A Comprehensive Characterization of Post-COVID-19 Syndrome in a Diverse Population

ALEXANDRA S. LEE

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Sean N. Parker Center for Allergy & Asthma Research
Stanford University School of Medicine

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• As of September 17, 2021, SARS-CoV-2 is attributed to at least 226 million infections and 4.6 million deaths worldwide (COVID-19 Dashboard, WHO. 2021)

• Post-Acute Sequelae of SARS-CoV-2 infection (PASC) includes fatigue, shortness of breath (SOB), and sleep disturbances (Collins, NIH. 2021; Nasserie et al., JAMA Netw Open. 2021)

• PASC affects a diverse range of patients (Lund et al., Lancet Infect Dis. 2021)

• There is no clear definition and a lack of systematic evaluations on PASC’s development, persistence, and relationship with treatments (Phillips et al., N Engl J Med. 2021)
Methods

• Adult inpatients and outpatients with a positive SARS-CoV-2 result by RT-PCR from March 11, 2020, to February 17, 2021, were enrolled

• Participants were seen for in-person visits at diagnosis and every 1-3 months

• Visits included nasal swabs, blood draws, and symptom questionnaires

• Nasal swabs were screened for SARS-CoV-2 reinfection by RT-PCR

• Blood samples were tested for presence of SARS-CoV-2 antigens, including the nucleocapsid (N) and spike (S) proteins, and their respective antibodies

Source: Jason McLellan/University of Texas at Austin
(Science 2020 DOI: 10.1126/science.abb2507)

Methods

• Time to first resolution of all symptoms (TTFR): time from COVID-19 diagnosis to the first visit where no symptoms were documented

• Time to sustained symptom resolution (TTSR): time from COVID-19 diagnosis to the visit where participants reported resolution of all symptoms and no recurring symptoms for at least 1 month or longer until the end of the study period

Source: BMJ Journals – COVID-19 Podcasts
blogs.bmj.com/covid-19/2020/05/14/bmjs-covid-19-podcasts
• 617 of 627 participants included for analysis

• 105 participants were enrolled for ≥6 months post-diagnosis

• 16 participants deceased as of March 19, 2021, 9 had critical COVID disease

• There were no recurrent COVID-19 infections per RT-PCR testing at every visit as of March 2021

• Underlying lung disease (asthma or COPD) was associated with longer TTFR/TTSR
Results

Three months after diagnosis:
- 57.5% reported persistent symptoms (n=179)
- Fatigue (35.2%), headache (26.8%), myalgia (24.6%)

Six months … :
- 40% reported persistent symptoms (n=105)
- Fatigue (21.9%), headache (17.1%), myalgia (16.2%)

12 months … :
- Four reported upper respiratory, neurologic, and constitutional symptoms (n=21)

- Number of symptoms increased after the second month in participants with moderate, severe, or critical disease
- 83 symptom recurrences after TTFR
- Frequently reported co-occurring symptoms include (1) ageusia and anosmia (2) cough and SOB (3) chills, fever, fatigue, headache, SOB, myalgia, cough

Figure 2

Confidential
Results

- More severe disease at baseline associated with higher N and S antigen concentrations
- Higher anti-N IgG concentrations at first week after diagnosis were associated with shorter TTSR
- More severe disease at diagnosis was associated with higher IgG antibody levels
- In general, IgG increased in month one before significantly decreasing
- Higher N antigen levels in the first week after diagnosis were associated with longer TTFR but not TTSR
- Antibodies remained positive for most participants up to nine months after diagnosis
- S antigen levels in the first week were not significantly associated with TTFR or TTSR
- IV Remdesivir use had no effect on TTSR

Discussion

- All disease severities have a similar risk of PASC
- Prolonged inflammation and prolonged low-level infection may be linked to PASC
- Higher anti-nucleocapsid antibody levels at diagnosis were significantly associated with faster sustained symptom resolution
- Anti-N IgG levels may be an independent predictor of COVID-19 symptom duration
- Antibodies may be correlated with some protection against COVID-19 for a prolonged period after initial illness
Podium to practice takeaways:

• 40% of patients reported symptoms at six months after diagnosis
• No significant difference in symptom duration among severe vs. mild disease
• Comorbid lung disease was associated with longer duration of symptoms
• Remdesivir use had no effect on TTSR
• Higher baseline anti-N IgG was associated with shorter TTSR
• Antibodies to SARS-CoV-2 persisted for at least 9 months after diagnosis

Conclusion

Future Direction

• Larger study population and longer follow-up period
• Long-term control group without SARS-CoV-2 infection for comparison
• Exploration of N protein in vaccine development for possible PASC prophylaxis
• Exploration of viral RNA in the small bowel and development of prolonged symptoms

Question 1

A patient has comorbid lung disease, but they also have high S antigen levels within the first week after diagnosis. These observations suggest which of the following for the patient?

