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Eosinophilic Esophagitis Patients Are Not At Increased Risk of Severe COVID-19: A Report from a Global Registry

Running Title: COVID-19 in EoE

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Abstract

Background: The impact of COVID-19 on eosinophilic esophagitis (EoE) and eosinophilic gastrointestinal diseases (EGID) is unknown.

Objective: We aimed to characterize EoE and EGID patients 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, de-identified 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); 73% male). Most had atopy (73%), and 80% had isolated EoE. Prior to 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 PPIs 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 ICU admissions or deaths were reported. Mean time from first symptoms to resolution in symptomatic patients was 10 days (range 1-90). 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 EoE patients are at increased risk for severe COVID-19 infection or that COVID-19 leads to EGID flares.

Highlights Box

1. What is already known about this topic?

No data has been published on the outcome of COVID-19 in EoE/EGID patients.

2. What does this article add to our knowledge?

COVID-19 severity in EoE patients appears to be comparable to that of the general population.

3. How does this study impact current management guidelines?

EoE/EGID patients with COVID-19 may be managed following guidelines for the general population.

Keywords: Corona virus, COVID-19, Eosinophilic Oesophagitis, EGID, eosinophilic GI disease, epidemiology, outcome, risk factor

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68 **Abbreviations:** ACE2 - Angiotensin Converting Enzyme-2; COVID-19 - coronavirus disease 2019;
69 EoE - Eosinophilic Esophagitis; EGID - Eosinophilic Gastrointestinal Diseases; GI –
70 Gastrointestinal; PPI - Proton Pump Inhibitors; SARS-CoV-2 - severe acute respiratory syndrome
71 coronavirus 2, TH2 – T helper 2.

Introduction

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 corona virus disease 2019 (COVID-19)(1). 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, ACE2, is expressed in multiple human tissues, including the esophagus(2) and intestines(3). Binding of the SARS-CoV-2 spike protein to ACE2 and proteolytic cleavage by TMPRSS2, a cellular serine protease, facilitate viral entry into cells(4). While the infection remains asymptomatic or mild in most patients, a minority may progress to moderate/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(5, 6).

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(7-9). 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 (PPI) and steroids) which have been implicated in the risk for more severe COVID-19(10-13). Furthermore, while normal and elevated peripheral eosinophil counts have been found to be associated with better outcomes in COVID-19(14, 15), it is theoretically possible that eosinophil depleting drugs, which are sometimes used for treatment of EoE/EGID, may induce more severe disease(16).

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(17). A clear understanding of the impact that pre-existing EoE/EGID 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/EGID 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 eosinophilic gastrointestinal diseases, and was based on similar work in inflammatory bowel disease(13). The project was endorsed and promoted by Gastroenterology Societies in Europe, North America, and Latin America, Allergy and Immunology societies, and patient advocacy groups (**Supplemental Table E1**). Following 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 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). 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 final outcome prior to data analysis. We utilized 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.

De-identified 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 prior to COVID-19), laboratory test values prior to 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) (**Supplemental Figure E1**).

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

Statistical analysis was performed using IBM SPSS statistics 27 (Armonk NY: IBM Corp). 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 (IQR; range). Associations of non-parametric variables with 2 independent samples were calculated with the Mann-Whitney test. Binary variables were analyzed by Pearson Chi-Square Test. A P-value <0.05 was considered significant.

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

Results

During the 12-month period from April 2020-March 2021, 94 patients were entered into the database from 8 countries. Most patients were from the United States (US) (70), and Spain (9) (**Supplemental Figure E2**). Within the United States, patients resided in 17 different States (**Supplemental Figure E2**), the majority from the Northeastern and Southwestern US. The median age was 21years (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 which 43% had active disease based on either use of beta-agonists twice weekly, prophylactic inhaler use, or an asthma related hospitalization in the previous year. The vast majority (98%) were non-smokers. (**Table 1**). The median (IQR) BMI of patients over 16 years of age was 23.5 (21.8-26.9).

Insofar as the segment of the GI tract involved in the eosinophilic disease, while the majority 90 (96%) had esophageal involvement, only 75 (79.8%) had isolated EoE, 2 (2.1%) had isolated eosinophilic colitis, and one 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 1). The majority were in clinical remission (54%) at the time of the last assessment prior to COVID-19, though only 34% reported combined clinical and histological remission at the time of the last gastroenterologist follow-up prior to COVID-19. Seventeen patients (18%) had mild and 20 (21%) had moderate disease activity, while 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 (**Supplemental Table E2**). Treatment for EoE/EGID at the time of SARS-COV-2 infection included PPIs 49 (52%), topical steroids (budesonide or fluticasone) 48 (51%), 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±1mg. Two patients each were receiving systemic steroids or enteric budesonide, one received azathioprine/6-mercaptopurine, and 4 patients were receiving a biologic treatment (**Table 1**). Feeding tubes were reported by three patients; five patients had undergone esophageal dilation in the three months prior to COVID-19.

