Gastrointestinal Manifestations of COVID-19
Latest Data on Symptoms, Stool Testing, and Clinical Outcomes

MONDAY, MAY 18, 2020 Webinar
8:00 to 9:30 pm Eastern Daylight Time

Presenters
• Brennan M. R. Spiegel, MD, MSHS, FACG
• Paul Y. Kwo, MD, FACG
• Millie D. Long, MD, MPH, FACG
• Jordan E. Axelrad, MD, MPH

Moderators
• Mark B. Pochapin, MD, FACG
• David A. Greenwald, MD, FACG

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- COVID-19 Patient Resources
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Resources

- IBD Circle: [https://ibd-circle.within3.com/public/sign_in](https://ibd-circle.within3.com/public/sign_in)
  - Posts of previous questions and answers
  - Can post your questions for the faculty
- ACG website: [gi.org](https://gi.org)
  Education Universe: [http://universe.gi.org/](http://universe.gi.org/)
- Crohn’s & Colitis Foundation
  [https://www.crohnscolitisfoundation.org/coronavirus/professional-resources](https://www.crohnscolitisfoundation.org/coronavirus/professional-resources)
  [https://www.crohnscolitisfoundation.org/coronavirus/what-ibd-patients-should-know](https://www.crohnscolitisfoundation.org/coronavirus/what-ibd-patients-should-know)
Resources

• [https://covidibd.org](https://covidibd.org)
  – Open access data
  – Can report your patients easily
• International Organization of IBD: [https://www.ioibd.org](https://www.ioibd.org)
  – [https://www.gastrojournal.org/article/S0016-5085(20)30465-0/fulltext](https://www.gastrojournal.org/article/S0016-5085(20)30465-0/fulltext)
  – IOIBD Recommendations (dd 17 April 2020) Infusion Center guidance (PDF)
  – IOIBD Recommendations (dd 19 April 2020) endoscopy (PDF)
• PDFs to be sent to all registrants

Friendly Reminders

• Your audio will be muted.

• We will be taking questions during the webinar via the “question” functionality of our webinar tool – which is located in the right-side panel of Go-to-Webinar. If you would like to ask a question via the “question” feature, type your question directly in to the space provided.

• Please contact technical support (855) 352-9002 during this event if you have any questions or need assistance with the webinar tool.

• This call is being recorded and will be available on the IBD Circle. All IBD Circle members will receive a link to access the recording in an upcoming IBD Circle digest.
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The American College of Gastroenterology is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

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ACG will submit MOC points on the first of each month. Please allow 3-5 business days for your MOC credit to appear on your ABIM account.

If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement.

THESE ANSWERS WILL BE REVIEWED
Disclosures:

Moderators:
Samir A. Shah, MD, FACG
Dr. Shah has indicated no relevant financial disclosures.
Jean-Paul Achkar, MD, FACG
Dr. Achkar has indicated no relevant financial disclosures.

Faculty:
David T. Rubin, MD, FACG
Advisory Committee/Board Member: CCFA, Janssen
Consultant: AbbVie Pharmaceuticals, Algenonics, Allergan, Biomica, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Check-cap, Dusal Pharmaceuticals, Galen Pharma/Atlantic, Genentech, Gilead Sciences, Ichos Sciences S.A. (formerly Glenmark Pharmaceuticals), GSK, Janssen, Lilly, Narconon River Mgmt.; Pfizer, Prometheus, Reinsurance, Shire, Takeda, Teichlab, Inc.
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Consulting - AbbVie, BMS, Janssen, Pfizer, Takeda

Sunanda V. Kane, MD, MSPH, FACG
Consultant- Gilead, Samsung Bioepis

ACG and the Crohn's & Colitis Foundation IBD Circle
May 12th, 2020 Webinar
IBD in the COVID-19 Era: Update for the Busy Clinician

- Review knowledge on risk of COVID-19 in IBD patients and how COVID-19 affects medical management of immunomodulators and biologics in IBD
- Discuss data gathered from a large research registry: SECURE-IBD
- Review the real-life clinical experience with COVID-19 from a highly impacted area (NYC)
Agenda

• 8:00-8:05 pm  Welcome and Overview of IBD-COVID resources. Dr. Samir A. Shah
• 8:05-8:25 pm  Management of the IBD patient in the COVID-19 era. Dr. David Rubin
• 8:25-8:40 pm  What are we learning from the SECURE-IBD registry? Drs. Ryan Ungaro and Erica Brenner
• 8:40-8:50 pm  What have we learned from the NYC experience? Dr. David Hudesman
• 8:50-9:30 pm  Panel discussion with faculty: Drs. Sunanda Kane, David Rubin, Ryan Ungaro, Erica Brenner, and David Hudesman

