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COVID-19 infection in hypereosinophilic syndrome: A survey-based analysis

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The role of eosinophils in coronavirus disease 2019 (COVID-19) infection remains controversial. As in other febrile illnesses, including sepsis and influenza, decreased blood eosinophil levels are frequent in COVID-19 infection and have been associated with increased disease severity. Moreover, retrospective studies of patients with asthma and eosinophilic gastrointestinal disorders suggest that eosinophilia and/or type 2 inflammatory responses may be protective against severe manifestations of COVID-19 infection. Although these data led some to suggest early in the pandemic that eosinophil-depleting biologics may be detrimental in COVID-19 infection, published studies examining the association between biologic therapy and the incidence and severity of COVID-19 infections in patients with asthma do not support this hypothesis. Moreover, increased eosinophilic pulmonary inflammation has been reported in patients with fatal COVID-19 infection, consistent with a possible pathogenic role of eosinophils in the most severe cases.

Hypereosinophilic syndromes (HESs) are a heterogeneous group of rare disorders defined by hypereosinophilia and eosinophil-related disease manifestations. Although any organ system can be involved in HESs, the skin, respiratory, and gastrointestinal tracts are most commonly affected. HESs can be divided into clinical subtypes, including myeloid, lymphoid, and idiopathic variants, which have implications with respect to etiology, clinical manifestations, response to therapy, and prognosis. To explore the effects of HES treatment and COVID-19 in patients with HESs, 238 participants with HES actively enrolled on a natural history study of eosinophilic disorders (NCT00001406), who had previously consented to email correspondence, were invited to participate in serial REDCap surveys (see Figure E1 in this article’s Online Repository at www.jaci-inpractice.org). The first surveys were distributed in November 2020 and included questions about demographic characteristics, HES status, and COVID testing. Follow-up surveys, which included vaccination and Centers for Disease Control and Prevention (CDC) guideline adherence questions, were emailed in July 2021 to all 238 participants. Because of the study time frame (November 1, 2020, to October 1, 2021), none of the COVID-19 cases were likely due to the Omicron variant, first reported in the United States by the CDC on November 22, 2021.

A total of 160 unique participants responded to at least 1 survey between November 18, 2020, and October 1, 2021, of which 98 responded to follow-up surveys between July 1, 2021, and October 1, 2021. Of the 160 unique responders, 51.3% were males; 82.5% identified as White, 6.3% as Black, and 4.4% as Asian (Table I). A total of 105 (65.6%) participants had been tested for COVID-19 at least once, of which 23 (21.9%) tested positive between March 2020 and September 2021 (HESCOVID+). There were no demographic differences between the HESCOVID+ participants and those who reported no history of COVID-19 (HESWELL). The geographic distribution of the reported cases of COVID-19 infection closely mirrors that of the total participants (see Figure E2 in this article’s Online Repository at www.jaci-inpractice.org).

The distribution of HES subtypes was significantly different between the HESWELL and HESCOVID+ groups (P < .005, Freeman-Halton test), with a significantly decreased proportion of idiopathic HES and nearly significantly increased proportion of lymphoid variant HES in the HESCOVID+ group compared with the entire cohort (0% vs 18.5%, P = .017, and 34.8% vs 10.9%, P = .052, respectively, central Fisher exact test corrected for multiple comparisons (Table I). The prevalence rates of asthma and diabetes were similar in the HESCOVID+ and HESWELL groups (47.8% vs 40.9% and 0% vs 10.2%, respectively; P = nonsignificant), as was the proportion of participants taking medication for HES (82.6% vs 83.9%; P = nonsignificant). Most participants (83.8%) were taking HES medications, including 62 who were receiving an eosinophil-lowering biologic (mepolizumab or benralizumab) (Table II). Although the numbers are small, no significant differences in prevalence were detected for any of the medications or medication categories between the HESWELL and HESCOVID+ groups.

