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Clinical science

Characteristics of and risk factors for COVID-19 breakthrough infections in idiopathic inflammatory myopathies: results from the COVAD study

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Abstract

Objectives: The objective of this study was to explore the prevalence, characteristics and risk factors of COVID-19 breakthrough infections (BIs) in idiopathic inflammatory myopathies (IIMs) using data from the COVID-19 Vaccination in Autoimmune Diseases (COVAD) study.

Methods: A validated patient self-reporting e-survey was circulated by the COVAD study group to collect data on COVID-19 infection and vaccination in 2022. BIs were defined as COVID-19 occurring $\geq$14 days after two vaccine doses. We compared BI characteristics and severity among patients with IIMs, patients with other autoimmune rheumatic and non-rheumatic diseases (AIRD, nrAID), and healthy controls (HCs). Multivariable Cox regression models were used to assess the risk factors for BI, severe BI ,and hospitalizations among patients with IIMs.

Results: Among the 9449 included responses, BIs occurred in 1447 respondents (15.3%). The median age was 44 years [interquartile range (IQR) 21], 77.4% were female, and 182 BIs (12.9%) occurred among the 1406 patients with IIMs. Multivariable Cox regression among the data for patients with IIMs showed increasing age to be a protective factor for BIs [hazard ratio (HR) = 0.98, 95% CI = 0.97–0.99], and HCQ and SSZ use were risk factors (HR = 1.81, 95% CI = 1.24–2.64, and HR = 3.79, 95% CI = 1.69–8.42, respectively). Glucocorticoid use was a risk factor for a severe BI (HR = 3.61, 95% CI = 1.09–11.8). Non-white ethnicity (HR = 2.61, 95% CI = 1.03–6.59) was a risk factor for hospitalization. Compared with other groups, patients with IIMs required more supplemental oxygen therapy (IIMs = 6.0% *vs* AIRDs = 1.8%, nrAIDs = 2.2% and HCs = 0.9%), intensive care unit admission (IIMs = 2.2% *vs* AIRDs = 0.6%, nrAIDs and HCs = 0%), advanced treatment with antiviral or monoclonal antibodies (IIMs = 34.1% *vs* AIRDs = 25.8%, nrAIDs = 14.6% and HCs = 12.8%) and had more hospitalization (IIMs = 7.7% *vs* AIRDs = 4.6%, nrAIDs = 1.1% and HCs = 1.5%).

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Conclusion: Patients with IIMs are susceptible to severe COVID-19 BIs. Age and immunosuppressive treatments were related to the risk of BIs.

Keywords: idiopathic inflammatory myopathies, COVID-19, breakthrough infection, autoimmune diseases, hospitalization.

Rheumatology key messages

- Severe cases of COVID-19 BIs were more common in patients with IIMs than in other groups.
- The risk of a severe BI was higher among IIM patients on glucocorticoids and among non-white participants.

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Introduction

Vaccines have emerged as a safe and effective intervention for reducing severe COVID-19 outcomes [1]. However, emerging evidence of vaccine breakthrough COVID-19 infections (BIs) suggest that the protection offered may wane with time, though reassuringly BIs appear to be less severe than for pre-vaccination COVID-19 [2–4]. However, given the susceptibility of patients with autoimmune rheumatic diseases (AIRDs), particularly idiopathic inflammatory myopathies (IIMs), to poor COVID-19 outcomes, owing to frequent AIRD sequelae, comorbidities, and immunosuppression, even relatively milder BIs may represent a cause for concern in this vulnerable group [4–6]. This is reflected by the rare, yet non-negligible incidence of hospitalization, the requirement for oxygen supplementation, and even mortality associated with COVID-19 BIs in these patients, though the majority of cases remain mild [4, 7].