Moderators: Drs. Samir A. Shah and Jean-Paul Achkar

IBD IN THE COVID-19 ERA: UPDATE FOR THE BUSY CLINICIAN
Tuesday, May 12, 2020 at 8 pm EDT
Management of the IBD Patient in the COVID-19 Era

David T. Rubin, MD, FACP
Joseph B. Kirsner Professor of Medicine
Chief, Section of Gastroenterology, Hepatology and Nutrition
University of Chicago

Coronavirus

- Enveloped, single-stranded RNA viruses
- Endemic coronaviruses are frequent causes of respiratory infections globally
- New human coronaviruses include severe acute respiratory syndrome (SARS, 2002) and Middle East Respiratory Syndrome (MERS, 2012)
- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the most recently identified human coronavirus
Current World Numbers


Incubation Period

- **Incubation period**: 1-14 days with an average of 5 days
- **Infectiousness**: around 12 hours prior to symptoms onset to 5-6 days after
- Symptomatic individuals are 50% more infectious than asymptomatic ones
- Two-thirds of infected individuals are symptomatic (many mild)

Long incubation period without any obvious symptoms

Possible Disease Course

- Stage I (Early Infection)
  - Viral response phase
  - Mild constitutional symptoms
    - Fever
    - Dry cough
    - Diarrhea
    - Fatigue
  - Lymphocytosis, increased
  - Proinflammatory cytokines
    - Increased IL-6 and CRP

- Stage II (Pulmonary Phase)
  - Host inflammatory response phase
  - Shortness of breath
  - Hypoxia (Hypoxic pulmonary vasoconstriction)
  - Abscess and necrotic lung
  - Elevated inflammatory markers
    - CRP, IL-6, IL-8, IL-10
    - Troponin, NT-ProBNP elevation
  - ARDS
  - Cardiac failure

- Stage III (Hyperinflammation Phase)
  - 8-10 days


IBD Circle
A Partnership of the American Gastroenterological Association
and the Crohn’s & Colitis Foundation
When to Suspect COVID-19

- Cough
- Shortness of breath or difficulty breathing

*Or at least two of these symptoms:*
- Fever
- Chills
- Repeated shaking with chills
- Muscle pain
- Headache
- Sore throat
- New loss of taste or smell
- Known exposure to infected person
- Abnormal chest imaging
- Lymphopenia (low wbc)
- Elevated CRP (blood test)

What about GI symptoms?


Frequency of COVID-19 Hospitalized Patients with or without Digestive Symptoms

- Without digestive, nor respiratory symptoms (n=20)
- With digestive symptoms, without respiratory (n=7, most patients have fever, except 1)
- With respiratory symptoms, without digestive symptoms (n=85)
- With digestive and respiratory symptoms (n=92)

What We Know So Far About GI Symptoms and Viral Detection in Stool

<table>
<thead>
<tr>
<th>Author</th>
<th>Journal</th>
<th>Year Published</th>
<th>N of Patients</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jin X, et al</td>
<td>Gut</td>
<td>2020</td>
<td>651</td>
<td>- 11.45% with one GI symptom (nausea, vomiting, diarrhea)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>- Identified novel methylation site in S protein that changed from SARS to Wuhan and some differences to the strain in Zhenjiang Province may account for change in frequency of GI symptoms</td>
</tr>
<tr>
<td>Xiao F, et al</td>
<td>Gastroenterology</td>
<td>2020</td>
<td>73</td>
<td>- 39 (53%) had positive stool RNA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Stool remained positive in 17 patients (23.29%) after respiratory samples were negative</td>
</tr>
<tr>
<td>Wu Y, et al</td>
<td>Lancet Gastroenterol Hepatol</td>
<td>2020</td>
<td>74</td>
<td>- 41 (55%) had positive stool samples</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Fecal samples were positive for a mean of 27.9 days (vs. respiratory samples – mean 16.7 days)</td>
</tr>
<tr>
<td>Wolfel R, et al</td>
<td>Nature</td>
<td>2020</td>
<td>9</td>
<td>- Viral RNA detected in sputum and stool samples</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Live virus was not isolated from stool samples</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Virus in stool is not thought to be infectious</td>
</tr>
</tbody>
</table>

Risk Factors for Poor Outcomes

Table 4: Bivariate Cox Regression of Factors Associated With ARDS Development or Progression From ARDS to Death