Four (17.4%) of the HESCOVID+ participants were hospitalized, all of whom had significant risk factors for severe COVID (body mass index > 35 [n = 3], severe asthma [n = 3], and cardiovascular disease [n = 3]) in 3 patients, and a history of vaping tobacco in the fourth). One patient died of bacterial sepsis after COVID-19 infection. All 4 hospitalized patients had lymphoid variant HES and were receiving 1 or more treatment for HES (prednisone [n = 3], ruxolitinib [n = 1], mepolizumab [n = 1]) at the time of COVID-19 infection, although eosinophilia was uncontrolled in 2 of the 4 (>1500/mm3 at the visit before infection). The hospitalization rate in the HESCOVID+ group (17.4%) was similar to that reported by the CDC for all individuals who tested positive for SARS-CoV-2 between February 12, 2020, and March 28, 2020 (21%; P = nonsignificant), but higher than the 9% hospitalization rate reported for individuals with no underlying health condition. Although there was a trend toward a lower rate in the HESCOVID+ group compared with that in patients with chronic lung disease in the same CDC report (37.5%; P = .051), rates of COVID-19 infection in a large cohort of patients with asthma that included a significant proportion of patients on biologic therapy reported hospitalization rates (26.1%) similar to those in the current study.

Clinical Implications

This survey-based study of participants with hypereosinophilic syndrome suggests that neither eosinophilia nor depletion of eosinophils impact the severity of coronavirus disease infection and that there is no increased risk of vaccination against coronavirus disease 2019 in this patient population.
A total of 116 (72.5%) participants responded to the vaccination questions. The vaccination rate in the HESCOVID+ group was lower than that in the HESWELL group (71.4% vs 90.5%; \(P = .029\)). Three of the 15 HESCOVID+ vaccinated participants were immunized before their reported COVID-19 infection. Five of the 101 vaccinated participants reported an increase in eosinophil count or eosinophil-related symptoms after immunization. In only 1 case did this lead to a change in HES therapy (a transient increase in prednisone dose 2 weeks after the second dose of the Pfizer vaccine).

Consistent with published data in patients with other eosinophil-associated disorders,\(^1\) the data from this survey suggest that patients with HESs are no more likely to have severe COVID-19 infection than the general population and that treatment does not represent a major risk factor for severe disease. Equally important, despite isolated reports of the development of eosinophilic disorders temporally related to COVID-19 vaccination, clinically significant exacerbation of HESs (ie, requiring alteration of therapy) was reported in less than 1% of vaccinated participants.

Although encouraging, this study has limitations. As in any survey-based study, the reliability of the data is limited by the accuracy of patient reporting and bias can be introduced if one of the study outcomes (eg, COVID-19 infection) results in reduced response rates. Although the number of participants was small due to the rarity of HESs, the response rate was high (67.2%), and the demographic and clinical characteristics of the participants are comparable to those in the 604 participants currently or previously enrolled on the same natural history protocol. Moreover, chart review of the 78 survey nonresponders revealed 44 participants for whom data were available regarding COVID-19 infection over the entire study period identified only 2 additional cases of COVID-19 infection in 44 participants, neither of whom had a severe presentation. Finally, the variability in COVID-19 infection rates and the introduction of immunization during the study time

### TABLE I. Demographic and clinical characteristics of the study participants

| Characteristic                  | HESWELL cohort* (n = 137) | HES COVID+ cohort (n = 23) |
|---------------------------------|---------------------------|---------------------------|
| **Sex: female, n (%)**          | 65 (47.4)                 | 12 (52.2)                 |
| **US resident, n (%)**          | 130 (94.9)                | 21 (91.3)                 |
| **White, n (%)**                | 110 (80.3)                | 22 (95.7)                 |
| **Age (y), median (range)**     | 53 (6-88)                 | 50 (21-73)                |
| **Additional risk factors**     |                           |                           |
| Current smoker, n (%)\(^1\)    | 9 (6.6)                   | 3 (13.0)                  |
| Asthma, n (%)                   | 56 (40.9)                 | 11 (47.8)                 |
| Diabetes, n (%)                 | 14 (10.2)                 | 0 (0)                     |
| Cardiovascular disease, n (%)   | 28 (20.4)                 | 4 (17.4)                  |
| Geo mean BMI (range)            | 25.4 (14.1-38.5)          | 27.8 (16.6-56.3)          |
| **HES subtype, n (%)**          |                           |                           |
| MHES                            | 19 (13.9)                 | 1 (4.3)                   |
| LHES                            | 15 (10.9)                 | 8 (34.8)                  |
| Overlap                         | 63 (46.0)                 | 14 (60.9)                 |
| IHES                            | 36 (26.3)                 | 0                         |
| HEUS                            | 4 (2.9)                   | 0                         |
| Symptoms in month before filling out survey (patient report), n (%) | 55 (40.1) | 9 (39.1) |
| Change in therapy in 3 mo before filling out survey (patient report), n (%) | 19 (13.9) | 5 (21.7) |

