Seroconversion Following SARS-CoV-2 Infection or Vaccination in Pediatric IBD Patients

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Introduction

Protective immunity to SARS-CoV-2, either naturally induced by infection or artificially induced or augmented by vaccination, is vital to reducing the transmission of SARS-CoV-2 and the burden of severe coronavirus disease 2019 (COVID-19). Data on the impact of immunomodulatory therapies used to treat inflammatory bowel disease (IBD) on both types of protective immunity have been scant, with initial reports of attenuation of natural immunity and vaccine efficacy by TNF antagonists.¹,² However, 2 doses of COVID-19 vaccine or a single dose in those with a history of SARS-CoV-2 infection have both been shown to induce seroconversion in a large majority of patients.²,³ There is little data on seroconversion in pediatric IBD, a population that may have distinct immunologic responses to SARS-CoV-2, given that increased age has been associated with lower antibody concentrations after COVID-19 vaccination.² Understanding seroconversion is particularly important as vaccination becomes more widely available in pediatrics with the recent emergency use approval of BNT162b2 (Pfizer-BioNTech) down to 12 years of age.⁴ We therefore sought to evaluate and compare serologic responses to SARS-CoV-2 infection and vaccination in a pediatric IBD cohort.

Methods

We conducted a retrospective chart review of all IBD patients younger than 21 years old in whom a SARS-CoV-2 immunoglobulin G (IgG) antibody assay was performed between April 2020 and May 2021 at our tertiary care center. The COVID-SeroKlir (Kantaro Biosciences, LLC, New York, NY) semiquantitative SARS-CoV-2 IgG antibody assay, an enzyme-linked immunosorbent assay (ELISA) measuring IgG antibody to the full-length SARS-CoV-2 spike protein with emergency use authorization, was routinely collected at infusion and outpatient clinic visits.⁵ The study was approved by the Mount Sinai institutional review board.

Electronic medical records were reviewed, and data were collected on demographics, IBD location and behavior (Paris classification),⁶ exposure(s) to SARS-CoV-2, and history of SARS-CoV-2 infection/symptoms. Indication for antibody testing and titer levels, which were described as high titer or strongly positive (≥960 titer or >40 AU/mL), moderately positive (320–960 titer or 16–39 AU/mL), weakly positive (80–160 titer or 5–15 AU/mL), and negative⁵ were recorded.

Patients meeting World Health Organization (WHO) criteria for confirmed (laboratory confirmation of COVID-19 infection) or probable COVID-19 (either meeting defined clinical criteria with contact with a probable or confirmed case of COVID-19 or recent onset of anosmia/ageusia without an identified cause) were classified as having prior COVID-19 infection.⁷ Standard descriptive statistics, including frequency for categorical variables and median (interquartile range [IQR]) for continuous variables, were calculated unless otherwise stated. Univariate analyses were performed using Fisher exact and χ² test for categorical variables and Mann-Whitney and Spearman Rank Coefficient for continuous variables where appropriate. Statistical analyses were performed using R 3.6.3 (The R Foundation for Statistical Computing, 2018) and SAS OnDemand for Academics 3.8 (SAS Institute Inc., Cary, NC, 2020). A P value ≤.05 was considered statistically significant.

Results

One or more SARS-CoV-2 IgG antibody assay(s) was performed in 340 pediatric patients; 15% (n = 51) were confirmed or probable for COVID-19; 2% (n = 7) were suspected for COVID-19; 16% (n = 54) were exposed to or had close contact with SARS-CoV-2 infection without clinical symptoms; 61% (n = 208) did not have any prior symptoms or exposures; and 6% (n = 20) had a history of COVI-19 vaccination. In the 51 patients with confirmed or probable...
COVID-19, 90% had seroconversion (Supplementary Table 1). Of the 5 patients without evidence of seroconversion, 3 had confirmed and 2 had probable COVID-19. Those that did not seroconvert were similar in age to the rest of the postinfection cohort (median 20 [17–20] years old, \( P = .15 \)), with a trend to a higher proportion of patients with UC/IBD-U (60%, \( P = .07 \)); 4 patients (80%) were on a biologic therapy (3 infliximab, 1 ustekinumab), and the remaining patient was on 5-aminosalicylate (5-ASA). There was a significantly longer time interval between infection and titer level measurement in those with a negative titer (negative, 257 [167–340] days; positive, 112 [41–180] days; \( P = .03 \)); however, titer level was not correlated with time from infection in the entire postinfection cohort (\( P = −0.06, P = .74 \)).

Within the 16% of patients with exposure to SARS-CoV-2 without clinical symptoms, 23 (43%) had a positive SARS-CoV-2 antibody assay. There were no identified clinical characteristics associated with seroconversion in the group exposed to SARS-CoV-2 without clinical symptoms (Supplementary Table 2).