A) Greater risk of prolonged symptoms, due to comorbid lung disease
B) No increased risk of prolonged symptoms, due to comorbid lung disease
C) Greater risk of prolonged symptoms, due to S antigen levels
D) No increased risk of prolonged symptoms, due to S antigen levels


Question 2

A patient experiences persistent anosmia 6 months after COVID-19 diagnosis. Which of the following is most likely a co-occurring symptom?

A) Ageusia
B) Cough
C) SOB
D) Myalgia

Acknowledgements

Clinical and Research Teams at the Sean N. Parker Center for Allergy & Asthma Research:

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Angela Rogers, Monica Vel, and Samuel Yang

Thank you!

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The International Cannabis KAP (Knowledge, Attitudes and Practice) Allergist Survey Study

ACAAI Conference 2021, New Orleans

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https://cannaresearchfoundation.org/

Disclosures

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Background

- Knowledge among physicians is lagging behind patient usage.
- Many physicians are unaware of the endocannabinoid system and its impact on disease states.
- The qualifying conditions for a medical cannabis card is also unknown to many physicians.
- Allergists should be well-versed about different routes of administration in order to counsel patients more effectively.

Background (2)

- If cannabis use is not found contraindicated in a patient, counseling should include appropriate methods of consumption.
  - Especially because patients are reluctant to initiate conversations.
  - A study of allergic/asthmatic patients showed only 37.5% wanted to talk to their physician about cannabis.
  - Almost 70% used cannabis for pain & 22% had a medical card.
  - 54.3% smoked cannabis and 35.2% vaped.
  - And, 19.3% reported coughing, 6% wheeze, & 7% shortness of breath.
  - Plus, of those with uncontrolled asthma, 50% SMOKED cannabis.

Zeiger, JS et al. (2021) Ann Allergy Asthma Immunol 126 (401-410)
Knowledge-Attitudes-Practice (KAP)

- Early theories: Attitudes directly guide practice.
- New theories: Intervening variables (i.e. mediators) exist in the relationship. Attitudes is a mediator that explains the underlying mechanism of the relationship between Knowledge (IV) and Cannabis Practice (DV)


Objectives

To test the knowledge-attitudes-practice paradigm in ACAAI members.

This cross-sectional survey is part of a larger international collaboration with the Canadian Society of Allergy and Clinical Immunology and the European Academy of Allergy and Immunology.
Consort Diagram

1. English-speaking allergists who see patients contacted through the ACAAI
2. Enrollment on RedCap from 6/10/21 to 7/21/21 (N=215)
3. Completed surveys (N=193)

Questionnaire

1. Demographics.
2. Have you ever used cannabis?
   Yes or No.
4. Attitudes about cannabis: 13 questions.
5. Clinical practice regarding cannabis:
   Intake forms, verbally ask about use, cannabis allergy, comfortable discussing cannabis with patients.
**Methods: Cluster Analysis**

1. Cluster analysis on attitudes questions.
   - Divides data into smaller groups with similar characteristics (think of the sorting hat in Harry Potter).
2. SPSS Two Step cluster analysis was used with BIC goodness-of-fit to determine final cluster solution.
3. Post-hoc tests used to determine cluster validity.

**Methods: Knowledge**

1. Seven questions, each with a single right answer.
2. Scores summed and total scores ranged 0-7.
3. Chi-square was used to determine whether there were differences in knowledge scores and practice by attitudes clusters.
Results (n=193)

- Male: 59.6%
- 57-64 years old: 43.5%
- Ever used cannabis: 34.4%
- Even seen a patient with cannabis allergy: 32.6%

Patients and cannabis use

- Never ask patients about use: 22.0%
- Cannabis use not on Intake form: 61.2%
- Uncomfortable speaking to patients: 32.2%
**Attitudes Clusters**

- Attitudes-1 less supportive than Attitudes-2.
- Significant difference between the two groups on 10/13 questions.

**Knowledge by Attitudes Cluster**

- Total (n=183)
- Attitudes-2 (n=75)
- Attitudes-1 (n=108)

10 participants marked preferred not to answer
## Attitudes by Cannabis Use

**Ever Used Cannabis *\(^{*}\)**

<table>
<thead>
<tr>
<th>Attitudes</th>
<th>Attitudes Clusters [N (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Attitudes-1 (n=100)</td>
</tr>
<tr>
<td>Yes</td>
<td>27 (27.0)</td>
</tr>
<tr>
<td>No</td>
<td>73 (73.0)</td>
</tr>
</tbody>
</table>

*Chi-square, p<0.001; Missing participants marked preferred not to answer

## Attitudes by Comfort Talking to Patients

**Are you comfortable talking to your patients about cannabis? *\(^{*}\)**

<table>
<thead>
<tr>
<th>Attitudes</th>
<th>Attitudes Clusters [N (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Attitudes-1 (n=108)</td>
</tr>
<tr>
<td>Yes</td>
<td>64 (59.3)</td>
</tr>
<tr>
<td>No</td>
<td>19 (17.6)</td>
</tr>
<tr>
<td>Unsure</td>
<td>25 (23.1)</td>
</tr>
</tbody>
</table>