| Vaccinated, n (%)\(^4\)         | 86 of 95 (90.5)           | 15 of 21 (71.4)           |
| Moderna (mRNA-1273) vaccine     | 37 of 86 (43.0)           | 1 of 15 (6.7)             |
| Pfizer (BNT162b2) vaccine       | 48 of 86 (55.8)           | 12 of 15 (80.0)           |
| J&J (INJ-78436735) or AstraZeneca (ChAdOx1-S) | 1 of 86 (1.2) | 2 of 15 (13.3) |
| Vaccinated before infection, n (%) | NA                      | 3 of 15 (20.0)           |
| Hospitalized for treatment of COVID, n (%) | NA                    | 4                         |
| Died from COVID-related complications, n (%) | NA                     | 1                         |

\(^4\)Not available/applicable.
\(^1\)Includes tobacco or other inhaled substances.
\(^2\)HES subtypes: MHES, myeloid HES defined by clinical or molecular evidence of an eosinophilic myeloid neoplasm; LHES, lymphoid variant HES defined by the presence of an aberrant and/or clonal T-cell population; overlap HES, single-organ HES or defined eosinophilic syndrome that overlaps in clinical presentation with idiopathic HES (eg, eosinophilic gastrointestinal disorders or eosinophilic granulomatosis with polyangiitis), HEUS, hypereosinophilia of undetermined significance defined as hypereosinophilia without symptoms or clinical manifestations; and IHES, idiopathic HES defined as HES that does not fit in any of the other categories.

### TABLE II. HES medications

| Medication                        | HESWELL cohort\(^*\) (n = 137) | HES COVID+ cohort (n = 23) |
|-----------------------------------|---------------------------------|---------------------------|
| Any HES medication                | 115 (83.9)                      | 19 (82.6)                 |
| Glucocorticoids                   | 58 (42.3)                       | 9 (39.1)                  |
| Oral                              | 45 (32.8)                       | 8 (34.8)                  |
| Swallowed                         | 13 (9.5)                        | 1 (4.3)                   |
| Inhaled therapy\(^†\)             | 53 (38.7)                       | 9 (39.1)                  |
| Biologic therapy                  | 55 (40.1)                       | 11 (47.8)                 |
| Mepolizumab                       | 37 (27.0)                       | 8 (34.8)                  |
| Benralizumab                      | 16 (11.7)                       | 1 (4.3)                   |
| Other\(^†\)                       | 2 (1.5)                         | 2 (8.7)                   |
| Tyrosine kinase inhibitors        | 19 (13.9)                       | 2 (8.7)                   |
| Imatinib or nilotinib (PDGFR)     | 11 (8.0)                        | 1 (4.3)                   |
| Ruxolitinib or tofacitinib (JAK)  | 8 (5.8)                         | 1 (4.3)                   |
| Cytotoxic therapy                 | 11 (8.0)                        | 1 (4.3)                   |
| Hydroxyurea                       | 6 (4.4)                         | 0                         |
| Methotrexate                      | 5 (3.6)                         | 1 (4.3)                   |
| Immunomodulatory therapy         | 13 (9.5)                        | 0                         |
| IFN-\(\alpha\)                   | 4 (2.9)                         | 0                         |
| Mycophenolate motefil             | 4 (2.9)                         | 0                         |
| Cyclosporine                      | 3 (2.2)                         | 0                         |
| Other immunomodulatory\(†\)      | 2 (1.5)                         | 0                         |
| Other\(^†\)                       | 3 (2.2)                         | 0                         |