<table>
<thead>
<tr>
<th>Patient characteristics and findings</th>
<th>ARDS HR (95% CI)</th>
<th>P value</th>
<th>Death HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (≥65 vs &lt;65), y</td>
<td>3.26 (2.69-3.11)</td>
<td>&lt;.001</td>
<td>6.17 (3.26-11.67)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Gender (male vs female)</td>
<td>1.47 (0.92-2.36)</td>
<td>.11</td>
<td>0.64 (0.30-1.05)</td>
<td>.07</td>
</tr>
<tr>
<td>Highest patient temperature (≥39 °C vs &lt;39 °C)</td>
<td>1.77 (1.11-2.84)</td>
<td>.02</td>
<td>0.43 (0.21-0.92)</td>
<td>.01</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Hypertension (yes vs no)</td>
<td>1.82 (1.13-2.93)</td>
<td>.01</td>
<td>1.70 (0.52-5.24)</td>
<td>.09</td>
</tr>
<tr>
<td>Diabetes (yes vs no)</td>
<td>2.34 (1.25-4.39)</td>
<td>.002</td>
<td>1.30 (0.80-2.13)</td>
<td>.19</td>
</tr>
</tbody>
</table>

p<0.01

BMI ≥35 kg/m² (n=38)
BMI 30-35 kg/m² (n=24)
BMI 25-30 kg/m² (n=48)
BMI <25 kg/m² (n=17)

Notes:
Profile of Antibodies in Patients with Pneumonia Due to SARS-CoV


Are IBD Patients at Unique Risk?

• Management of IBD often involves immunosuppressive or immune modifying therapies

• Known increased risk of some viral infections with IBD therapies (influenza, VZV, CMV...)

• Exposures:
  – Patients with IBD may be receiving infusions in infusion centers
  – Patients with IBD require routine and diagnostic endoscopic procedures

• Pathophysiology (in theory): bowel expresses ACE2 receptor
Questions of Concern Related to IBD and COVID-19

- What is the risk of infection with SARS-CoV-2?
- Does bowel inflammation increase risk of infection with SARS-CoV-2?
- What is the risk of COVID-19?
- Do patients with IBD have different outcomes with COVID-19?
- Do IBD therapies increase risk of infection or COVID-19?
- Are any IBD therapies protective against COVID-19?
- Should patients with IBD modify their therapies during the pandemic?


Viral Infections and IBD Therapies

- Increased risk of varicella zoster infection with tofacitinib\(^1\)
- Reactivation of hepatitis B with anti-TNF therapy\(^2\)
- Cases of viral warts associated with thiopurines\(^3\)
- IBD patients have an increased influenza risk compared with those without IBD\(^4\)
- Systemic corticosteroids were found to be independently associated with influenza (Table)\(^4\)

Task Forces
- Clinical trials task force
- Endoscopy task force
- Hospitalization task force
- Research task force
  - Epidemiology
  - Etiology
  - Prognosis and natural history
  - Prevention
  - Outcomes and quality of life
  - Clinical Practice
- Telemedicine task force

Publications
- Management of IBD Patients during COVID-19 Pandemic¹
- Recommendations for Surgery in IBD Patients during COVID-19 Pandemic²

Management of Patients with Crohn’s Disease and Ulcerative Colitis During the COVID-19 Pandemic: Results of an International Meeting

David T. Rubin, Maria T. Abreu, Victoria Bai, Corey A. Siegel on behalf of the International Organization for the Study of Inflammatory Bowel Disease

Acknowledgments:
The authors thank all the participants of the RAND panel.

IOIBD Members:

Additional invited participants:
Eric J. Brenner, Britt Christensen, Ferdinando D’Amico, Chris M. Griffiths, Peter D. Higgins, Michael D. Kappelman, Charlie Lee, Miguel O. Uguero, Joel R. Ross, Ryan Ungaro

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Demographics of Participants by Specialty (N=66)

Statements developed by steering committee → Survey sent to participants → Webinar → Statements modified → Participants re-surveied

Survey Results

<table>
<thead>
<tr>
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<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
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<tbody>
<tr>
<td>Inappropriate Statement</td>
<td>Pre-Survey (N=64) 69 Statements</td>
<td>Post-Survey (N=66) 76 Statements</td>
<td>Agreement (based on post-survey)</td>
<td>Disagreement (based on post-survey)</td>
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<td>Appropriate Statement</td>
<td>16</td>
<td>26</td>
<td>18</td>
<td>8</td>
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<td>Uncertain Statement</td>
<td>24</td>
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<td>15</td>
<td>4</td>
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<td>0</td>
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<td>Total Statements:</td>
<td>64</td>
<td>12</td>
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Disagreement Index (DI) = \( \frac{66 \text{ \%ile} - 33 \text{ \%ile}}{2.35 + \left( \frac{1.5 \cdot (66 \text{ \%ile} - 33 \text{ \%ile})}{2} \right)} \)
Are IBD Patients at a Higher Risk?