*Chi-square, p<0.05; 10 participants marked preferred not to answer
Knowledge by Allergist Cannabis Use

- Total (n=165)
- Yes (n=63)
- No (n=102)

Missing participants marked preferred not to answer

Knowledge by Comfortable Patient Discussions

- Total (n=183)*
- Yes (n=124)
- No (n=27)
- Unsure (32)

*Ten participants declined to answer this question
Knowledge and attitudes separately impact practice

- Allergists who used cannabis had significantly more supportive attitudes toward cannabis & significantly more knowledge about cannabis.
- Allergists with more knowledge about cannabis and more supportive attitudes toward cannabis were significantly more likely to feel comfortable speaking to patients about cannabis.

We thank the allergists who participated in The International Canna KAP Allergists Survey.

We also want to thank ACAAI, CSACI, and EAACI for their support.
One vs Two-Day Aspirin Desensitization in Aspirin Exacerbated Respiratory Disease: A Quality Improvement Project

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Disclosures

• There is nothing to disclose.
Background

• Aspirin-exacerbated respiratory disease (AERD) is a chronic inflammatory condition of the sinuses and lungs.
• Formerly known as Samter’s Triad.
• Aspirin hypersensitivity is a common condition.
• The cause of mucosal inflammation of AERD is not fully understood.

Background

• AERD is diagnosed and treated medically in a stepwise approach that includes aspirin challenge and desensitization.
• Variety of protocols that differ in the medications used, doses, and time course for the ASA desensitization.
Study Objective

• To assess the implementation of a one-day versus a two-day aspirin desensitization protocol in patients with aspirin-exacerbated respiratory disease (AERD).

Methods

• AERD Patients: Mayo Clinic Florida
• A retrospective chart review was performed, and data was uploaded to REDCap.
Methods

- Pre-/post-intervention, quality improvement design to compare the completion rates, reaction rates, estimated costs and time reduction of a two versus one-day aspirin desensitization.
  - Pre-intervention: November 2017-December 2020
  - Post-intervention: January-June 2021
- Success defined by tolerance of 325 mg ASA dose.

Methods

- The cost for each desensitization was estimated based on 2017-2020 US Medicare standards.
- We included the pre-desensitization variables:
  - Pre-bronchodilator forced expiratory volume in one second (FEV1)
  - Urinary leukotriene E4 (LTE-4)
  - Absolute eosinophil count (AEC)
  - Total IgE
Methods

• Descriptive statistics were performed in all variables.
• Categorical variables were summarized as frequencies and percentages, numerical variables were summarized as means and standard deviations.
• To determine statistical difference between groups we used Fisher’s Exact Test for categorical variables, and Mann Whitney U tests for numerical variables.

Table 1. Two versus one-day aspirin desensitization protocol.

<table>
<thead>
<tr>
<th>Day One</th>
<th>Day One</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>Medication and Dose</td>
</tr>
<tr>
<td>0900</td>
<td>Ketorolac-1 spray in 1 nostril*</td>
</tr>
<tr>
<td>0930</td>
<td>Ketorolac-2 sprays in each nostril</td>
</tr>
<tr>
<td>1000</td>
<td>Ketorolac-3 sprays in each nostril</td>
</tr>
<tr>
<td>1100</td>
<td>Aspirin-60 mg orally</td>
</tr>
<tr>
<td>1200</td>
<td>Aspirin-60 mg orally</td>
</tr>
<tr>
<td>1300</td>
<td>Instructions and discharge</td>
</tr>
</tbody>
</table>

Day Two:

<table>
<thead>
<tr>
<th>Time</th>
<th>Medication and Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0800</td>
<td>Aspirin: 150 mg orally</td>
</tr>
<tr>
<td>1100</td>
<td>Aspirin: 325 mg orally</td>
</tr>
<tr>
<td>1400</td>
<td>Instructions and discharge</td>
</tr>
</tbody>
</table>