\(^*\)Cohort that had no history of COVID or positive COVID test (does not include the COVID+ cohort).
\(^†\)Inhaled steroids and/or \(\beta\)-agonists.
\(^\dag\)Dupilumab (n = 2), omalizumab (n = 1), and liresentinumab (n = 1).
\(^\ddagger\)Intravenous immunoglobulin (n = 1) and lenalidomide (n = 1).
\(\ddagger\)Desmopresins (n = 1), montelukast (n = 1), romipolin (n = 1).

\(\ddagger\)JAK, Janus kinase; PDGFR, platelet derived growth factor receptor.

Values are \(n\) (%).

A total of 116 (72.5%) participants responded to the vaccination questions. The vaccination rate in the HESCOVID+ group was lower than that in the HESWELL group (71.4% vs 90.5%; \(P = .029\)). Three of the 15 HESCOVID+ vaccinated participants were immunized before their reported COVID-19 infection. Five of the 101 vaccinated participants reported an increase in eosinophil count or eosinophil-related symptoms after immunization. In only 1 case did this lead to a change in HES therapy (a transient increase in prednisone dose 2 weeks after the second dose of the Pfizer vaccine).

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Although encouraging, this study has limitations. As in any survey-based study, the reliability of the data is limited by the accuracy of patient reporting and bias can be introduced if one of the study outcomes (eg, COVID-19 infection) results in reduced response rates. Although the number of participants was small due to the rarity of HESs, the response rate was high (67.2%), and the demographic and clinical characteristics of the participants are comparable to those in the 604 participants currently or previously enrolled on the same natural history protocol. Moreover, chart review of the 78 survey nonresponders revealed 44 participants for whom data were available regarding COVID-19 infection over the entire study period identified only 2 additional cases of COVID-19 infection in 44 participants, neither of whom had a severe presentation. Finally, the variability in COVID-19 infection rates and the introduction of immunization during the study time
frame complicated selection of an appropriate database for comparison of infection and hospitalization rates, and, perhaps more important, the application of the findings to Omicron (and future variants) is uncertain. Despite these limitations, the findings from this study suggest that patients with HESs are at no greater risk of COVID-19 infection, complications from COVID, or adverse events following immunization with currently available COVID-19 vaccines.

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COVID-19 Assessment in HES

Dear research participant,

We are collecting information regarding experience with COVID-19 testing, symptoms and treatment in patients with hyper eosinophilia. In the following survey we will use “you” or “patient” to refer to the participant with hyper eosinophilia. Whether or not you have been diagnosed with confirmed COVID-19, we invite you to fill out this survey.

Filling out this survey should take no more than 5-10 minutes of your time. We may contact you again over the next year to gather additional information and/or send you additional surveys.

Note that this survey is best taken on a laptop or desktop computer in one sitting, as you will not be able to return to a partially completed survey.

Thank you for your participation!

---

**Assigned EOS number**

[EOS: #### (0001 - 1500)]

---

**If the patient is being assisted in completing this assessment, or if this assessment is being completed by another party, please specify relationship of this person to the patient**

- [ ] Not applicable
- [ ] Spouse or partner
- [ ] Parent
- [ ] Child
- [ ] Sibling
- [ ] Friend
- [ ] Other

---

**Specify other relationship**

---

**FIGURE E1.** RedCap survey questionnaires.
Patient information

If you are filling out this form for a family member or friend with HES, please try your best to fill the form out as accurately as possible. Hereafter "you" will refer to the patient in question. If you do not know the answer to a question please select "don't know" or "unknown."

