Adverse Events & Serological Responses Following SARS-CoV-2 Vaccination in Individuals with Inflammatory Bowel Disease

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Background

- The rapid development of SARS-CoV-2 vaccines has raised concerns over vaccine safety in immunocompromised populations including for those with inflammatory bowel disease (IBD)
- We described adverse events (AEs) following SARS-CoV-2 vaccination in those with IBD and determined relationships between AEs and post-vaccination antibody titres

Methods

- Individuals with IBD were assessed for anti-SARS-CoV-2 spike antibody (anti-S) concentration within 1–12 weeks following 1st, 2nd, 3rd, and/or 4th dose of vaccine
- AEs following vaccination were collected via telephone interview after each dose, using the Adverse Events Following Immunization form
- Antibodies against the SARS-CoV-2 spike protein (Anti-S) concentration was defined as geometric mean titre (GMT), and AEs were classified using binary definitions
- Multivariable logistic regression was used to model the effect of independent predictors on injection site reaction by vaccine dose
- Flare of IBD within 30 days of vaccination was collected via chart review

Results

- Multivariable logistic regression determined no associations between anti-S concentration and injection site reaction for all doses
- Age above 65 years was associated with decreased injection site reaction with 1st and 3rd doses
- Female sex and mRNA vaccine type were associated with increased injection site reaction with 1st and 2nd doses
- Prior COVID-19 infection, IBD type, and medication class were not associated with injection site reaction with any dose
- No flares were reported within 30 days of any vaccination. However, one participant was diagnosed with a severe AE requiring hospitalization: Immune thrombocytopenic purpura (ITP) following 2nd dose

Discussion

- AEs following SARS-CoV-2 vaccination are generally mild and become less common with each consecutive dose
- SARS-CoV-2 vaccines are not associated with IBD flares
- Females, those under 65 years of age, and those administered mRNA vaccines are more likely to experience injection site reaction following vaccination
- Prior COVID-19 infection, IBD type, and medication class do not predict injection site reaction

Table 1. Participant characteristics and adverse events following 1st, 2nd, 3rd, and 4th dose of a SARS-CoV-2 vaccine

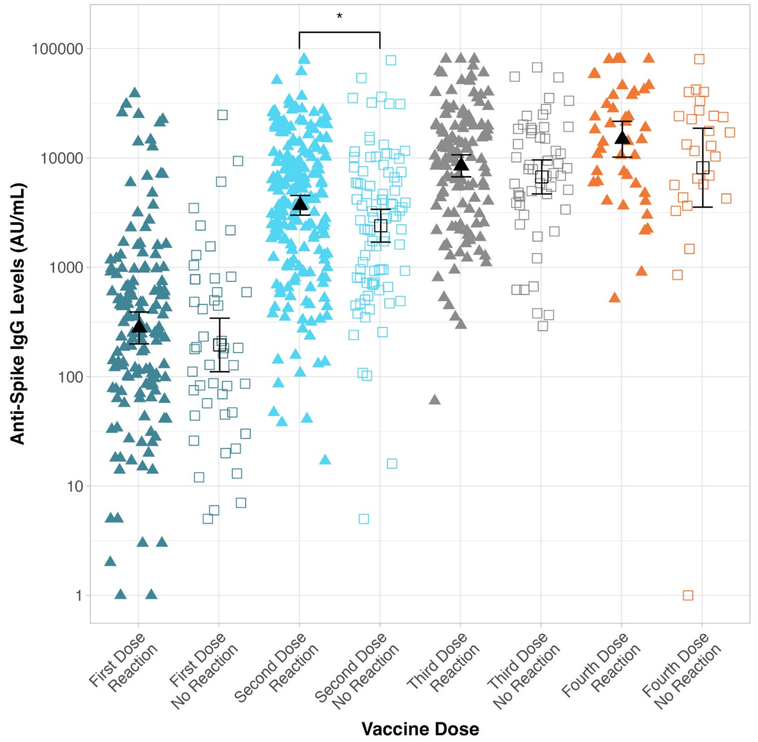
Characteristics	Dose 1 (/331)	Dose 2 (/331)	Dose 3 (/195)	Dose 4 (/100)
Sex, *n* (%)				
Male	155 (46.8%)	155 (46.8%)	86 (44.1%)	49 (49.0%)
Female	176 (53.2%)	176 (53.2%)	109 (55.9%)	51 (51.0%)
Mean age (SD)	52.05 (14.52)	52.05 (14.52)	51.81 (15.20)	57.98 (14.01)
IBD Type, *n* (%)				
Crohn's Disease	238 (71.9%)	238 (71.9%)	150 (76.9%)	75 (75.0%)
Ulcerative Colitis & IBD-U	93 (28.1%)	93 (28.1%)	45 (23.1%)	25 (25.0%)
Medication, *n* (%)				
No immunosuppressives	33 (10.0%)	32 (9.7%)	14 (7.2%)	27 (27.0%)
Anti-TNF only	118 (35.7%)	119 (36.0%)	74 (38.0%)	20 (20.0%)
Immunomodulators only	7 (2.1%)	7 (2.1%)	5 (2.6%)	<5
Vedolizumab only	37 (11.2%)	39 (11.8%)	19 (9.7%)	9 (9.0%)
Ustekinumab only	76 (23.0%)	74 (22.4%)	42 (21.5%)	16 (16.0%)
Tofacitinib only	5 (1.5%)	5 (1.5%)	<5	—
Combination therapy	49 (14.8%)	47 (14.2%)	36 (18.5%)	18 (18.0%)
Oral Corticosteroids	6 (1.8%)	8 (2.4%)	<5	7 (7.0%)
Vaccine Type, n (%)				
Pfizer-BioNTech	271 (81.9%)	275 (83.1%)	179 (91.8%)	82 (82.0%)
Moderna	45 (13.6%)	49 (14.8%)	16 (8.2%)	18 (18.0%)
AstraZeneca	15 (4.5%)	7 (2.1%)	—	—
Adverse Events	**Dose 1 (/331)**	**Dose 2 (/331)**	**Dose 3 (/195)**	**Dose 4 (/100)**
Injection site, *n* (%)	250 (75.5%)	231 (70%)	138 (70.8%)	55 (55.0%)
Lymph node swelling, *n* (%)	1 (0.3%)	9 (2.7%)	14 (7.2%)	1 (1.0%)
Gastrointestinal, *n* (%)	17 (5.1%)	16 (4.8%)	6 (3.1%)	2 (2.0%)
Fatigue or malaise, *n* (%)	86 (26.0%)	87 (26.3%)	45 (23.1%)	22 (22.0%)
Fever or chills, *n* (%)	27 (8.2%)	35 (10.6%)	19 (9.7%)	5 (5.0%)
Musculoskeletal, *n* (%)	34 (10.3%)	41 (12.4%)	25 (12.8%)	9 (9.0%)
Headache or migraine, *n* (%)	34 (10.3%)	46 (13.9%)	23 (11.8%)	11 (11.0%)
Other, *n* (%)	16 (4.8%)[α]	14 (4.2%)[β]	7 (3.6%)[γ]	2 (2.0%)[δ]
Any symptoms, *n* (%)	275 (83.3%)	261 (79.1%)	151 (77.4%)	67 (67.0%)

