input type="checkbox"/> work contact <input type="checkbox"/> travel out of the country of residence <input type="checkbox"/> neighbor <input type="checkbox"/> other <input type="checkbox"/> unknown
<b>Presenting symptoms</b> <b>*mark as many as apply</b>	<input type="checkbox"/> Asymptomatic <input type="checkbox"/> Low fever (38°c-39°c) <input type="checkbox"/> Highest fever>39°c <input type="checkbox"/> Cough <input type="checkbox"/> Dyspnea <input type="checkbox"/> Runny nose <input type="checkbox"/> Other
<b>Severity of COVID 19 infection</b>	<input type="radio"/> asymptomatic <input type="radio"/> mild <input type="radio"/> moderate <input type="radio"/> severe <input type="radio"/> unknown
<b>COVID-19 related hospitalization</b>	<input type="radio"/> Yes <input type="radio"/> No
<b>Total days from symptoms to clinical resolution of the infection</b>	<input type="text"/>
<b>Were there residual symptoms related to COVID-19 at time of report?</b>	<input type="radio"/> Yes <input type="radio"/> No
<b>Did the patient receive any antiviral medication</b>	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Unknown

FIGURE E1. Continued.

Did the infection induce a flare of the EOE/EGID?	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Unknown	↕
Did you stop the EOE/EGID treatment because of the COVID-19 infection?	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Unknown	↕
Death	<input type="radio"/> Yes <input type="radio"/> No	↕
Any other comments?	<div style="border: 1px solid black; height: 40px; width: 100%;"></div>	Expand
<div style="border: 1px solid black; padding: 2px; display: inline-block; margin: 5px;">✓</div> <div style="border: 1px solid black; padding: 2px; display: inline-block; margin: 5px;">Save &amp; Return Later</div>		

FIGURE E1. Continued.



**FIGURE E2.** (A) Country and (B) state of residence (US only) of eosinophilic esophagitis/eosinophilic gastrointestinal disease patients with coronavirus disease 2019.

**TABLE E1.** Organizations endorsing and supporting the COVID-EoE/EGID initiative

Endorsing organizations	Promoting patient advocacy groups	Promoting organizations
Consortium of Eosinophilic Gastrointestinal Disease Researchers	Campaign Urging Research for Eosinophilic Disease foundation (United States)	American College of Gastroenterology
United European Gastroenterology	American Partnership for Eosinophilic Disorders (United States)	Academy of Allergy, Asthma & Immunology
European Society for Pediatric Hepatology and Nutrition EGID working group	Eosinophilic Family Coalition (United States)	Israeli Society for Pediatric Gastroenterology, Hepatology, and Nutrition
European Consortium for Eosinophilic Diseases of the GI Tract	Eos Network (United Kingdom)	Latin American Society for Pediatric Gastroenterology, Hepatology, and Nutrition
North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition	Israeli Eosinophilic Esophagitis Patient Advocacy Group (Lehedva) (Israel)	British Society of Gastroenterology
		British Society for Pediatric Gastroenterology, Hepatology, and Nutrition
		Belgian Society for Pediatric Gastroenterology, Hepatology, and Nutrition
		European Society for Pediatric Gastroenterology, Hepatology, and Nutrition

COVID, Coronavirus disease; EGID, eosinophilic gastrointestinal disease; EoE, eosinophilic esophagitis.

**TABLE E2.** Comorbidities in eosinophilic esophagitis/eosinophilic gastrointestinal disease patients

Comorbidity	N
Anxiety disorder	4
Attention deficit and hyperactivity disorder	3
Celiac disease	2
Inflammatory bowel disease	2
Mast cell activation syndrome	2
Hypertension	1
Gastroesophageal reflux disease	1
Gastroparesis	1
Epilepsy	1
Irritable bowel syndrome	1
Raynaud's phenomenon	1
Ehlers-Danlos syndrome	1
Hashimoto's disease	1
Migraine	1
Esophageal atresia	1
Fragile X syndrome	1
Juvenile idiopathic arthritis	1
Thalassemia minor	1
Intermittent porphyria	1
Multiple endocrine neoplasia, type 2B	1
Von Willebrand disease	1
Squamous cell carcinoma	1