Results of an International Consensus Meeting

• The risk of infection with SARS-CoV-2 is the same whether a patient has IBD or does not have IBD.
• Independent of treatment, patients with CD or UC do not have a greater risk of infection with SARS-CoV-2 than the general population.
• It is uncertain if active inflammation from IBD increases the risk of getting SARS-CoV-2.
• Patients with an ostomy are not at increased risk for COVID-19.
• Patients with a J pouch are not at increased risk for COVID-19.

What about Special Situations?

Results of an International Consensus Meeting

• Elective surgeries and endoscopies should be postponed at this time.
• It is uncertain if healthcare workers with IBD on immune modifying medications working in an environment with known or suspected COVID-19 patients should continue working in that same environment.
• Patients with IBD on immune modifying medications should discontinue any non-essential travel.
• It is safe to continue infusions in an infusion center, assuming the infusion center has a screening protocol in place.
What About IBD Therapy?

<table>
<thead>
<tr>
<th>S-ASA</th>
<th>BUD</th>
<th>PRED (≤20mg/d)</th>
<th>AZA/6MP</th>
<th>MTX</th>
<th>Anti-TNF</th>
<th>VEDO</th>
<th>UST</th>
<th>TOFA</th>
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</table>

**To prevent SARS-CoV-2 infection.**

**If infected with SARS-CoV-2 but don't have COVID-19.**

**Confirmed COVID-19.**

- Continue Therapy
- Unsure
- Hold/Delay/Stop Therapy

Treatment of IBD After SARS-CoV-2 Infection

**Results of an International Consensus Meeting**

- In an IBD patient who tests positive for SARS-CoV-2 and whose IBD meds have been stopped because of this, IBD meds can be restarted:
  - after 14 days (provided they have not developed COVID-19).
  - after COVID-19 symptoms resolve.
  - after 2 nasopharyngeal PCR tests are negative.
Management of IBD Patients During COVID-19

When Do You Restart Therapy?

- Unclear
- Options:
  - When patient is asymptomatic
  - When patient is asymptomatic for more than 3 days (?)
  - When patient has PCR test for SARS-CoV-2 negative (once or twice?) (maybe not1)
  - When patient is in convalescent phase of illness (IgG positive, IgM negative)

Limitations to Our Current Approach

• Limited data.
• Long half life of many drugs makes holding them of questionable benefit.
• Unclear denominator of infected IBD patients.
• No distinction between infectious and inflammatory phases of COVID-19.

Outcomes of COVID-19 in 79 patients with IBD in Italy

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>COVID-19 related pneumonia</th>
<th>COVID-19 related death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR [95%CI]</td>
<td>P-value</td>
</tr>
<tr>
<td>Age &gt; 65</td>
<td>5.87 [1.15, 29.66]</td>
<td>0.03</td>
</tr>
<tr>
<td>CCI* score &gt; 1</td>
<td>2.91 [1.06, 9.21]</td>
<td>0.04</td>
</tr>
<tr>
<td>UC diagnosis</td>
<td>2.72 [1.06, 6.99]</td>
<td>0.03</td>
</tr>
<tr>
<td>Active IBD</td>
<td>10.25 [2.11, 49.73]</td>
<td>0.003</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>4.94 [0.95, 25.55]</td>
<td>0.05</td>
</tr>
<tr>
<td>Thiopurines</td>
<td>1.21 [0.22, 6.40]</td>
<td>0.82</td>
</tr>
<tr>
<td>Anti-TNF</td>
<td>1.18 [0.47, 2.97]</td>
<td>0.71</td>
</tr>
<tr>
<td>Vedolizumab</td>
<td>0.53 [0.16, 1.73]</td>
<td>0.29</td>
</tr>
</tbody>
</table>

*Charlson Comorbidity Index

COVID-19 in Immune-Mediated Diseases
Case Series from New York (NYU)

- N = 86
- RA, IBD, psoriatic arthritis, ankylosing spondylitis, psoriasis...
- 59 PCR confirmed COVID-19
- HTN, DM, COPD were associated with higher hospitalization

<table>
<thead>
<tr>
<th>Medication</th>
<th>Total (n=59)</th>
<th>Ambulatory (n=45)</th>
<th>Hospitalized (n=14)</th>
<th>Adjusted OR [95%CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxychloroquine</td>
<td>7 (11.9)</td>
<td>4 (8.9)</td>
<td>3 (21.4)</td>
<td>1.43 [1.04, 1.97]</td>
</tr>
<tr>
<td>MTX</td>
<td>14 (23.7)</td>
<td>8 (17.8)</td>
<td>6 (42.9)</td>
<td>1.37 [1.06, 1.78]</td>
</tr>
<tr>
<td>Steroids</td>
<td>7 (11.9)</td>
<td>3 (6.7)</td>
<td>4 (28.6)</td>
<td>1.40 [1.01, 1.93]</td>
</tr>
</tbody>
</table>


