Physician Practice Patterns in Holding Inflammatory Bowel Disease Medications due to COVID-19, in the SECURE-IBD Registry

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Abstract

Background: We aimed to describe physician practice patterns in holding or continuing IBD therapy in the setting of COVID-19 infection, using the Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease [SECURE-IBD] registry.

Methods: IBD medications that were stopped due to COVID-19 were recorded in the SECURE-IBD registry in addition to demographic and clinical data. We conducted descriptive analyses to understand characteristics associated with stopping IBD medications in response to active COVID-19 infection.

Results: Of 1499 patients, IBD medications were stopped in 518 [34.6%] patients. On bivariate and multivariable analyses, a diagnosis of ulcerative colitis or IBD-unspecified was associated with a lower odds of stopping medication compared with Crohn's disease (adjusted odds ratio [aOR] 0.6, 95% confidence interval [CI] 0.48, 0.75). When evaluating specific medications, 5-aminosalicylic acid was more likely to be continued \( p < 0.001 \) whereas anti-tumour necrosis factor therapy and immunomodulator therapy were more likely to be stopped [global \( p < 0.001 \)]. Other demographic and clinical characteristics did not affect prescription patterns.

Conclusions: IBD medications other than immunomodulators were continued in the majority of IBD patients with COVID-19, in the international SECURE-IBD registry. Future studies are needed to understand the impact of stopping or continuing IBD medications on IBD- and COVID-19 related outcomes.

Key Words: Inflammatory bowel disease; Crohn’s disease; ulcerative colitis; coronavirus disease 2019; IBD therapy