1. Patient's current age

2. Country of residence
   - USA
   - Other

2a. Specify other country

2b. State of residence in the USA
   (e.g.: CA, MN, WA)

3. Gender
   - Male
   - Female
   - Non-binary/third gender
   - Other
   - Prefer not to say

3.1 Specify other gender

4. Race
   - White
   - Black
   - American Indian/Native Alaskan
   - Asian
   - Native Hawaiian/Pacific Islander
   - Unknown/NA
   - Other
   - Prefer not to say

4a. Specify other race

5. Ethnicity
   - Latino/Latina/Latino
   - Not-Latino/Latina/Latino
   - Unknown
   - Other
   - Prefer not to say

5a. Specify other ethnicity

6. Patient's weight

6. Or weight
   - Unknown/Prefer not to say

6a. Weight units
   - kg
   - lb
Confidential

---

7. Patient's height

[###]

7. Or height

- [ ] Unknown/Prefer not to say

7a. Height units

- [ ] cm
- [ ] inches

---

FIGURE E1. Continued
## Patient's HES Information

1. Date of HES diagnosis (year)
   - 2000
   - 2001
   - 2002
   - 2003
   - 2004
   - 2005
   - 2006
   - 2007
   - 2008
   - 2009
   - 2010
   - 2011
   - 2012
   - 2013
   - 2014
   - 2015
   - 2016
   - 2017
   - 2018
   - 2019
   - 2020
   - 2021
   - Other
   - Not applicable
   - Unknown

1a. Specify other year

---

2. List HES symptoms and health problems associated with HES experienced at the time of diagnosis

---

3. Currently taking medication for HES? (please include medications within the past month even if recently stopped)
   - Yes
   - No
   - Don't know

3a. Currently taking oral HES medications?
   - Yes
   - No

3a1. Please select all that apply
   - Hydroxyurea
   - Tyrosine kinase (e.g. imatinib, nilotinib, dasatinib)
   - JAK inhibitors (e.g., tofacitinib, ruxolitinib)
   - Methotrexate
   - Cellcept (mycophenolate mofetil)
   - Cyclosporine
   - Azathioprine
   - Oral Corticosteroids (e.g. prednisone, medrol)
   - Swallowed budesonide
   - Swallowed fluticasone
   - Other

3a1. Specify other oral HES medication(s)

---

3b. Currently receiving biologic or injectable medications?
   - Yes
   - No

---

**FIGURE E1.** Continued
3b1. Please select all that apply
- Benralizumab
- Dupilumab
- Omalizumab
- Reslizumab
- Mepolizumab
- Methotrexate inj
- Interferon alpha inj
- Other

3b1. Specify other biologic or injectable medication(s)

| 3c. Currently using inhaled medications? |
|-----------------------------------------|
| Yes                                     |
| No                                      |

3c1. Please specify all that apply
- Advair
- Albuterol
- Symbicort
- Dulera
- Flovent
- Quvar
- Other

3c1. Specify other inhaled medication(s)

| 3c2. If having used inhalers in the past month, have they been used regularly as prescribed? |
|---------------------------------------------------------------------------------------------|
| Yes                                                                                          |
| No                                                                                           |

4. Have you ever been diagnosed with any of these conditions?
   (indicate all that apply)
- Coronary artery disease
- Heart failure
- Heart rhythm abnormality
- High blood pressure
- History of stroke or heart attack
- Other heart problems
- Diabetes
- Asthma
- COPD (emphysema)
- Other lung disease
- Chronic kidney disease
- Chronic liver disease
- Other
- None of the above

4a. Please specify other

4b. Please specify if:
Other heart problems, other lung disease or chronic liver disease

| 4c. Currently taking any medications for the conditions indicated above? |
|------------------------------------------------------------------------|
| Yes                                                                    |
| No                                                                     |

4c1. Please list the medications being taken

5. Currently smoke cigarettes?
   - Yes
   - No
5a. How many cigarettes smoked? (1-50)

5b. [hes5a] cigarettes smoked per
   - Day
   - Week
   - Month

5c. Number of years smoking? (1-70)

6. Ever smoked cigarettes in the past?
   - Yes
   - No

6a. How many cigarettes smoked? (1-50)