The diagnosis of COVID-19 was made by naso-pharyngeal swab PCR 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

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 diagnosis of EoE/EGID to COVID-19 was 5.0 ± 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 gastrointestinal complaints during the duration of their COVID-19. These included diarrhea (8%), nausea/vomiting (5%), and abdominal pain (4%), with only three 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 2**). 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 ($p=0.07$). There was a single, mild flare of EoE during mildly symptomatic COVID-19 reported in a 34 year old, non-atopic, male 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 prior to COVID-19. There were two 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 three were over 40 years old, and none needed mechanical ventilation or extracorporeal membrane oxygenation (ECMO). The first was a 40 year old non-atopic, non-obese 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, non-asthmatic, overweight (BMI 26) male with EoE treated with topical fluticasone (0.8mg/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 male 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 three days with high fever, cough, dyspnea, rhinorrhea and diarrhea. It is unknown if he received anti-viral treatment. His symptoms fully resolved after 60 days.

In order 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 seven US centers who responded, there were 39 COVID-19 cases out of 4,391 patients giving an incidence of 1:113 (8,850/1 million). On a world-wide basis, there were 57 COVID-19 cases out of 5,549 patients, giving an incidence of 1:97 (10,309/ 1 million). This is compared to 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(18).

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 collaborative efforts are necessary to assess outcomes of rare diseases such as EoE/EGIDs. While 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 U.S. and worldwide populations. In our cohort, no cases of long COVID-19 were reported, however patients may have been entered into the database soon after primary recuperation, and thus long COVID-19 missed. To date there have been no patient series (and to the best of our knowledge even case reports) reporting COVID-19 outcomes in EoE/EGID patients. Both Savarino et al.(8) and Franceschini et al.(9) 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 to 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 reported 81% mild disease, and 19% severe/critical(19). In contrast to their cohort in which only 2% of patients were under the age of 18 years, in our EoE/EGID cohort 29/94 (31%) of patients were in this age group which generally have 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(6) while in our cohort the oldest patient was 53 years old. Furthermore, our patients had relatively few significant co-morbidities that are known risk factors for severe COVID-19 disease. It is unclear if the low frequency of COVID associated co-morbidities is representative of the broader EoE/EGID patient population. Additionally, a recent systematic review and meta-analysis(20) 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 which 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.(21) 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 towards lower TMPRSS2 expression than non-atopic 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 gastrointestinal 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(14, 15, 22). These studies further support the notion that individuals whom harbor a TH2 predominant milieu have better outcomes, possibly because this profile protects from the damaging effects of a TH1 associated cytokine storm(9, 21). 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(23, 24). 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), the fact that the vast majority had relatively mild disease, and our study construct, we could not assess for this association in EoE/EGID patients.

In our study, neither the use of PPI nor of swallowed topical steroids were 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(10) as well as poorer COVID-19 outcomes(10-12), though recent data have challenged this(25). Similarly, patients using chronic systemic steroids in inflammatory bowel diseases(13) and rheumatic disease(26, 27) have had more severe COVID-19 outcomes. However, inhaled steroids used for asthma and COPD maintenance treatment appear to be safe(28, 29). 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(30-32). 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 which must be acknowledged. First, while 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. In order 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 IBD or chronic liver disease, patients with EoE/EGID may not be in as 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 incidences 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 which 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. Since formal guidelines on the nomenclature of disease severity were only developed as the pandemic advanced, and differ between time periods, reporting countries and guidelines(33), these were not specifically queried nor reported. Furthermore, we do not have data on the need for supplemental oxygen or COVID19 associated imaging which 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(34, 35). Due to the rarity of COVID-19 in our population, we chose to include the few cases which were not confirmed by testing rather diagnosed epidemiologically based on 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 which 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(36) and of other EGIDs between 3.3-8.4/100,000(37) 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 three hospitalizations, no deaths and none having reported non-resolving 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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Table 1. Patient Characteristics