1. Introduction

The impact of holding immunosuppressive and other therapies for inflammatory bowel diseases [IBD] in the context of coronavirus disease 2019 [COVID-19] is unknown. In the interim, expert consensus is to hold corticosteroids, immunosuppressants, and biologics, but not 5-aminosalicylic acid [5-ASA], at the time of suspected or confirmed diagnosis of COVID-19 infection until fever and other symptoms are resolved. There are currently no
| Characteristic
description | All patients on ≥1 medication | IBD medication stopped | IBD medication not stopped | p-value |
|-----------------|------------------------------|-----------------------|----------------------------|---------|
| N               | [mean] % [SD]                | N [mean] % [SD]       | N [mean] % [SD]            |         |
| Total number of patients | 1499 518 31.8% 981 60.2% - | - | - | - |
| Age             | 44 17.88 43 16.77 44 18.43 0.276 | 43 16.77 44 18.43 | 44 18.43 | 0.276 |
| Female sex      | 752 48% 242 47% 485 49% 0.290 | 485 49% | 485 49% | 0.290 |
| Race            | White 1221 81% 420 81% 801 82% 0.787 | 801 82% | 801 82% | 0.787 |
|                | Black or African American 96 6% 35 7% 61 6% 0.685 | 61 6% | 61 6% | 0.685 |
|                | American Indian/Native Alaskan 2 0% 1 0% 1 0% 0.646 | 1 0% | 1 0% | 0.646 |
|                | Asian 87 6% 33 6% 54 6% 0.495 | 54 6% | 54 6% | 0.495 |
|                | Native Hawaiian/Pacific Islander 0 0% 0 0% 0 0% - | 0 0% | 0 0% | 0.016 |
|                | Other 115 8% 47 9% 68 7% 0.138 | 68 7% | 68 7% | 0.138 |
| Hispanic/Latino | Yes 262 17% 100 19% 162 17% 0.409 | 162 17% | 162 17% | 0.409 |
|                | No 930 62% 314 61% 616 63% 0.409 | 616 63% | 616 63% | 0.409 |
|                | Unknown 186 12% 66 13% 120 12% 0.409 | 120 12% | 120 12% | 0.409 |
|                | Missing 121 8% 38 7% 83 8% 0.409 | 83 8% | 83 8% | 0.409 |
| Country         | USA 514 34% 172 33% 342 35% 0.520 | 342 35% | 342 35% | 0.520 |
|                | Spain 225 15% 80 15% 145 15% 0.732 | 145 15% | 145 15% | 0.732 |
|                | France 90 6% 32 6% 58 6% 0.837 | 58 6% | 58 6% | 0.837 |
|                | Italy 74 5% 16 3% 58 6% 0.016 | 58 6% | 58 6% | 0.016 |
|                | UK 71 5% 26 5% 45 5% 0.708 | 45 5% | 45 5% | 0.708 |
|                | Iran 53 4% 20 4% 33 3% 0.620 | 33 3% | 33 3% | 0.620 |
|                | Russian 79 5% 32 6% 47 5% 0.253 | 47 5% | 47 5% | 0.253 |
|                | Brazil 50 3% 24 5% 26 3% 0.042 | 26 3% | 26 3% | 0.042 |
|                | Other 343 23% 116 22% 227 23% 0.744 | 227 23% | 227 23% | 0.744 |
| Disease type    | Crohn's disease 821 55% 325 63% 496 51% <0.001 | 496 51% | 496 51% | <0.001 |
|                | Ulcerative Colitis 649 43% 187 36% 462 47% | 462 47% | 462 47% | 0.702 |
|                | IBD-unspecified 24 2% 4 1% 20 2% | 20 2% | 20 2% | 0.702 |
| IBD disease activity | Remission 854 57% 292 56% 562 57% | 562 57% | 562 57% | 0.702 |
|                | Mild 273 18% 92 18% 181 18% 0.153 | 181 18% | 181 18% | 0.153 |
|                | Moderate 240 16% 90 17% 150 15% 0.153 | 150 15% | 150 15% | 0.153 |
|                | Severe 80 5% 24 5% 56 6% 0.620 | 56 6% | 56 6% | 0.620 |
| Comorbid conditions | Any condition 555 37% 194 37% 361 37% 0.804 | 361 37% | 361 37% | 0.804 |
|                | Cardiovascular disease 109 7% 32 6% 77 8% 0.236 | 77 8% | 77 8% | 0.236 |
|                | Diabetes 88 6% 32 6% 56 6% 0.713 | 56 6% | 56 6% | 0.713 |
|                | Lung disease 144 10% 42 8% 102 10% 0.133 | 102 10% | 102 10% | 0.133 |
|                | Hypertension 194 13% 75 14% 119 12% 0.198 | 119 12% | 119 12% | 0.198 |
|                | Cancer 33 2% 10 2% 23 2% 0.603 | 23 2% | 23 2% | 0.603 |
|                | History of stroke 19 1% 5 1% 14 1% 0.447 | 14 1% | 14 1% | 0.447 |
|                | Chronic renal disease 33 2% 8 2% 25 3% 0.208 | 25 3% | 25 3% | 0.208 |
|                | Chronic liver disease 52 3% 17 3% 35 4% 0.774 | 35 4% | 35 4% | 0.774 |
|                | Other 214 14% 77 15% 137 14% 0.636 | 137 14% | 137 14% | 0.636 |
| Current smoker | 63 4% 18 3% 45 5% 0.307 | 45 5% | 45 5% | 0.307 |
| BMI            | BMI <30 925 62% 315 61% 610 62% 0.491 | 610 62% | 610 62% | 0.491 |
|                | BMI >=30 249 17% 82 16% 167 17% | 167 17% | 167 17% | 0.491 |
|                | Missing 325 22% 121 23% 204 21% | 204 21% | 204 21% | 0.491 |
| COVID-19 related emergency room visit | 549 37% 188 36% 361 37% 0.847 | 361 37% | 361 37% | 0.847 |
| COVID-19 related hospitalisation | 422 28% 147 28% 275 28% 0.887 | 275 28% | 275 28% | 0.887 |

Statistically significant associations are in bold.

IBD, inflammatory bowel disease; SD, standard deviation; BMI, body mass index.

aUnless otherwise specified, percentages do not include missing values or ‘unknown’. For all characteristics, unless noted above, less than 4% of data were missing and unknown, respectively, for each category.

bPercentages and n from each subcategory may not add up to the exact number of total reported cases, due to missing values and/or non-mutually exclusive variables.

cBy physician global assessment [PGA] at time of COVID-19 infection.
data on physician practice patterns regarding IBD therapy in the setting of COVID-19.