Case Reports of IBD and COVID-19

<table>
<thead>
<tr>
<th>Author</th>
<th>Journal, year</th>
<th>Patient Characteristics</th>
<th>Presentation</th>
<th>Management/Outcome</th>
</tr>
</thead>
</table>
- Received 3 doses of infliximab in the past and went into clinical remission  
- Self-discontinued medications 6 years ago | - Abdominal pain, diarrhea, hematochezia, and urgency for 6 weeks -> hospitalized for UC flare -> treated with methotrexate and discharged  
- 2 days later, worsening bloody diarrhea and abdominal pain, no respiratory symptoms | - B-hcg positive, confirmed intrauterine pregnancy  
- Tested positive for SARS-CoV-2  
- Started on iv methylprednisolone, was unable to transition to oral, so was given iv cyclosporine  
- Developed pleuritic chest pain, ruled out PE and was started on hydroxychloroquine + azithromycin  
- Experienced a spontaneous abortion on day 9 |
| Wolf DC, Wolf CH, Rubin DT | Am J Gastroenterol, 2020 [submitted] | - 85 year old man with CD on no therapy for his disease  
- Takes loperamide PRN | - 4 liquid stools per day, anorexia, fatigue, 13-pound weight loss in 10 days  
- Persistent non-productive cough despite azithromycin | - Telehealth management, started on bismuth subsalicylate (BSS) 525 mg PO 2-3x a day while waiting for labs  
- Tested positive for SARS-CoV-2  
- Diarrhea improved within 48 hours, 80% improvement of all other symptoms by day 6, near resolution by day 10  
- Patient remained on BSS throughout course of illness |
| Jacobs J, Clark-Snustad K, Lee S | Inflamm Bowel Dis, 2020 [Epub ahead of print] | - 33 year old woman with a 13 year history of UC  
- Started tofacitinib 10 mg BID in June 2019  
- Achieved clinical remission after 5 months of therapy | - Fever, chills, cough, myalgia, sore throat, fatigue, and night sweats  
- No GI symptoms | - Tested positive for SARS-CoV-2  
- Tofacitinib 10 mg BID was continued  
- Respiratory sx resolved after 5 days  
- Remained well with no symptoms after 2 weeks |
Vitamin D Supplementation Can Reduce the Clinical Effects of COVID-19

- Vitamin D deficiency can be implicated in ARDS, heart failure, and sepsis.

- These can all be manifestations of critically ill COVID-19 patients.

- To reduce the risk of infection, it is recommended that people at risk of influenza and/or COVID-19 consider taking vitamin D3.

- Randomized controlled trials and large population studies should be conducted to evaluate these recommendations.

<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>Findings from Vitamin D Supplementation Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of CAP with Vitamin D</td>
<td>Did not significantly result in complete resolution. Baseline 25(OH)D was 20 ng/mL. Achieved 25(OH)D in the treatment arm was 40 ng/mL.</td>
</tr>
<tr>
<td>Increased production of pro-inflammatory cytokines such as IL-6</td>
<td>Reduces concentration of IL-6</td>
</tr>
<tr>
<td>Increased CRP</td>
<td>Reduces CRP in diabetic patients</td>
</tr>
<tr>
<td>Increased risk of sepsis</td>
<td>No reduction in mortality rate found for adults with sepsis supplemented with vitamin D. Most trials included participants with 25(OH)D =20 ng/mL. Vitamin D3 doses between 250 and 600 thousand IU.</td>
</tr>
<tr>
<td>Risk of ARDS</td>
<td>Vitamin D deficiency contributes to development of ARDS</td>
</tr>
</tbody>
</table>


Reliable References to Stay Updated

- who.int/health-topics/coronavirus
- cdc.gov/coronavirus/2019-ncov
- coronavirusupdates.uchicago.edu
- crohnscolitisfoundation.org/coronavirus
- covidibd.org
- ioibd.org
- clinicaltrials.gov
- rubinlab.uchicago.edu/blog
- twitter.com/IBDMD
Update on Impact of COVID-19 in Inflammatory Bowel Disease Patients

Erica Brenner, MD (University of North Carolina at Chapel Hill)
Ryan Ungaro, MD MS (Icahn School of Medicine at Mount Sinai, New York)
Jean-Frederic Colombel, MD (Icahn School of Medicine at Mount Sinai, New York)
Michael Kappelman MD, MPH (University of North Carolina at Chapel Hill)

Background

- Coronavirus disease 2019 (COVID-19) has rapidly spread throughout the world and is now an international pandemic
- Almost 80% of patients with severe COVID-19 (requiring intensive care) have at least one underlying comorbidity¹
- Inflammatory bowel disease (IBD) patients are frequently on immunosuppressive treatments that increase the risk of infection
- To date, there are limited data on the disease course of COVID-19 in IBD patients including impact of clinical characteristics and medications