Patient Characteristics (n=94)	n (%) or median (IQR)
Age	
At EoE/EGID Diagnosis	17 (10-31)
At time of COVID-19	21 (16-35)
Male	69 (73%)
Race	82% white
GI region involved in EoE/EGID	
Esophagus	90 (96%)
Stomach	11 (12%)
Small Bowel	11 (12%)
Colon	5 (5%)
EoE/EGID activity at time of COVID-19	
Complete remission	32 (34%)
Clinical remission but Histologic activity	19 (20%)
Mild activity	17 (18%)
Moderate activity	20 (21%)
Severe activity	6 (6%)
Treatment at time of COVID-19	
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/6mercaptopurine	1 (1%)

[Ⓢ] anti-IL5, anti-IL5r, dupilumab, vedolizumab

Table 2. COVID-19 severity stratified by EoE/EGID treatment at the time of infection.

	Moderate/Severe COVID-19 (n=13)	Asymptomatic COVID-19 (n=80)	P value
Diet	4	30	0.45
Oral topical steroids	6	41	0.77
Systemic steroids	0	2	1
PPI	8	40	0.44
AZA-6MP	0	1	1
Enteric budesonide	0	2	1
Anti-IL5	0	1	1
Benralizumab	1	0	0.14
Dupilumab	1	0	0.14
Vedolizumab	0	1	1
Cromolyn sodium	1	1	0.26