While the characteristics and risk factors for BIs, including vaccine type, homologous/heterologous vaccination, newer SARS-CoV-2 variants, employment in health-care professions, and immunosuppressants have been described in the general population and AIRDs, BIs in patients with IIMs remain understudied [2–4, 8–11]. In a retrospective study of 11 468 rheumatic disease patients, patients on B cell–depleting therapy, CTLA4-antibody, MMF, IL-6 inhibitors, and JAK inhibitors reported higher frequency of BIs compared with the users of HCQ [9]. Important aspects of AIRDs, such as disease type and immunosuppressant drugs, the cornerstone of the management of these patients, remain underexplored as potential risk factors for BIs, including severe BIs [4, 7, 9–11]. In another study, immunosuppressed patients were found to be at three times higher risk of contracting BIs [11]. IIMs are heterogeneous diseases with a higher interferon signature and higher use of steroids and immunosuppression compared with other AIRDs [12, 13]. There is no data on the prevalence and characteristics of BIs after booster vaccination and advanced treatment for COVID among patients with IIMs, other than the preliminary insights into early BIs published by the COVAD group previously [4].

Thus, the primary aim of this study was to investigate the prevalence and characteristics of BIs, severe BIs, and all-cause hospitalization in a large sample of patients with IIMs. The secondary aim was to identify risk factors for BIs among patients with IIMs and compare the prevalence and characteristics of BIs in patients with IIMs with those for patients with other AIRDs, non-rheumatic autoimmune diseases (nrAIDs) and healthy controls (HCs). We further explored BIs among patients with subtypes of IIMs, and the characteristics of a second BI.

Methods

Study design and ethics

We analysed data from the 2nd COVAD study, an international multicentre cross-sectional patient self-reporting electronic survey [14]. Respondents were informed regarding the survey via cover letter at the beginning of the survey, and they consented electronically in lieu of written consent [15]. No financial incentives were offered for survey completion, and we obtained prior ethical approval from the institutional ethics committee of Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India [16]. We adhered to The Checklist for Reporting Results of the Internet E-Surveys (CHERRIES) when reporting results [17].

Data collection and eligibility criteria

The validated COVAD-2 study questionnaire was hosted on the www.surveymonkey.com platform in multiple languages; it was circulated by the global study group of 157 collaborators across 106 countries in their clinics, across patient support groups, and on social media platforms. We collected data on demographics, AIRD details (including diagnosis, treatment history, and current symptom status), COVID-19 infection history, including symptoms, duration, and complications (hospitalization due to COVID-19 and requirement of oxygen therapy), and COVID-19 vaccination details in patients with autoimmune diseases and HCs from 1 January 2022, to 31 July 2022. Our methods are further detailed in the previously published protocol [14, 18].

We included a convenience sample of all adult participants (≥18 years old) with IIMs, AIRDs, nrAIDs and HCs who had received at least two COVID-19 vaccine doses in the analysis. Participants answered a closed-ended question 'Did you ever test positive for COVID-19?' and specified the number of events and the dates of occurrence. Incomplete responses, those vaccinated prior to June 2020 (probable trial participants), and patients who received the primary series with a single vaccine dose were excluded. Respondents without autoimmune diseases were considered HCs. The definitions of IIMs, AIRDs and nrAIDs are detailed in the Supplementary Material online.

Outcome measures and covariates

BIs were defined as COVID-19 infections occurring ≥14 days after the second vaccine dose [19]. BIs requiring hospitalization, intensive care unit (ICU) or high-dependency unit (HDU) admission, oxygen requirement, or advanced treatment (antivirals or mAbs) were defined as severe. Hospitalizations due to COVID-19 included respondents

who were hospitalized for COVID-19 infections or BIs. Data on age, gender, ethnicity, comorbidities, country by Human Development Index, first vaccine dose, vaccine type, number of vaccine doses, myositis subtype, and immunosuppressive medications (not mutually exclusive groups) were collected and analysed as covariates.

We used the validated Patient Reported Outcomes Measurement Information System (PROMIS®) Fatigue 4a tool to assess fatigue in the past 7 days prior to survey completion through four questions, with a total score ranging from 4 (lowest fatigue) to 20 (highest fatigue) [20, 21]. Therefore, the current fatigue status was considered a long-term outcome following BIs and was compared among patients with IIMs after several vaccine doses.