Table 2. Multivariable logistic regression model for predictors of injection site reaction by vaccine dose

Variables	Post-1st Dose (*n* = 188)		Post-2nd Dose (*n* = 277)		Post-3rd Dose (*n* = 154)	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	p-value
Age						
<65 years*	**0.24 (0.11, 0.55)**	**0.001**	0.72 (0.36, 1.44)	0.349	**0.39 (0.17, 0.90)**	**0.027**
65+ years						
Sex						
Female*	**0.40 (0.19, 0.85)**	**0.017**	**0.48 (0.27, 0.85)**	**0.011**	0.86 (0.40, 1.84)	0.700
Male						
IBD Type						
Ulcerative colitis / IBD-U*	0.62 (0.24, 1.64)	0.336	0.76 (0.39, 1.47)	0.412	0.93 (0.36, 2.45)	0.888
Crohn's disease						
Medication						
No immunosuppressives*	—	—	—	—	—	—
Anti-TNF only	0.72 (0.20, 2.60)	0.619	0.86 (0.33, 2.22)	0.748	0.18 (0.02, 1.69)	0.133
Immunomodulators only	0.85 (0.05, 13.52)	0.909	1.49 (0.14, 16.46)	0.744	0.12 (0.01, 2.30)	0.159
Vedolizumab only	1.61 (0.32, 7.99)	0.563	1.56 (0.48, 5.08)	0.460	0.34 (0.03, 4.48)	0.412
Ustekinumab only	0.74 (0.20, 2.72)	0.646	1.50 (0.52, 4.34)	0.457	0.29 (0.03, 2.85)	0.286
Tofacitinib only	0.17 (0.01, 2.91)	0.223	0.47 (0.06, 3.57)	0.466	—	—
Combination therapy[a]	0.85 (0.19, 3.76)	0.828	1.41 (0.43, 4.64)	0.575	0.46 (0.04, 4.86)	0.516
Corticosteroids[b]	—	—	1.98 (0.29, 13.49)	0.484	0.15 (0.01, 3.14)	0.222
Vaccine Type						
Viral vector vaccine*	**7.78 (1.85, 32.81)**	**0.005**	**6.34 (1.08, 37.30)**	**0.041**	—	—
mRNA vaccine						
Prior COVID-19						
No*	1.07 (0.27, 4.25)	0.924	1.09 (0.38, 2.65)	0.987	1.51 (0.38, 5.95)	0.560
Yes						
Anti-S Antibody Level						
Per $\log_{10}$ (AU/mL)	1.00 (0.55, 1.83)	0.998	1.39 (0.85, 2.27)	0.193	1.41 (0.67, 2.97)	0.366

* Indicates reference group
[a] Combination therapy refers to any combination of two or more of the following therapies: anti-TNF, immunomodulators, vedolizumab, ustekinumab, and tofacitinib
[b] Oral prednisone at any dose or with any other drug class

Figure 1. Log-transformed anti-SARS-CoV-2 spike antibody concentration across four doses of SARS-CoV-2 vaccine for participants who reported injection site reactions compared to participants who did not



Additional data is available through our interactive data visualization website: https://kaplan-gi.shinyapps.io/COVID_Serology/

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