6b. [hes6a] cigarettes smoked per
   - Day
   - Week
   - Month

6c. Number of years smoked? (1-70)

7. Currently vaporize other tobacco products?
   - Yes
   - No

7a. How many times? (1-50)

7b. [hes7a] times per
   - Day
   - Week
   - Month

8. Currently smoke anything else?
   - Yes
   - No

8a. Please specify what else

8b. How many times smoked? (1-50)

8c. [hes8a] times per
   - Day
   - Week
   - Month

8d. For how long been smoking [hes8a]?
   (months or years) (1-70)

FIGURE E1. Continued
FIGURE E1. Continued

Specify time unit

- Months
- Years
| Patient's current HES status (prior to COVID-19) |
|-----------------------------------------------|
| 1. Had any HES symptoms in the past month?     |
| ☐ Yes                                         |
| ☐ No                                          |
| 1a. Specify what symptoms were experienced    |
|                                              |
| 1b. How often have the symptoms occurred?     |
| ☐ Daily                                       |
| ☐ Often                                       |
| ☐ Sometimes                                   |
| ☐ Rarely                                      |
| 1c. How severe are the symptoms?              |
| ☐ Mild                                        |
| ☐ Moderate                                    |
| ☐ Severe                                      |
| 2. Had to change medications to control HES symptoms or eosinophil counts in the past 3 months? |
| ☐ Yes                                         |
| ☐ No                                          |
| 2a. Please specify                            |
|                                              |
### Patient COVID-19 Screening Questions

1. Did patient or doctor suspect any COVID-19 infection?  
   - [ ] Yes  
   - [x] No

1.1 Did you report this episode in the previous survey?  
   - [ ] Yes  
   - [x] No

1a. What was the approximate date when this suspicion arose?  

2. Did the patient have any known exposure to coronavirus?  
   - [ ] Yes  
   - [ ] No  
   - [ ] Don't know

2a. Exposed how?  
   (select all that apply)  
   - [ ] Occupational exposure  
   - [ ] Travel  
   - [ ] Household contact  
   - [ ] Other

   [ ] Please specify other

2b. What was the approximate date of the exposure?  

3. Was the patient tested for COVID-19?  
   - [ ] Yes  
   - [x] No

3a. Reason for testing?  
   - [ ] Known exposure  
   - [ ] Symptomatic  
   - [ ] Occupational screening program  
   - [ ] Other

   [ ] Specify other

3a1. If patient was symptomatic, how many days were symptoms experienced before being tested?  
   - [ ] 0 - 45 days

3b. What type of test was used?  
   (select all that apply)  
   - [ ] Nasal swab (PCR)  
   - [ ] Antibody test (blood test)  
   - [ ] Other

   [ ] Specify other

3c. What was the date of the first test?  

3d. Were any of the tests positive for COVID-19?  
   - [ ] Yes  
   - [ ] No  
   - [ ] Don't know
3d1. Which test(s) was/were positive for COVID-19? (select all that apply)
- Nasal swab (PCR)
- Antibody test (blood test)
- Other
- Don't know

3d1. Specify other

Thank you for participating. We may make contact in the future for a similar survey.
**COVID-19 Questions**