¹. MMWR Morb Mortal Wkly Rep 2020;69:382-386
Aim

• To define the impact of COVID-19 on patients with IBD

• To evaluate associations between age, co-morbidities, IBD characteristics, and IBD treatments and COVID-19 outcomes

Methods

• Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease (SECURE-IBD) is an international registry of IBD patients who have had COVID-19

• Health care providers invited to report cases on a web-based platform

• Cases reported after a minimum of 7 days from symptom onset and sufficient time has passed to observe the disease course through resolution of acute illness or death

• Data collected include patient demographics, IBD type, co-morbidities, disease activity (by physician global assessment), BMI, smoking, and IBD medications at time of COVID-19 infection

• COVID-19 outcomes: hospitalization, need for intensive care unit (ICU), need for ventilator, and death
Methods

- Descriptive statistics reported on cohort characteristics and outcomes
- Age-standardized mortality ratios (SMRs) calculated using reference populations from China, Italy, and the United States\(^1\)\(^-\)\(^3\)
- Primary outcome was severe COVID-19, defined as a composite of ICU admission, ventilator use, and/or death, consistent with existing COVID-19 literature
- Multivariable logistic regression estimated the independent effects of age, sex, disease (CD vs UC/IBD-U), disease activity, smoking, BMI \(\geq 30\), number of comorbidities (0, 1, \(\geq 2\)), systemic corticosteroids, TNF antagonists, and mesalamines (5-ASA) / sulfasalazine on the primary outcome

1. Onder G et al. JAMA 2020
2. Zhonghua Liu Xing Bing Xue Za Zhi 2020
3. Centers for Disease Control and Prevention 2020

Results: Cohort Characteristics

- Analysis based on first 525 cases
- 33 different countries
- Median age 41 years
- 53% men, 84% white
- 59.4% Crohn’s disease
- IBD disease activity at time of infection
  - 60% Remission
  - 18% Mild
  - 19% Moderate/Severe
  - 1% Unknown
- Outcomes
  - 30.7% Hospitalized
  - 4.6% ICU
  - 4% Ventilator
  - 3% Death
  - 7% Severe COVID-19 (composite)
## Results: Age-Standardized Mortality Ratios

<table>
<thead>
<tr>
<th>Reference Country Population</th>
<th>SMR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>1.76 (0.90-2.62)</td>
</tr>
<tr>
<td>Italy</td>
<td>1.45 (0.74-2.16)</td>
</tr>
<tr>
<td>United States</td>
<td>1.66 (0.85-2.47)</td>
</tr>
</tbody>
</table>

## Outcomes by Age

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total N</th>
<th>Outpatient only, n (%)</th>
<th>Hospitalized, n (%)</th>
<th>Death, n (%)</th>
<th>ICU/Ventilator/Death, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>525</td>
<td>363 (69)</td>
<td>161 (31)</td>
<td>16 (3)</td>
<td>37 (7)</td>
</tr>
<tr>
<td>Age Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-9 years</td>
<td>3</td>
<td>3 (100)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>10-19 years</td>
<td>26</td>
<td>23 (88)</td>
<td>3 (12)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>20-29 years</td>
<td>116</td>
<td>93 (80)</td>
<td>23 (20)</td>
<td>0 (0)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>30-39 years</td>
<td>108</td>
<td>87 (81)</td>
<td>20 (19)</td>
<td>1 (1)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>40-49 years</td>
<td>95</td>
<td>64 (67)</td>
<td>31 (33)</td>
<td>2 (2)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>50-59 years</td>
<td>74</td>
<td>45 (61)</td>
<td>29 (39)</td>
<td>2 (3)</td>
<td>6 (8)</td>
</tr>
<tr>
<td>60-69 years</td>
<td>54</td>
<td>30 (56)</td>
<td>24 (44)</td>
<td>3 (6)</td>
<td>11 (20)</td>
</tr>
<tr>
<td>70-79 years</td>
<td>24</td>
<td>7 (29)</td>
<td>17 (71)</td>
<td>2 (8)</td>
<td>3 (13)</td>
</tr>
<tr>
<td>&gt;=80 years</td>
<td>23</td>
<td>9 (39)</td>
<td>14 (61)</td>
<td>6 (26)</td>
<td>6 (26)</td>
</tr>
</tbody>
</table>
Outcomes by Medication Class