Estimated Cost: $1597.81
Estimated Time: 13 hours

*Mix 2 mL of Ketorolac (60 mg/2 mL) with 2.75 mL preservative-free normal saline. This mixture is in a spray bottle that delivers 0.1 mL per spray ~1.26 mg of Ketorolac mixture.
Results: Demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>One-Day Protocol (n=5)</th>
<th>Two-Day Protocol (n=15)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female Sex</td>
<td>N (%)</td>
<td>N (%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2 (40)</td>
<td>9 (60)</td>
<td>.61</td>
</tr>
<tr>
<td>Age, in years, Mean/SD</td>
<td>45±20</td>
<td>57±12</td>
<td>.23</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>5 (100)</td>
<td>11 (86.6)</td>
<td></td>
</tr>
<tr>
<td>Non-White</td>
<td>0 (0)</td>
<td>2 (13.3)</td>
<td>.55</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never Smoker</td>
<td>2 (40)</td>
<td>11 (73.3)</td>
<td></td>
</tr>
<tr>
<td>Former Smoker</td>
<td>2 (40)</td>
<td>4 (26.7)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (20)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Components of AERD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic Rhinitis with Nasal Polyva</td>
<td>5 (100)</td>
<td>11 (86.7)</td>
<td>1</td>
</tr>
<tr>
<td>Asthma</td>
<td>5 (100)</td>
<td>15 (100)</td>
<td>1</td>
</tr>
<tr>
<td>Adverse Reaction to ASA or NSAIIDs</td>
<td>3 (60)</td>
<td>7 (46.7)</td>
<td>1</td>
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<tr>
<td>Body Mass Index (BMI), Mean/SD</td>
<td>25±2±2.2</td>
<td>28±1±2.2</td>
<td>.42</td>
</tr>
<tr>
<td>Number of Polypropylene Before</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desensitization, Mean/SD</td>
<td>3.8±1.78</td>
<td>2.8±1.56</td>
<td>.26</td>
</tr>
<tr>
<td>Time Between Last Polypropylene and</td>
<td>39.2±25.9</td>
<td>196±35±13</td>
<td>.025</td>
</tr>
<tr>
<td>Desensitization (Days), Mean/SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-desensitization parameters, Mean/SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1 (%)</td>
<td>83±18±3</td>
<td>76±16±9</td>
<td>.6</td>
</tr>
<tr>
<td>LTE-4 (ng/ml)</td>
<td>302±109</td>
<td>106±1154</td>
<td>.2</td>
</tr>
<tr>
<td>Absolute Eosinophil Count (cells/mL)</td>
<td>572±435</td>
<td>686±445</td>
<td>.74</td>
</tr>
<tr>
<td>Total IgE (AUS)</td>
<td>186±85</td>
<td>735±1028</td>
<td>.5</td>
</tr>
</tbody>
</table>

Results: Desensitization Completion Rates and the Number of Reactions Requiring Treatment

- **P=1**
- **P=0.14**

Graphs showing completion rates and number of reactions requiring treatment for One-Day and Two-Day desensitization protocols.
Results: Mean Follow-Up Time, Cost and Time Reduction

- Mean Follow-Up Time in Months
  - One-Day (n=5)
  - Two-Day (n=15)

**Estimated Post-Intervention Cost Reduction:** $762

**Estimated Intervention Time Reduction:** 6 hours

Implications for Practice

I. In this cohort, the implementation of a one-day aspirin desensitization protocol showed similar rates of completion to a two-day protocol without an increase of adverse drug reactions.

II. A one-day protocol yielded lower associated costs with an estimated cost reduction of $762 and time reduction of 6 hours.

III. Further prospective studies are necessary to confirm these findings.
References


Thank you!
Characteristics And Outcomes Among Immunodeficiency Patients Hospitalized With SARS-CoV-2 In The New York City Area

John Accarino, M.D.

Immunodeficient Patients with COVID-19

- “A possible role for B cells in COVID-19? Lesson from patients with agammaglobulinemia” ¹
- “Coronavirus disease 2019 in patients with inborn errors of immunity: An international study” ²
- “Preexisting Autoantibodies to Type I IFNs Underlie Critical COVID-19 Pneumonia in Patients with APS-1” ³

Immunodeficient Patients with COVID-19

• “COVID-19 in patients with primary and secondary immunodeficiency: The United Kingdom experience”
  • 60 with primary immunodeficiency (PID)
  • 33 with symptomatic secondary immunodeficiency (SID)
  • 7 with other inborn errors of immunity including autoinflammatory diseases and C1 inhibitor deficiency

• “In comparison to the general population, adult patients with PID and symptomatic SID display greater morbidity and mortality from COVID-19”

What outcomes can we expect for hospitalized patients with PID/SID and COVID-19?

What outcomes can we expect for hospitalized patients with PID/SID and COVID-19?

How does this compare to the hospitalized general population?

Inclusion Criteria – I. PCR Positive & Hospitalized

• Admitted Patients

• Confirmed SARS-CoV-2
Inclusion Criteria – II. Immunodeficiency Diagnoses

• Primary Immunodeficiency
  • Inborn errors of immunity 2019 classification table compiled by the International Union of Immunological Societies (IUIS) 5

• Secondary Immunodeficiency
  • Agency for Healthcare Research and Quality (AHRQ) QI™
  • ICD-10-CM/PCS Specification Version 6.0
  • Immunocompromised State Diagnosis and Procedure Codes 6

(5) Inborn errors of immunity committee (iei) » iuis. IUIS. https://iuis.org/committees/iei/