1. If suspected or confirmed to have COVID-19, which of the following symptoms were experienced?

| Symptom                          | Mild | Moderate | Severe | No  | Don’t know |
|----------------------------------|------|----------|--------|-----|------------|
| a. Fatigue                       | ☐    | ☐        | ☐      | ☐   | ☐          |
| b. Fever                         | ☐    | ☐        | ☐      | ☐   | ☐          |
| c. Chills                         | ☐    | ☐        | ☐      | ☐   | ☐          |
| d. Headache                      | ☐    | ☐        | ☐      | ☐   | ☐          |
| e. Sore throat                    | ☐    | ☐        | ☐      | ☐   | ☐          |
| f. Difficulty breathing          | ☐    | ☐        | ☐      | ☐   | ☐          |
| g. Malaise/Weakness              | ☐    | ☐        | ☐      | ☐   | ☐          |
| h. Muscle aches                  | ☐    | ☐        | ☐      | ☐   | ☐          |
| i. Nausea                        | ☐    | ☐        | ☐      | ☐   | ☐          |
| j. Vomiting                      | ☐    | ☐        | ☐      | ☐   | ☐          |
| k. Abdominal Pain                | ☐    | ☐        | ☐      | ☐   | ☐          |
| l. Loss of appetite              | ☐    | ☐        | ☐      | ☐   | ☐          |
| m. Diarrhea                      | ☐    | ☐        | ☐      | ☐   | ☐          |
| n. Runny nose or congestion      | ☐    | ☐        | ☐      | ☐   | ☐          |
| o. Loss of smell                 | ☐    | ☐        | ☐      | ☐   | ☐          |
| p. Loss of taste                 | ☐    | ☐        | ☐      | ☐   | ☐          |
| q. Confusion                     | ☐    | ☐        | ☐      | ☐   | ☐          |
| r. Other                         | ☐    | ☐        | ☐      | ☐   | ☐          |

1b. What was the highest temperature experienced?  

[° ° °]

1b. Temperature units  

- ☐ Celsius  
- ☐ Fahrenheit

1r. Specify other

2. Did the patient visit an emergency room for suspected COVID-19 infection?  

- ☐ Yes  
- ☐ No

2a. Was the patient hospitalized?  

- ☐ Yes  
- ☐ No

2a1. How many days was the patient hospitalized for?  

[1 - 99]

2a2. Placed on nasal or high flow oxygen?  

- ☐ Yes  
- ☐ No

2a3. Placed on non-invasive ventilation (BiPAP)?  

- ☐ Yes  
- ☐ No

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**FIGURE E1.** Continued
2a4. Treated in the intensive care unit (ICU)?
   ○ Yes
   ○ No

2a5. Intubated/placed on a respirator?
   ○ Yes
   ○ No

3. Were any regular HES medications changed because of a suspected or proven COVID19 diagnosis?
   ○ Yes
   ○ No
   ○ Unknown

3a. Please specify what was stopped or changed

4. Did the patient develop any complications of COVID19 infection?
   (such as kidney problems, heart problems, blood clots, or bacterial infections)
   ○ Yes
   ○ No

4a. Select all that apply
   □ Kidney problems (e.g. kidney failure or need for dialysis)
   □ Heart problems (e.g. myocarditis (inflammation of the heart) or heart failure)
   □ Blood clots
   □ Bacterial infection
   □ Other

4a. Specify other

5. Did the patient receive any experimental treatment?
   ○ Yes
   ○ No

5a. Please select all that apply
   □ Azithromycin
   □ Chloroquine
   □ Hydroxychloroquine
   □ Favipiravir
   □ Intravenous immunoglobulin (IVIG)
   □ Lopinavir/ritonavir
   □ Oseltamivir
   □ Remdesivir
   □ Ruxolitinib (JAK inhibitor)
   □ Steroids (such as prednisone or dexamethasone)
   □ Tocilizumab (IL-6 inhibitor)
   □ Plasma from recovered patients
   □ Other

5a. Specify other

5b. Was this treatment received as part of a clinical trial?
   ○ Yes
   ○ No
   ○ Unknown

6. Did COVID-19 symptoms resolve?
   ○ Yes
   ○ No
6a. What symptoms are still being experienced?

6b. How many days in total did the patient experience symptoms?

(0 - 99)
Confidential

Vaccination Status

Please complete the Vaccination Status survey.

Thank you!
**Vaccination Status**

Have you been vaccinated against SARS-CoV-2?
- ☐ Yes
- ☐ No

a. Which vaccine did you receive?
- ☐ Moderna
- ☐ Pfizer-BioNTech
- ☐ J&J / Janssen
- ☐ AstraZeneca
- ☐ Other
- ☐ Don't know

b. Specify other

b. When did you receive your first vaccine?