Statistical methods

The characteristics of the major subgroups of participants with BIs were compared using the Mann–Whitney *U* test for continuous variables (age, days until the first BI) and the χ^2 test for categorical variables.

Predictors of BIs, severe BIs, and hospitalization among patients with IIMs were evaluated by univariable and multivariable Cox regression, and the results were presented as hazard ratios (HRs) with a 95% CI. The multivariable Cox regression models were adjusted for age, gender, ethnicity, and those covariates with a $P < 0.2$ in the univariable analysis. Those covariates not following the proportional hazards assumption (model using time-dependent interaction terms) were excluded from the model.

COVID-19 BI symptoms and severity among patients with IIMs were compared with those for patients with AIRDs, patients with nrAIDs, and HCs individually using the Kruskal–Wallis test, with Bonferroni's posthoc test for continuous variables (days until symptoms resolution) and the χ^2 test for categorical variables. Comparison of Fatigue 4a scores between the BIs in patients with IIMs after different number of vaccine doses were adjusted for time since BI using a linear regression model.

Additional exploratory analysis of COVID-19 BIs after different number of vaccine doses, comparison of symptoms and severity among IIMs subgroups (DM, anti-synthetase syndrome, IBM, necrotizing autoimmune myositis, overlap myositis and PM), and characteristics of the second BI among the major subgroups of participants was performed using χ^2 for categorical variables and the Kruskal–Wallis test for continuous variables. Statistical significance was defined as a two-sided *P*-value <0.05 unless otherwise stated. Statistical analyses were performed using IBM SPSS version 28.0.

Results

Study population

Among the total 17 612 survey respondents, 10 783 completed the survey in full. From these, we excluded the unvaccinated ($n = 734$), single COVID-19 vaccine dose recipients ($n = 319$), primary series vaccination with a single vaccine dose ($n = 277$), and those vaccinated prior to June 2020 (probable trial participants) ($n = 4$), finally including 9449 respondents who had received at least two vaccine doses in the final analysis.

BI prevalence and characteristics

COVID-19 BIs occurred in 1447 (15.3%) respondents in total, median age 44 years [interquartile range (IQR) 35, 56], 77.4% female, 54.7% white, of whom 12.5% ($n = 182$) were patients with IIMs, 49.4% ($n = 716$) were patients with AIRDs, 6.1% ($n = 89$) were patients with nrAIDs, and 31.7% ($n = 460$) were HCs. The prevalence of BIs among patients with IIMs was 12.9% (182/1406). Comorbidities were common, with mental health disorders (28.5%), hypertension (16.5%) and dyslipidaemia (12.1%) being the most prevalent. The first BI occurred after a median of 117 days (IQR 59, 176) following the second COVID-19 vaccine dose and did not differ between the different groups. Other baseline characteristics of the respondents experiencing BIs are detailed in Table 1.

Risk factors for COVID-19 BIs, severe BIs, and hospitalization among IIMs

In the multivariable Cox model, increasing age (HR = 0.98, 95% CI = 0.97–0.99) was protective; HCQ (HR = 1.81, 95% CI = 1.24–2.64), and SSZ therapy (HR = 3.79, 95% CI = 1.69–8.42) were associated with increased risk of BIs (Tables 2 and 3). Glucocorticoid use was associated with severe BIs, with an adjusted HR = 3.61 (95% CI = 1.09–11.8) in the multivariable model (Table 3). Having non-white ethnicity was an additional risk factor for hospitalization among patients with IIMs (HR = 2.61, 95% CI = 1.03–6.59) (Table 3).