SARS-CoV-2 in NYC Area - Demographics

<table>
<thead>
<tr>
<th>Comparison of Data Sets</th>
<th>Immunodeficiency Population</th>
<th>General Population Richardson et al7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Hospitalizations</td>
<td>214</td>
<td>5700</td>
</tr>
<tr>
<td>Hospitals</td>
<td>12 hospitals in NYC, Long Island, and Westchester County</td>
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<td>March 1, 2020-December 1, 2020</td>
<td>March 1,2020-April 4, 2020</td>
</tr>
<tr>
<td>Inclusion Criteria</td>
<td>Hospitalized Patients PCR+ for SARS-CoV-2</td>
<td>Hospitalized Patients PCR+ for SARS-CoV-2</td>
</tr>
<tr>
<td></td>
<td>ICD10 for PID and/or SID</td>
<td></td>
</tr>
</tbody>
</table>

Median Age (IQR)
- Immunodeficiency Population: 67 years (54-78)
- General Population: 63 years (52-75)

### SARS-CoV-2 in NYC Area - Demographics

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<td>Hospitalized Patients PCR+ for SARS-CoV-2</td>
</tr>
<tr>
<td>Median Age (IQR)</td>
<td>67 years (54-78)</td>
<td>63 years (52-75)</td>
</tr>
<tr>
<td>Gender (%)</td>
<td>Male – 122 (57%) Female – 92 (43%)</td>
<td>Male – 3437 (60.3%) Female – 2263 (39.7%)</td>
</tr>
</tbody>
</table>


### SARS-CoV-2 in NYC Area - Demographics

<table>
<thead>
<tr>
<th>Race</th>
<th>Immunodeficiency Population</th>
<th>General Population Richardson et al(^7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. Respondents</td>
<td>208</td>
<td>5441</td>
</tr>
<tr>
<td>White</td>
<td>111 (53.4%)</td>
<td>2164 (39.8%)</td>
</tr>
<tr>
<td>Black/African-American</td>
<td>36 (17.3%)</td>
<td>1230 (22.6%)</td>
</tr>
<tr>
<td>Asian</td>
<td>14 (6.7%)</td>
<td>473 (8.7%)</td>
</tr>
<tr>
<td>Other/Multiracial</td>
<td>47 (22.6%)</td>
<td>1574 (28.9%)</td>
</tr>
</tbody>
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<tbody>
<tr>
<td>No. Respondents</td>
<td>208</td>
<td>5441</td>
</tr>
<tr>
<td>White</td>
<td>111 (53.4%)</td>
<td>2164 (39.8%)</td>
</tr>
<tr>
<td>Black/African-American</td>
<td>36 (17.3%)</td>
<td>1230 (22.6%)</td>
</tr>
<tr>
<td>Asian</td>
<td>14 (6.7%)</td>
<td>473 (8.7%)</td>
</tr>
<tr>
<td>Other/Multiracial</td>
<td>47 (22.6%)</td>
<td>1574 (28.9%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. Respondents</td>
<td>185</td>
<td>5341</td>
</tr>
<tr>
<td>Hispanic</td>
<td>35 (18.9%)</td>
<td>1230 (23.0%)</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>150 (81.1%)</td>
<td>4111 (77.0%)</td>
</tr>
</tbody>
</table>


Comorbidities of Population

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Count, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease</td>
<td>104, 48.8%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>86, 40.4%</td>
</tr>
<tr>
<td>Chronic kidney disease stages I-IV</td>
<td>74, 34.7%</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>52, 24.4%</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>30, 14.1%</td>
</tr>
<tr>
<td>Chronic gastrointestinal disease</td>
<td>7, 3.3%</td>
</tr>
<tr>
<td>No other comorbidities</td>
<td>41, 19.2%</td>
</tr>
</tbody>
</table>
Immunodeficiencies of Population

- PID (6%)
- SID (78%)
- Both PID and SID (5%)
- Immunodeficiency, Unspecified (11%)

Examples of Included Primary Immunodeficiency Diagnoses

- Humoral Defects:
  - CVID (4)
  - Defects of Specific Antibody Subtypes (10)
- Defects in the Complement System (1)
- DiGeorge Syndrome (1)
- Febrile Neutrophilic Dermatosis (3)
Examples of Included Secondary Immunodeficiency Diagnoses

- Hematologic/Oncologic Diagnoses:
  - Myelodysplastic Disease (49)
  - Lymphoid/Hematopoietic Neoplasms (35)
  - Histiocytosis Syndromes (19)
- H/o Solid Organ or Stem Cell Transplant (63)
- Stage 5 CKD/End-Stage Renal Disease (52)
- Protein-Calorie Malnutrition (30)
- Leukopenia:
  - Chemotherapy or Other Drug-Induced (3)
  - Unspecified (5)
  - Immunocompromising Infection (3)