OR
- ☐ Don't know

b. Don't know

c. Have you or will you receive a second dose?
- ☐ Yes
- ☐ No

c1. Date of 2nd dose

OR
- ☐ Don't know

c1. Don't know

d. Did you have any adverse reactions to one or both doses?
- ☐ Yes
- ☐ No
  (If 'Yes', indicate severity of reactions experienced.)

| Adverse Reaction                          | No | Mild | Moderate | Severe |
|-------------------------------------------|----|------|----------|--------|
| i. Redness at the injection site          | ☐  | ☐    | ☐        | ☐      |
| ii. Pain at the injection site            | ☐  | ☐    | ☐        | ☐      |
| iii. Swelling at the injection site       | ☐  | ☐    | ☐        | ☐      |
| iv. Fever                                 | ☐  | ☐    | ☐        | ☐      |
| v. Chills                                 | ☐  | ☐    | ☐        | ☐      |
| vi. Muscle/joint/body aches               | ☐  | ☐    | ☐        | ☐      |
| vii. Headache                             | ☐  | ☐    | ☐        | ☐      |
| viii. Fatigue                             | ☐  | ☐    | ☐        | ☐      |
| ix. Nausea                                | ☐  | ☐    | ☐        | ☐      |
| x. Other                                  | ☐  | ☐    | ☐        | ☐      |

x. Specify other

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**FIGURE E1.** Continued
| Question                                                                 | Yes | No  |
|-------------------------------------------------------------------------|-----|-----|
| Did you experience worsening of your eosinophil count or eosinophil-related symptoms after receiving either dose of the vaccine? |     |     |
| e1. After which dose?                                                   |     |     |
| e2. What got worse?                                                     |     |     |
| e3. Did you have an eosinophil count checked?                           |     |     |
| e3a. Please provide the absolute eosinophil count OR WBC count and % eosinophils |     |     |
| (We may contact you to obtain these results.)                           |     |     |
| f. Did you stop, start or change the dose of any of your eosinophil therapies in the 2 weeks BEFORE you got either dose of the vaccine? |     |     |
| f1. After which dose?                                                   |     |     |
| f2. Which medication?                                                   |     |     |
| f3. Please describe the change                                          |     |     |
| g. Did you stop, start or change the dose of any of your eosinophil therapies in the 2 weeks AFTER you got either dose of the vaccine? |     |     |
| g1. After which dose?                                                   |     |     |
| g2. Which medication?                                                   |     |     |
| g3. Please describe the change                                          |     |     |
| Do you plan to be vaccinated?                                           |     |     |

**FIGURE E1.** Continued
a. Why?

Are you currently working?  
- Yes  
- No

a. Are you currently working outside of your home?  
- Yes  
- No

a1. When did you start working outside of your home after the start of the COVID-19 pandemic?

OR

a1. Not applicable  
(Have been working outside of my home throughout the pandemic)
**FIGURE E1.** Continued

| During 2020, what precautions did you follow in an indoor setting (e.g. grocery store, restaurant)? | All of the time | Most of the time | Some of the time | Never |
|---|---|---|---|---|
| a. Wear a mask | | | | |
| b. Stay 5 feet away from people not part of your household | | | | |
| c. Wash/sanitize hands frequently | | | | |
| d. Avoid crowds/large gatherings | | | | |
What precautions do you CURRENTLY follow in an indoor setting (e.g. grocery store, restaurant)?

| Precaution                                      | All of the time | Most of the time | Some of the time | Never |
|-------------------------------------------------|-----------------|------------------|------------------|-------|
| a. Wear a mask                                  | ○               | ○                | ○                | ○     |
| b. Stay 6 feet away from people not part of your household | ○               | ○                | ○                | ○     |
| c. Wash/sanitize hands frequently               | ○               | ○                | ○                | ○     |
| d. Avoid crowds/large gatherings                | ○               | ○                | ○                | ○     |
FIGURE E2. Geographic distribution of survey responders living in the United States. The number of participants by state is shown for all US survey responders (n = 151) in blue and for only the HESCVID+ participants (n = 21) in red. Nine additional participants resided outside of the continental United States.