Twenty patients had antibody testing after vaccination (Table 1). All patients seroconverted following vaccination, and all patients receiving mRNA vaccination had high titer levels. The patient who received a single dose of JNJ-78436735 (Johnson & Johnson) had a moderate titer level. All but 1 (95%) of those receiving a 2-series mRNA vaccination had completed both vaccinations in the series; the single patient with an assay performed after only 1 dose of BNT162b2, with no prior history of SARS-CoV-2 infection, seroconverted. Titer level was not significantly associated with type of biologic or small molecule therapy (Figure 1); patients receiving mRNA-1273 (NIH-Moderna) did have significantly higher titer levels compared to BNT162b2 and JNJ-78436735 (\( P = .005 \)).

### Discussion

Herein we report robust serologic antibody responses to SARS-CoV-2 infection and COVID-19 vaccination in a pediatric IBD cohort. All of our patients seroconverted after vaccination even in the setting of biologic and small molecule usage, which was similar to the findings in an adult IBD study published out of our center.\(^3\) Moreover, nearly all (90%) of our patients had seroconversion following SARS-CoV-2 infection, which was higher than the rates seen in Kennedy et al, suggesting improved postinfection seroconversion in pediatrics.\(^3\) The high titer levels achieved in a large number of those who seroconverted are thought to confer protection; however, the association with elapsed time from SARS-CoV-2 exposure to negative level warrants continued investigation into the longevity of the protection conferred and more detailed cataloging of the complexities of the immunoprotective response beyond IgG antibodies. Although we are limited by our small sample size and variable times to assay, this study provides important reassurances to pediatric gastroenterologists, patients, and families and lends further support to expert consensus recommendations for vaccination of IBD patients.\(^8\)

| Table 1. Clinical characteristics of pediatric patients with IBD who received COVID vaccination. |
|-----------------------------------------------|
| **Clinical Characteristic** | **Vaccination +/- Prior Infection** |
| Demographics | | |
| Male, N (%) | 12 (60) |
| Age (years), Median (IQR) | 18 (17–20) |
| Vaccination Type | | |
| BNT162b2 (Pfizer-BioNTech) | 14 (70) |
| mRNA-1273 (NIH-Moderna) | 5 (25) |
| JNJ-78436735 (Johnson & Johnson) | 1 (5) |
| IBD Subtype, N (%) | | |
| Crohn’s Disease | 15 (75) |
| Ulcerative colitis | 5 (25) |
| Age of Diagnosis, N (%) | | |
| Diagnosis <17 years | 17 (85) |
| Crohn’s Disease Location | | |
| Ileal | 4 (29) |
| Colonic | 1 (7) |
| Ileocolonic | 8 (57) |
| Isolated Upper Tract | 1 (7) |
| Crohn’s Disease Behavior, N (%) | | |
| Non-penetrating, nonstricturing | 11 (85) |
| Structuring | 1 (8) |
| Penetrating | 0 (0) |
| Structuring and Penetrating | 1 (8) |
| Perianal Disease | 2 (15) |
| Ulcerative Colitis/IBD-U, N (%) | | |
| Proctitis | 0 (0) |
| Left-sided | 1 (20) |
| Extensive/pancolitis | 4 (80) |
| IBD Therapy, N (%) (Supplementary Figure 1B) | | |
| Biologic Therapy | 19 (95) |
| Infliximab | 7 (37) |
| Adalimumab | 2 (11) |
| Ustekinumab | 10 (53) |
| Vedolizumab | 0 (0) |
| Tofacitinib | 2 (10)\(^a\) |
| Disease Activity, N (%) | | |
| Clinical remission\(^b\) at time of vaccination | 17 (89) |
| SARS-CoV-2 Antibody Testing | | |
| Antibody positive, N (%) | 20 (100) |
| Median (IQR) time from last vaccination to titer (days) | 29 (14–37)\(^b\) |
| High titer, N (%) | 18 (95)\(^b\) |
| History of Infection, N (%) | 5 (25) |

\(^a\)Clinical remission: partial Mayo Score <2 or Harvey-Bradshaw Index <4
\(^b\)Single patient with qualitative titer only available
\(^c\)One patient was on combination ustekinumab and tofacitinib
Supplementary Data
Supplementary data is available at Inflammatory Bowel Diseases online.

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Conflicts of Interest
M.C.D. is a consultant for Janssen, Abbvie, UCB, Takeda, Pfizer, Prometheus Labs, Genentech, Salix, Celgene Research Support, Takeda, Pfizer, and Janssen. M.T.D. is a consultant for Neurologic Corp., a subsidiary of Samsung Electronics Co., Ltd. The remaining authors disclose no conflicts.

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