SARS-CoV-2 Outcomes in NYC Area

<table>
<thead>
<tr>
<th>Variable</th>
<th>Immunodeficient Population</th>
<th>General Population Richardson et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalizations</td>
<td>214</td>
<td>5700</td>
</tr>
<tr>
<td>Total discharged alive or dead patients at end of study</td>
<td>214 (100%)</td>
<td>2634 (46%)</td>
</tr>
</tbody>
</table>

### SARS-CoV-2 Outcomes in NYC Area

<table>
<thead>
<tr>
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<td>214 (100%)</td>
<td>2634 (46%)</td>
</tr>
<tr>
<td>Length of Stay – Median days hospitalized (IQR)</td>
<td>8 (4-14) – Discharged Alive 12 (6-20.5) – Expired</td>
<td>3.9 (2.4-6.7) – Discharged Alive 4.8 (2.3-7.4) – Expired</td>
</tr>
</tbody>
</table>

### SARS-CoV-2 Outcomes in NYC Area

<table>
<thead>
<tr>
<th>Variable</th>
<th>Immunodeficient Population</th>
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</tr>
</thead>
<tbody>
<tr>
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</tr>
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<td>8 (4-14) – Discharged Alive 12 (6-20.5) – Expired</td>
<td>3.9 (2.4-6.7) – Discharged Alive 4.8 (2.3-7.4) – Expired</td>
</tr>
<tr>
<td>Invasive Mechanical Ventilation</td>
<td>58 (27.2%)</td>
<td>320 (12.2%)</td>
</tr>
<tr>
<td>Renal Replacement</td>
<td>33 (15.5%)</td>
<td>81 (3.2%)</td>
</tr>
</tbody>
</table>

“Podium to Practice” Takeaways

• Hospitalized immunodeficient patients may have worse clinical outcomes compared to the community from which they were drawn

• More to come…
  • Effects of multiple SIDs vs. single SID
  • Effects due to underlying ID vs. secondary comorbidities
  • Analysis of vital signs and labs throughout admission
References


Inborn errors of immunity committee (iei) » uuis. iuis. https://iuis.org/committees/iei/


Acknowledgements

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Artemio Jongco, MD, PhD, MPH
Christopher League, PhD
Jane Cerise, PhD
Determinants of Esophageal Eosinophilia and Eosinophilic Esophagitis in Children with Inflammatory Bowel Disease

RYAN EID, MD PGY V
EMILY MCGOWAN MD, PHD
UNIVERSITY OF VIRGINIA
DIVISION OF ALLERGY AND IMMUNOLOGY
DECEMBER 11TH, 2020

Background

- Eosinophilic esophagitis (EoE) and inflammatory bowel disease (IBD) are both chronic conditions that are increasing in prevalence worldwide.

- While the diagnosis of EoE requires the exclusion of other causes of esophageal eosinophilia (EE), the dual-diagnosis of IBD/EoE has recently become a topic of interest.

- Several studies have demonstrated that EoE and IBD can co-exist in the same individual and that the prevalence of IBD/EoE is rising more rapidly than either single disease alone.\textsuperscript{1-4}

Fan et al, Moore et al, Mintz et all, Limketkai et al
Objective/Hypothesis

- **Objective**: Examine the prevalence of EE and EoE in the pediatric IBD population at the University of Virginia (UVA) and identify clinical characteristics associated with co-occurring disease.

- **Hypothesis**: The prevalence of EE and EoE will be higher in the pediatric IBD population than in the general pediatric population. Atopy will be associated with a risk of concomitant EE/IBD.

Methods

- We performed a retrospective study of children with IBD who were seen at UVA from October 2015 to June 2020.
- Patients with IBD were identified using ICD-10 codes, and the diagnosis was validated through chart review. Those who had an upper endoscopy were identified.
- EE was defined as $\geq 1$ eosinophil per high power field (eos/hpf)
- EoE was defined as $\geq 15$ eos/hpf and symptoms of esophageal dysfunction.
- Multivariable logistic regression was used to identify risk factors for EE among patients with IBD.
- All analyses were conducted using Stata/IC 15.1 (StatCorp)
- This study was approved by the UVA Institutional Review Board
Figure 1. Flow Diagram of Study Population