2. Methods

We analysed data from the Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease (SECURE-IBD) registry to determine physician practice patterns in IBD patients with confirmed COVID-19. Collection and categorisation of data have been previously reported.1 Reporters to SECURE-IBD were asked if any medications were stopped due to active COVID-19 infection and to indicate which specific drugs were stopped.

We conducted bivariate analyses to understand demographic and clinical characteristics associated with stopping at least one IBD medication due to COVID-19, and subsequently performed multivariable logistic regression to evaluate the independent effects on IBD disease activity [specified a priori] and other patient characteristics that were statistically significant on bivariate analyses. We also analysed country as a variable affecting stopping in multivariate analyses and included any country with ≥50 reported cases in SECURE-IBD. Additionally, among users of each medication class, we compared the proportion of patients who had discontinued treatment after diagnosis of COVID-19; p-values ≤0.05 were considered statistically significant.

3. Results

Of 1499 patients with available medication-related data in the SECURE-IBD registry, IBD medications were stopped in 518 [34.6%] patients and continued in 981 [65.4%] patients. Baseline characteristics of patients who stopped and did not stop at least one medication are reported in Table 1. On bivariate and multivariable analyses, a diagnosis of ulcerative colitis [UC] or IBD-unspecified [IBD-U] was associated with a lower odds of stopping medication compared with Crohn’s disease [CD] (adjusted odds ratio [aOR] 0.6, 95% CI 0.48, 0.75) [Table 2]. Compared with cases from other countries, those from Italy and Brazil were associated with higher odds of stopping IBD medication on bivariate analysis, but this was not significant in the multivariable model. Other demographic variables, physician global assessment of IBD activity, COVID-19 related emergency room visit, or hospitalisation were not associated with stopping IBD therapy in the setting of COVID-19.

When evaluating specific medications, 5-ASA was more likely to be continued [p <0.001] whereas anti-tumour necrosis factor [anti-TNF] therapy and immunomodulator therapy 96-mercaptopurine [6MP], azathioprine, methotrexate) were more likely to be stopped [global p <0.001] [Figure 1]. Of 156 patients on combination therapy with an anti-TNF and an immunomodulator, the anti-TNF alone was stopped in 10 [6.4%], immunomodulator alone in 33 [21.2%], and both medications in 53 [34%] patients. Sixty [38%] patients continued on combination therapy.

4. Discussion

In this brief report, we describe physician practice patterns in holding IBD medications, in an international registry of IBD patients with confirmed COVID-19. IBD medications were more likely to be continued in those with UC or IBD-U than with CD. This is likely due, at least in part, to a higher proportion of UC patients on 5-ASA therapy, which was the most likely medication to be continued. Conversely, anti-TNFs and immunomodulators, used alone or in combination, were the most frequently stopped classes of medications. These practice patterns are largely concordant with expert guidance on IBD medication management in setting of COVID-19.1

However, IBD medications were continued for nearly two-thirds of patients, and combination therapy with an anti-TNF and immunomodulator in nearly 40% of patients. It is important to note that biweekly or less frequent dosing of certain biologics could affect decision and feasibility to stop. Emergency room visit or hospitalisation due to COVID-19 did not impact on IBD medication management. Although variation in the discontinuation of IBD medications was significant by country in bivariate analyses, these associations did not remain statistically significant in a multivariable model. Notable trends that may have been limited by sample size include lower odds of medication discontinuation in patients from Italy and higher odds of discontinuation in patients from Brazil. These findings suggest the need to further study international variation in practice patterns and patient outcomes. In the absence of these data, we suggest following guidance laid out per expert consensus.1

Strengths of this study include the use of a large, international registry with a diverse adult and paediatric IBD patient population. Limitations include the considerable risk of reporting bias in this voluntary registry of IBD patients with COVID-19 patients. Another limitation is missing data, although this was <4% for all variables except ethnicity. In the present study, we were not able to evaluate

Table 2. Multivariable analysis to determine factors associated with odds of stopping IBD medication in IBD patients with COVID-19.