AZA-6MP – Azathioprine 6-mercaptopurine; PPI – Proton Pump Inhibitor

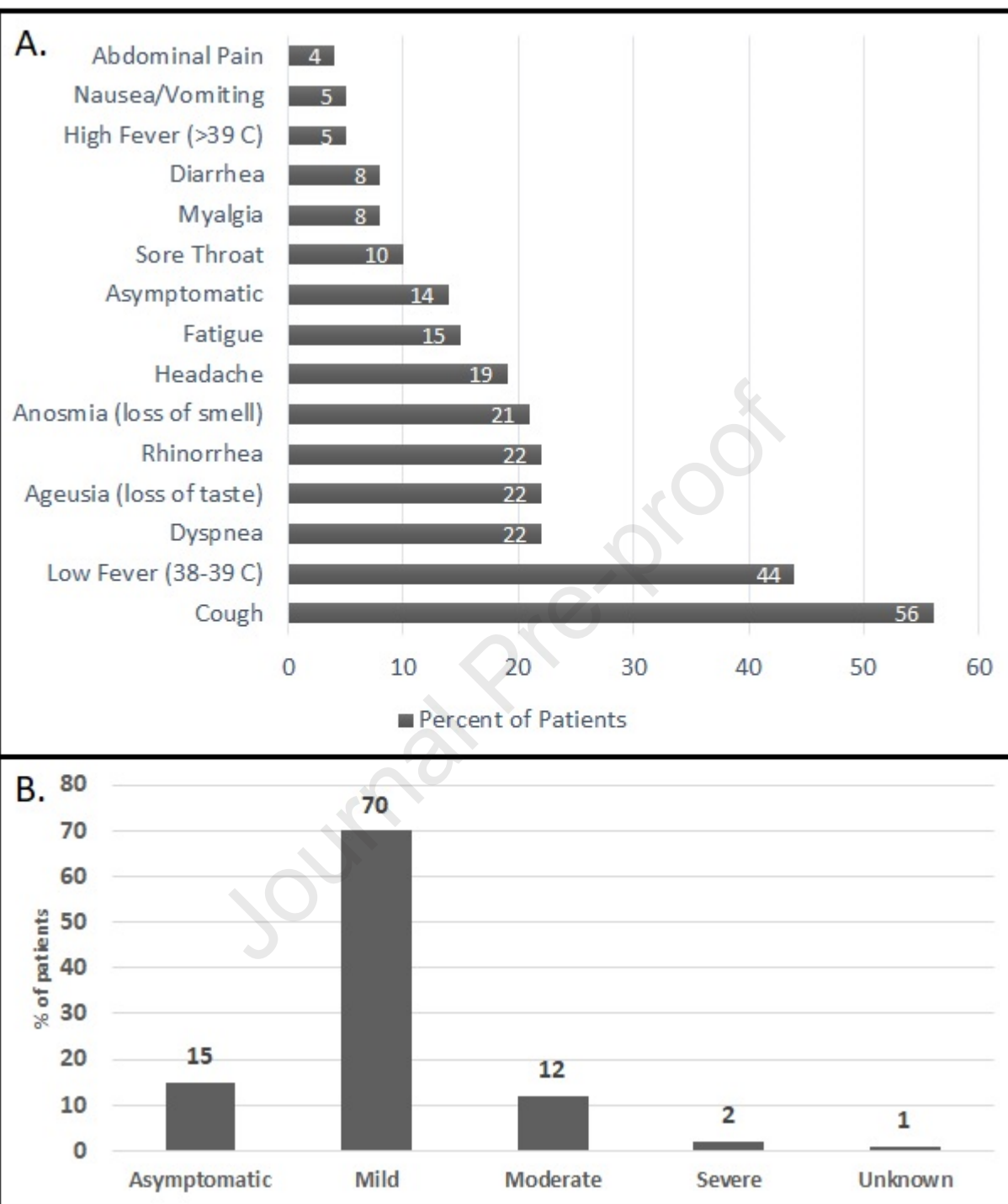
Figure Legends

Figure 1. A. Symptoms (n=80) and B. Severity (n=94) of EoE/EGID patients with COVID-19.

Supplemental Figure Legends:

Supplemental Figure E1 – COVID-EoE/EGID Base questionnaire

Supplemental Figure E2. A. Country and B. State of Residence (U.S. only) of EoE/EGID patients with COVID-19.



Supplementary Table E1. Organizations Endorsing and Supporting the COVID-EoE/EGID Initiative.

Endorsing Organizations	Promoting Organizations
Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR)	American College of Gastroenterology (ACG)
United European Gastroenterology (UEG)	Academy of Allergy, Asthma & Immunology (AAAAI)
European Society for Pediatric Hepatology and Nutrition (ESPGHAN) EGID working group	Israeli Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ISPGHAN)
European Consortium for Eosinophilic Diseases of the GI Tract (EUREOS)	Latin American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (LASPGHAN)
North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN)	British Society of Gastroenterology (BSG)
Promoting Patient Advocacy Groups	British Society for Pediatric Gastroenterology, Hepatology, and Nutrition (BSPGHAN)
Campaign Urging Research for Eosinophilic Disease (CURED) foundation. (United States)	Belgian Society for Pediatric Gastroenterology, Hepatology, and Nutrition (BeSPGHAN)
American Partnership for Eosinophilic Disorders (APFED) (United States)	European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN)
Eosinophilic Family Coalition (EFC) (United States)	
Eos Network (United Kingdom)	
Israeli Eosinophilic Esophagitis Patient Advocacy Group (Lehedva) (Israel)	

Supplementary Table E2. Comorbidities in EoE/EGID 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
MEN 2B	1
Von Willebrand Disease	1
Squamous Cell Carcinoma	1

COVID-19 and EOE/EGID



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.

Thank you!

Reporting center information

Name of reporting center

Name of treating physician

email address of treating physician

Patient Demographics

Is patient older than 89 years old?

☐ Yes ☐ No



Gender

☐ Male ☐ Female ☐ Other



Race/Ethnicity

*mark as many as apply

- ☐ Native American/Canadian/Alaska Native
- ☐ Black/ African American
- ☐ Arab
- ☐ Western European
- ☐ Native Australian
- ☐ Hispanic/Latino
- ☐ Eastern European
- ☐ South Asian (Indian)
- ☐ Asian
- ☐ White
- ☐ Other

Country of residence

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Smoking status

- ☐ No exposure
- ☐ Active smoker
- ☐ Passive exposure

↻

Does patient have Asthma?

- ☐ Yes ☐ No ☐ Unknown

↻

Does the patient have Atopic dermatitis?

- ☐ Yes ☐ No ☐ Unknown

↻

Does the patient have Allergic rhinitis?

- ☐ Yes ☐ No ☐ Unknown

↻

Does the patient have food allergy?

- ☐ Yes ☐ No ☐ Unknown

↻

Does the patient suffer from any other chronic disease other than EOE/EGID?