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total N</th>
<th>Outpatient only, n (%)</th>
<th>Hospitalized, n (%)</th>
<th>Death, n (%)</th>
<th>ICU/Ventilator/Death, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfasalazine/mesalamine</td>
<td>117</td>
<td>60 (51)</td>
<td>57 (49)</td>
<td>9 (8)</td>
<td>20 (17)</td>
</tr>
<tr>
<td>Budesonide</td>
<td>18</td>
<td>9 (50)</td>
<td>9 (50)</td>
<td>1 (6)</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Oral/parenteral steroids</td>
<td>37</td>
<td>11 (30)</td>
<td>26 (70)</td>
<td>4 (11)</td>
<td>9 (24)</td>
</tr>
<tr>
<td>6MP/azathioprine monotherapy</td>
<td>53</td>
<td>29 (55)</td>
<td>24 (45)</td>
<td>1 (2)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Methotrexate monotherapy</td>
<td>5</td>
<td>2 (40)</td>
<td>3 (60)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>Anti-TNF without 6MP/AZA/MTX</td>
<td>176</td>
<td>150 (85)</td>
<td>25 (14)</td>
<td>1 (1)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Anti-TNF + 6MP/AZA/MTX</td>
<td>52</td>
<td>32 (62)</td>
<td>20 (38)</td>
<td>2 (4)</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Anti-integrin</td>
<td>50</td>
<td>34 (68)</td>
<td>16 (32)</td>
<td>0 (0)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>IL-12/23 inhibitor</td>
<td>55</td>
<td>51 (93)</td>
<td>4 (7)</td>
<td>0 (0)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>JAK inhibitor</td>
<td>8</td>
<td>7 (88)</td>
<td>1 (13)</td>
<td>1 (13)</td>
<td>1 (13)</td>
</tr>
</tbody>
</table>

Multivariable Analysis

<table>
<thead>
<tr>
<th>Variable (Referent group)</th>
<th>ICU/Vent/Death Odds Ratio (95% CI) (n = 517)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.04 (1.01-1.06)</td>
<td>0.002</td>
</tr>
<tr>
<td>Male (Female)</td>
<td>1.20 (0.55-2.60)</td>
<td>0.65</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crohn’s disease (ulcerative colitis/IBD unspecified)</td>
<td>0.76 (0.31-1.85)</td>
<td>0.54</td>
</tr>
<tr>
<td>Disease severity (remission)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active disease</td>
<td>1.14 (0.49-2.66)</td>
<td>0.76</td>
</tr>
<tr>
<td>Systemic corticosteroid (none)</td>
<td>6.87 (2.30-20.51)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TNF antagonist (none)</td>
<td>0.90 (0.37-2.17)</td>
<td>0.81</td>
</tr>
<tr>
<td>Current smoker</td>
<td>0.55 (0.06-4.94)</td>
<td>0.59</td>
</tr>
<tr>
<td>BMI ≥ 30</td>
<td>2.00 (0.72-5.51)</td>
<td>0.18</td>
</tr>
<tr>
<td>Comorbidities (none)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.22 (0.45-3.26)</td>
<td>0.70</td>
</tr>
<tr>
<td>≥2</td>
<td>2.87 (1.05-7.85)</td>
<td>0.04</td>
</tr>
<tr>
<td>5-ASA/sulfasalazine (none)</td>
<td>3.14 (1.28-7.71)</td>
<td>0.01</td>
</tr>
<tr>
<td>Variable (Referent group)</td>
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<tr>
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<tr>
<td>2</td>
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<td>0.04</td>
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<td>0.54</td>
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<tr>
<td>ulcerative colitis/IBD</td>
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<tr>
<td>Disease severity</td>
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<td></td>
</tr>
<tr>
<td>remission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active disease</td>
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<td>0.76</td>
</tr>
<tr>
<td>Systemic corticosteroid</td>
<td></td>
<td></td>
</tr>
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<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
</tr>
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<td></td>
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<td>≥2</td>
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<td>0.04</td>
</tr>
<tr>
<td>5-ASA/sulfasalazine</td>
<td>3.14 (1.28-7.71)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