| Effect                  | Crude odds ratio | 95% Wald confidence limits | p-value | Adjusted odds ratio | 95% Wald confidence limits | p-value |
|-------------------------|------------------|----------------------------|---------|---------------------|----------------------------|---------|
| Active vs remission     | 1.024            | 0.822, 1.277               | 0.8296  | 0.971               | 0.772, 1.221               | 0.8003  |
| Unknown vs remission    | 1.203            | 0.676, 2.14                | 0.5298  | 1.261               | 0.702, 2.266               | 0.4375  |
| UC/IBDU vs CD           | 0.607            | 0.489, 0.755               | <0.0001 | 0.597               | 0.478, 0.747               | <0.0001 |
| USA vs non-USA          | 0.929            | 0.742, 1.163               | 0.5203  | 0.943               | 0.704, 1.264               | 0.6965  |
| Spain vs non-Spain      | 1.053            | 0.783, 1.417               | 0.7311  | 1.13                | 0.791, 1.615               | 0.5015  |
| France vs non-France    | 1.048            | 0.671, 1.636               | 0.8361  | 1.029               | 0.63, 1.68                 | 0.9092  |
| Italy vs non-Italy      | 0.507            | 0.289, 0.892               | 0.0183  | 0.595               | 0.326, 1.087               | 0.0916  |
| UK vs non-UK            | 1.099            | 0.67, 1.803                | 0.7081  | 1.154               | 0.674, 1.975               | 0.6014  |
| Iran vs non-Iran        | 1.154            | 0.655, 2.032               | 0.6205  | 1.403               | 0.764, 2.577               | 0.2748  |
| Russia vs non-Russia    | 1.308            | 0.824, 2.078               | 0.2544  | 1.477               | 0.882, 2.472               | 0.1381  |
| Brazil vs non-Brazil    | 1.785            | 1.014, 3.141               | 0.0447  | 1.731               | 0.947, 3.167               | 0.0748  |

Statistically significant associations are in bold.
UC, ulcerative colitis; IBD-U, IBD-unspecified; CD, Crohn’s disease.
the impact of holding or continuing medications on COVID-19 outcomes, due to issues related to unmeasured confounding of COVID-19 severity and lack of data regarding duration of holding medication and timing of medication restarting.

In summary, we found that IBD medications other than immunomodulators were continued in the majority of IBD patients with COVID-19, in the international SECURE-IBD registry. Future studies are needed to understand the impact of stopping or continuing IBD medications on IBD-related outcomes as well as COVID-19 related outcomes. The data underlying this article are available in the article and in its online supplementary material.

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**Conflict of Interest**

The corresponding author confirms on behalf of all authors that there have been no involvements that might raise the question of bias in the work reported or in the conclusions, implications, or opinions stated. MA receives research support from the Dickler Family Fund, New York Community Trust, and Helmsley Charitable Trust Fund for SECURE-IBD. EJB is supported by an Institutional Training Grant from the National Institutes of Health [T32DK007634]. JFC reports receiving research grants from AbbVie, Janssen Pharmaceuticals, and Takeda; receiving consulting fees from AbbVie, Amgen, Arena Pharmaceuticals, Boehringer Ingelheim, Celgene Corporation, Celtrion, Eli Lilly, Enterome, Ferring Pharmaceuticals, Genentech, Janssen Pharmaceuticals, Landos, Ipsen, Medimmune, Merck, Novartis, Pfizer, Shire, Takeda, Tigenix, and Viela bio; and holds stock options in Intestinal Biotech Development and Genfit. MDK has consulted for Abbvie, Janssen, Pfizer, and Takeda, is a shareholder in Johnson & Johnson, and has received research support from Abbvie and Janssen. RCU has served as a consultant and/or advisory board member for Eli Lilly, Janssen, Pfizer, and Takeda. He has received research support from AbbVie, Boehringer Ingelheim, and Pfizer. He is supported by a Career Development Award from the National Institutes of Health [K23KD111995-01A1].

**Author Contributions**

MA: study concept and design, interpretation of data, drafting of manuscript, critical revision of the manuscript for important intellectual content; EJB: study concept and design, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content; JFC: study concept and design, interpretation of data, critical revision of the manuscript for important intellectual content; MDK: study concept and design, interpretation of data, critical revision of the manuscript for important intellectual content; RCU: study concept and design, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content.

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