Table 1. Comparison of Demographic and Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>IBD (n=261)</th>
<th>IBD with EE (n=25)</th>
<th>P-Value&lt;sup&gt;a&lt;/sup&gt;</th>
<th>IBD with EoE (n=7)</th>
<th>P-Value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Sex</td>
<td>134 (51.3%)</td>
<td>18 (72.0%)</td>
<td>0.059</td>
<td>7 (100.0%)</td>
<td>0.015</td>
</tr>
<tr>
<td>Non-Hispanic White Race</td>
<td>228 (87.4%)</td>
<td>22 (88.0%)</td>
<td>0.030</td>
<td>5 (71.4%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Age at IBD Diagnosis (y)</td>
<td>13 (11.16)</td>
<td>14 (8.15)</td>
<td>0.33</td>
<td>13 (7.15)</td>
<td>0.22</td>
</tr>
<tr>
<td>IBD Phenotype</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crohn’s Disease</td>
<td>176 (67.4%)</td>
<td>16 (64.6%)</td>
<td>0.007</td>
<td>4 (57.1%)</td>
<td>0.081</td>
</tr>
<tr>
<td>Ulcerative Colitis</td>
<td>83 (31.8%)</td>
<td>6 (24.0%)</td>
<td></td>
<td>2 (28.6%)</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>2 (0.8%)</td>
<td>3 (12.0%)</td>
<td></td>
<td>1 (14.3%)</td>
<td></td>
</tr>
<tr>
<td>Crohn’s Disease Location</td>
<td></td>
<td></td>
<td>0.085</td>
<td></td>
<td>0.25</td>
</tr>
<tr>
<td>Upper</td>
<td>4 (2.3%)</td>
<td>0 (0.0%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td></td>
</tr>
<tr>
<td>Ileal</td>
<td>39 (22.2%)</td>
<td>2 (11.1%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td></td>
</tr>
<tr>
<td>Ileo colonic</td>
<td>126 (71.6%)</td>
<td>13 (72.2%)</td>
<td>4 (80.0%)</td>
<td>1 (20.0%)</td>
<td></td>
</tr>
<tr>
<td>Colonic</td>
<td>4 (2.3%)</td>
<td>3 (16.7%)</td>
<td>1 (20.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perianal</td>
<td>3 (1.7%)</td>
<td>0 (0.0%)</td>
<td>0 (0.00%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crohn’s Disease Phenotype</td>
<td></td>
<td></td>
<td>0.11</td>
<td></td>
<td>0.27</td>
</tr>
<tr>
<td>Stricture</td>
<td>13 (7.4%)</td>
<td>3 (18.8%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penetrating</td>
<td>11 (6.2%)</td>
<td>2 (12.5%)</td>
<td>1 (25.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory</td>
<td>152 (86.4%)</td>
<td>11 (68.8%)</td>
<td>3 (72.0%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 1. Comparison of Demographic and Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>IBD (n=261)</th>
<th>IBD with EE (n=25)</th>
<th>P-Value&lt;sup&gt;c&lt;/sup&gt;</th>
<th>IBD with EoE (n=7)</th>
<th>P-Value&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atopic Conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eczema</td>
<td>12 (4.6%)</td>
<td>1 (7.8%)</td>
<td>1.00</td>
<td>1 (14.3%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Asthma</td>
<td>13 (5.0%)</td>
<td>5 (20.0%)</td>
<td>0.013</td>
<td>1 (14.3%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Food Allergy</td>
<td>23 (8.8%)</td>
<td>9 (36.0%)</td>
<td>&lt;0.001</td>
<td>2 (28.6%)</td>
<td>0.013</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>51 (19.5%)</td>
<td>12 (48.0%)</td>
<td>0.004</td>
<td>6 (85.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>2 (0.8%)</td>
<td>0 (0.0%)</td>
<td>1.00</td>
<td>0 (0.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>More than one Atopic Disease</td>
<td>13 (5.0%)</td>
<td>10 (40.0%)</td>
<td>&lt;0.001</td>
<td>4 (57.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Autoimmune conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Celiac Disease</td>
<td>3 (1.1%)</td>
<td>0 (0.0%)</td>
<td>1.00</td>
<td>0 (0.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>6 (2.3%)</td>
<td>0 (0.0%)</td>
<td>0.59</td>
<td>0 (0.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Arthritis</td>
<td>22 (8.4%)</td>
<td>2 (8.0%)</td>
<td>1.00</td>
<td>2 (28.6%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Inflammatory Spondyloarthropathy</td>
<td>1 (0.4%)</td>
<td>0 (0.0%)</td>
<td>1.00</td>
<td>0 (0.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>&gt;1 Autoimmune Condition</td>
<td>3 (1.1%)</td>
<td>0 (0.0%)</td>
<td>1.00</td>
<td>0 (0.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Laboratory Assays</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>11.5 (10.3-12.9)</td>
<td>12 (11.1-13.7)</td>
<td>0.13</td>
<td>11.1 (10.5-12.2)</td>
<td>0.85</td>
</tr>
<tr>
<td>Absolute Eosinophil Count (k/µL)</td>
<td>0.2 (0.1, 0.38)</td>
<td>0.22 (0.11, 0.505)</td>
<td>0.92</td>
<td>0.41 (0.2, 0.64)</td>
<td>0.085</td>
</tr>
<tr>
<td>Sedimentation Rate (mg/L)</td>
<td>34 (17.0, 55.0)</td>
<td>37 (16.49)</td>
<td>0.92</td>
<td>49 (44, 54)</td>
<td>0.17</td>
</tr>
<tr>
<td>C-reactive protein (mg/dL)</td>
<td>1.43 (0.4, 4.3)</td>
<td>.8 (0.3, 2.8)</td>
<td>0.14</td>
<td>1.7 (0.3, 2.2)</td>
<td>0.39</td>
</tr>
</tbody>
</table>