### Recent updates (5/12/2020)

- 1,074 cases reported from 42 different countries

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total N</th>
<th>Hospitalized (n, %)</th>
<th>Death (n, %)</th>
<th>ICU/Ventilator/Death (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfasalazine/mesalamine</td>
<td>294</td>
<td>145 (49%)</td>
<td>22 (7%)</td>
<td>49 (17%)</td>
</tr>
<tr>
<td>Budesonide</td>
<td>27</td>
<td>13 (48%)</td>
<td>2 (7%)</td>
<td>4 (15%)</td>
</tr>
<tr>
<td>Oral/parenteral steroids</td>
<td>85</td>
<td>56 (66%)</td>
<td>10 (12%)</td>
<td>22 (28%)</td>
</tr>
<tr>
<td>6MP/azathioprine monotherapy</td>
<td>104</td>
<td>38 (37%)</td>
<td>2 (2%)</td>
<td>10 (10%)</td>
</tr>
<tr>
<td>Methotrexate monotherapy</td>
<td>8</td>
<td>4 (50%)</td>
<td>1 (13%)</td>
<td>1 (13%)</td>
</tr>
<tr>
<td>Anti-TNF without 6MP/AZA/MTX</td>
<td>314</td>
<td>60 (19%)</td>
<td>3 (1%)</td>
<td>8 (3%)</td>
</tr>
<tr>
<td>Anti-TNF + 6MP/AZA/MTX</td>
<td>106</td>
<td>38 (36%)</td>
<td>3 (3%)</td>
<td>12 (11%)</td>
</tr>
<tr>
<td>Anti-integrin</td>
<td>107</td>
<td>31 (29%)</td>
<td>4 (4%)</td>
<td>9 (8%)</td>
</tr>
<tr>
<td>IL 12/23 inhibitor</td>
<td>102</td>
<td>13 (13%)</td>
<td>0 (0%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>JAK inhibitor</td>
<td>17</td>
<td>5 (29%)</td>
<td>1 (6%)</td>
<td>2 (12%)</td>
</tr>
<tr>
<td>Other IBD medication</td>
<td>49</td>
<td>17 (43%)</td>
<td>1 (3%)</td>
<td>3 (8%)</td>
</tr>
</tbody>
</table>
**Strengths**

- Robust, worldwide collaboration
- Large, geographically diverse sample of pediatric and adult IBD patients
- Reporting directly by physicians and trained staff

**Limitations**

- Convenience sample
- Only includes confirmed cases
- Risk of reporting bias
  - May over-represent severe cases and areas with readily available testing
  - May under-represent severely ill patients hospitalized at an outside hospital or die without physician’s awareness
Summary

• Increasing age, comorbidities, and corticosteroids are associated with severe COVID-19 outcomes
• TNF antagonist medications do not appear to be associated with severe COVID-19 outcomes
• More data needed to further understand signals in other drug classes (5-ASA, TNF antagonist combination therapy)

Thank you!

All reporting providers and our partners:

And many more organizations listed at https://covidibd.org/our-partners/
WHAT HAVE WE LEARNED FROM THE NYC EXPERIENCE?

David Hudesman, MD
Co-Director, IBD Center at NYULMC
Associate Professor of Medicine, NYU

Haberman et al., N Engl J Med. 2020 Apr 29

COVID-19 in Immune-Mediate Inflammatory Diseases

- Prospective case of 86 patients from NYU Langone Health with known (59) or highly suspected (27) COVID-19
  - Inflammatory Bowel Disease
  - Psoriatic Arthritis
  - Psoriasis
  - Rheumatoid Arthritis
  - Ankylosing Spondylitis
- Median age = 46, 49% Female
- 72% on a biologic or JAK inhibitor
- 16% (14/86) were hospitalized

Haberman et al., N Engl J Med. 2020 Apr 29
COVID-19 in Immune-Mediate Inflammatory Diseases

• Hospitalized patients were older and were more likely to have comorbidities
• Use of biologics or JAK inhibitors
  – 76% (55/72 patients) not hospitalized
  – 50% (7/14) hospitalized
• Multivariate analysis (adjusting for age, sex, and comorbidities)
  – Prednisone use: 29% hospitalized vs 6% ambulatory
  – Hydroxychloroquine use: 21% hospitalized vs 7% ambulatory
  – Methotrexate use: 43% hospitalized vs 15% ambulatory

Updated NYU IBD/COVID-19 Experience

• 72 patients with known or suspected COVID-19
• 6 hospitalizations
  – 3 patients home within 24-48 hours, never required oxygen (one male patient with moderate disease, 2 female patients in remission)
  – 1 patient hospitalized for severe UC flare during first trimester of pregnancy
  – 1 patient intubated in ICU: 73 year old male with UC on mesalamine with HTN and prostate cancer (IBD in remission)
  – 1 patient died: 80 year old male on adalimumab with Parkinsons (IBD in remission)
Managing an IBD Practice in the COVID era

- IBD patient with COVID-19
  - Personalized approach
- IBD patient who is in a presumed flare
  - Telehealth vs Office visit
  - Labs and stool studies
  - Change in medication
  - Colonoscopy
- IBD patient who is stable
  - Disease monitoring
  - Medication compliance
- Provider and staff concerns and well being

THANK YOU
Management of IBD Patients During COVID-19


Member-Only Online Community

A member-only online resource, the IBD Circle is a trusted source for professional advice, collaboration, support, and practice resources to help you deliver quality patient care. Join as a professional member to access.

Community Sponsored By: abbvie