- ☐ Yes ☐ No

↻

EOE/EGID information**Type of EOE/EGID**
***mark as many as apply**

- ☐ Eosinophilic Esophagitis (EOE)
- ☐ Eosinophilic Gastritis (EG)
- ☐ Eosinophilic Enteritis (EE)
- ☐ Eosinophilic Colitis (EC)

Year of diagnosis**Age at diagnosis****Lab work performed in the 4 months prior to the COVID-19 infection:****Eosinophils**

- ☐ $10^3/\mu\text{L}$ ☐ Not Done

↻

WBC

- ☐ $10^3/\mu\text{L}$ ☐ Not Done

↻

Hemoglobin

- ☐ (gr/L) ☐ (gr/dL) ☐ Not Done

↻

Albumin
☐ gr/L ☐ gr/dL ☐ Not Done
**ESR**
☐ mm/h ☐ Not Done
**CRP**
☐ mg/L
☐ mg/dL
☐ mg/%
☐ Not Done
**EOE/EGID-related disease activity****Global assessment of disease activity prior to COVID-19 exposure**
☐ Complete remission (clinically and, as much as known, also histologically)
☐ Clinical remission (but, as much as known, histologically active)
☐ Mild disease activity
☐ Moderate disease activity
☐ Severe disease activity
**Longitudinal physician global assessment - Make your global assessment of the patient's EoE/EGID disease severity in the year prior to infection.**

Remission Severe disease activity

**Imaging****Type of last imaging prior to COVID-19 infection**
☐ US
☐ MRE
☐ CTE
☐ Barium Swallow
**Year of last imaging test**

Imaging results

Expand

Endoscopic assessment (upper endoscopy or ileocolonoscopy or video endoscopy)**Year of last endoscopic assessment****Assessment of endoscopic severity**

- ☐ None
- ☐ Mild
- ☐ Moderate
- ☐ Severe

5

Please describe endoscopic results**EOE/EGID-related treatments****Please select current EOE/EGID medication (within 3 months of infection)*****Mark as many as apply****In this section, questions about stopping treatment refer to stopping PRIOR to the COVID-19 infection.**

- ☐ Dietary Elimination
- ☐ Swallowed Topical Steroids
- ☐ Systemic Steroids
- ☐ PPI
- ☐ Azathioprine/6mp
- ☐ Enteric Budesonide
- ☐ Anti IL-5 (Mepolizumab, Reslizumab)
- ☐ Anti IL-5 receptor (Benralizumab)
- ☐ Dupilumab
- ☐ Vedolizumab
- ☐ Omalizumab
- ☐ Anti Siglec-8 antibody
- ☐ Montelukast
- ☐ Cromolyn
- ☐ Ketotifen
- ☐ Other

Has the patient ever had an esophageal dilation?

☐ Yes ☐ No



Does the patient currently have a feeding tube?

☐ Yes ☐ No



Past EOE/EGID treatments (discontinued at least 3 months prior to infection)

- ☐ Dietary Elimination
- ☐ Swallowed Topical Steroids
- ☐ Systemic Steroids
- ☐ PPI
- ☐ Azathioprine/6mp
- ☐ Enteric Budesonide
- ☐ Anti IL-5 (Mepolizumab, Reslizumab)
- ☐ Anti IL-5 receptor (Benralizumab)
- ☐ Dupilumab
- ☐ Vedolizumab
- ☐ Omalizumab
- ☐ Anti Siglec-8 antibody
- ☐ Montelukast
- ☐ Cromolyn
- ☐ Ketotifen
- ☐ Other

Was patient receiving any other medication not related to EOE/EGID

☐ Yes ☐ No



COVID-19- related data

The COVID-19 diagnosis was

☐ Confirmed ☐ Suspected



Patient weight (kg) closest to COVID-19 infection

Patient height (cm) closest to COVID-19 infection

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Who was the index contagious case, if known

- ☐ parent
- ☐ spouse
- ☐ child
- ☐ work contact
- ☐ travel out of the country of residence
- ☐ neighbor
- ☐ other
- ☐ unknown

Presenting symptoms
***mark as many as apply**

- ☐ Asymptomatic
- ☐ Low fever (38°C-39°C)
- ☐ Highest fever >39°C
- ☐ Cough
- ☐ Dyspnea
- ☐ Runny nose
- ☐ Other

Severity of COVID 19 infection

- ☐ asymptomatic
- ☐ mild
- ☐ moderate
- ☐ severe
- ☐ unknown

↻

COVID-19 related hospitalization

- ☐ Yes ☐ No

↻

Total days from symptoms to clinical resolution of the infection

Were there residual symptoms related to COVID-19 at time of report?

- ☐ Yes ☐ No

↻

Did the patient receive any antiviral medication

- ☐ Yes ☐ No ☐ Unknown

↻

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Did the infection induce a flare of the EOE/EGID?☐ Yes ☐ No ☐ Unknown**Did you stop the EOE/EGID treatment because of the COVID-19 infection?**☐ Yes ☐ No ☐ Unknown**Death**☐ Yes ☐ No**Any other comments?**

Expand

**Save & Return Later**