### Table 2: Association between EE and Demographic and Clinical Characteristics (n=261)

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>p-value&lt;sup&gt;a&lt;/sup&gt;</th>
<th>aOR (95% CI)</th>
<th>p-value&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>1.73 (.93-3.24)</td>
<td>0.082</td>
<td>1.72 (.87-3.41)</td>
<td>0.118</td>
</tr>
<tr>
<td>Race</td>
<td>1.19 (.85-1.67)</td>
<td>0.314</td>
<td>1.14 (.80-1.63)</td>
<td>0.46</td>
</tr>
<tr>
<td>IBD Phenotype</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crohn’s Disease</td>
<td>REF</td>
<td>REF</td>
<td>REF</td>
<td>REF</td>
</tr>
<tr>
<td>Ulcerative Colitis</td>
<td>1.16 (.61-2.22)</td>
<td>0.65</td>
<td>1.23 (.61-2.49)</td>
<td>0.559</td>
</tr>
<tr>
<td>Mixed</td>
<td>8.50 (1.4-53.1)</td>
<td>0.022</td>
<td>7.80 (1.12-54.55)</td>
<td>0.024</td>
</tr>
<tr>
<td>Atopic Conditions</td>
<td>3.64 (1.95-6.77)</td>
<td>&lt;0.001</td>
<td>3.66 (1.87-7.14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESR</td>
<td>.99 (.98-1.01)</td>
<td>0.432</td>
<td>.98 (.97-1.00)</td>
<td>0.052</td>
</tr>
<tr>
<td>CRP</td>
<td>.98 (.94-1.02)</td>
<td>0.452</td>
<td>.99 (.95-1.03)</td>
<td>0.691</td>
</tr>
</tbody>
</table>

Data are presented as odds ratio (OR), adjusted OR (aOR), and 95% confidence intervals (95% CI).

See Table 1 and 2 legends for expansion of abbreviations.

<sup>a</sup> Hosmer and Lemeshow goodness-of-fit test p = 0.39

<sup>b</sup> Fully adjusted model for all other variables.
Table 3: Clinical Characteristics of Patients with concomitant EoE and IBD

<table>
<thead>
<tr>
<th>Subject #</th>
<th>Time between IBD and EoE diagnosis (Days)</th>
<th>Eosinophils on Biopsy (eos/hpf)</th>
<th>Endoscopic findings</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>18</td>
<td>Furrows</td>
<td>Heartburn</td>
</tr>
<tr>
<td>2</td>
<td>96</td>
<td>50</td>
<td>Rings, Furrows, Exudate, Edema</td>
<td>Heartburn, Dysphagia, Food-Impaction, Vomiting</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>50</td>
<td>None</td>
<td>Dysphagia</td>
</tr>
<tr>
<td>4</td>
<td>90</td>
<td>20</td>
<td>Edema</td>
<td>Abdominal Pain</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>92</td>
<td>None</td>
<td>Dysphagia, Vomiting</td>
</tr>
<tr>
<td>6</td>
<td>42</td>
<td>50</td>
<td>None</td>
<td>Dysphagia, Abdominal pain, Vomiting</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>72</td>
<td>None</td>
<td>Heartburn, Weight loss</td>
</tr>
</tbody>
</table>

Discussion

- The prevalence of EE in our study population was 16.34% which is several times greater than a cohort of pediatric patients with abdominal symptoms (5.2%).5–7
- The prevalence of EoE in our study population was 2.24% which is also several times greater than that of the general adult population (0.05-0.1%) and is similar to a recent study of pediatric patients with IBD (1.5%).2
- In this study, we found that EE and EoE were strongly associated with atopic disease, even after adjusting for potential confounders.
Limitations

- Symptomatology of EoE and IBD have considerable overlap in young children and it is difficult to differentiate these conditions on chart review alone.

- Our population was composed of subjects from a large tertiary care health system and may not be generalizable to the general population.

- A large number of patients with IBD in our study had never had an EGD, which could lead to an overestimate of the prevalence of EE.

Conclusions and future directions

- The prevalence of EE and EoE among pediatric IBD patients is higher than that of the general population.

- The presence of allergic conditions is strongly associated with EE and EoE. In atopic patients with IBD and symptoms of esophageal dysfunction, suspicion for EoE should be high.

- Future studies utilizing machine learning algorithms/deep learning computer vision or transcriptomic analysis in patients with IBD and concomitant EoE/EE would be helpful to identify histologic or genetic characteristics that could further differentiate these phenotypes.\textsuperscript{10}

- To fully understand the complex relationship between EoE and IBD, future studies should include genetic and environmental data.
Citations


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Program Leadership:
-Dr. Michael Nelson MD, PhD
-Dr. Monica Lawrence MD
Questions?