Comparison of BIs among patients with IIMs, patients with other autoimmune diseases, and HCs

BIs symptoms and severity were different among the major groups. For instance, symptoms resolution time was longer in patients with IIMs (median 12 days) and AIRDs (11 days) compared with patients with nrAIDs (8 days) and HCs (7 days, $P < 0.001$). Arthralgia, headache and chest pain were more common in patients with AIRDs (40.6%, 46.8% and 15.5%, respectively), while cough (67.6%) was more common in patients with IIMs. Difficulty breathing and nausea/vomiting were more common in both IIMs (19.2% and 12.1%, respectively) and AIRDs (21.2% and 12.0%, respectively). A full description of the symptoms for the various groups is depicted in Table 4.

Compared with other groups, patients with IIMs required more supplemental oxygen therapy (IIMs = 6.0%, AIRDs = 1.8%, nrAIDs = 2.2%, HCs = 0.9%, $P < 0.001$), intensive care unit admission (IIMs = 2.2%, AIRDs = 0.6%, nrAIDs and HC = 0%, $P < 0.007$), advanced treatment with antiviral or mAbs (IIMs = 34.1%, AIRDs = 25.8%, nrAIDs = 14.6% and HCs = 12.8%, $P < 0.001$), and had more all-cause hospitalization (IIMs = 7.7%, AIRDs = 4.6%, nrAIDs = 1.1% and HCs = 1.5%, $P < 0.001$).

BI after different vaccine doses, in patients with subtypes of IIMs

BIs were reported in 47 patients (24.4%) after two doses, 105 patients (11.2%) after three doses, and 30 (10.8%) after four vaccine doses among the patients with IIMs ($P < 0.001$ between the three groups, $P < 0.001$ between the two- and three-dose groups, $P = 0.861$ between the three- and four-dose groups). Notably, the severity of BIs in patients with IIMs did not differ after two, three, or four vaccine doses (Supplementary Table 1). The fatigue 4a score for BIs after

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Table 1. Characteristics of the major subgroups of participants with breakthrough infections

Characteristics during the first BI	Total (*n* = 1447)	IIMs (*n* = 182)	AIRDs (*n* = 716)	nrAIDs (*n* = 89)	HCs (*n* = 460)
Median age (25th–75th), years	44 (35–56)	56 (47–66)	46 (37–57)***	40 (33–47)***	38 (31–48)***
Female gender	1104 (77.4)	129 (71.7)	608 (86.1)***	71 (81.6)	296 (65.3)
Median (25th–75th) time to first BI (days)	117 (59–176)	110 (58.7–164)	120 (61–172)	112 (70–179)	113 (53–186)
Race and ethnicity					
African	57 (3.9)	9 (4.9)	40 (5.6)	1 (1.1)	7 (1.5)
Asian	229 (15.8)	22 (12.1)	119 (16.6)	10 (11.2)	78 (17.0)
White	792 (54.7)	128 (70.3)	397 (55.4)	61 (68.5)	206 (44.8)
Hispanic	198 (13.7)	10 (5.5)	70 (9.8)	8 (9.0)	110 (23.9)
Mixed	46 (3.2)	5 (2.7)	22 (3.1)	3 (3.4)	16 (3.5)
Native American	5 (0.3)	1 (0.5)	2 (0.3)	0 (0)	2 (0.4)
Others	74 (5.1)	3 (1.6)	43 (6.0)	4 (4.5)	24 (5.2)
Did not wish to disclose	46 (3.2)	4 (2.2)	23 (3.2)	2 (2.2)	17 (3.7)
Number of vaccine doses					
Two	449 (31.0)	47 (25.8)	196 (27.3)	29 (32.6)	177 (38.4)
Three	721 (49.8)	105 (57.6)	339 (47.3)	46 (51.7)	231 (50.2)
Four	277 (19.1)	30 (16.4)	181 (25.2)	14 (15.7)	52 (11.3)
Comorbidities					
Any comorbidities	601 (41.5)	124 (68.1)	329 (45.9)***	37 (41.6)***	111 (24.1)***
Asthma	168 (11.6)	36 (19.8)	86 (12.0)*	9 (10.1)	37 (8.0)***
Chronic kidney disease	46 (3.2)	9 (4.9)	35 (4.9)	0 (0)a	2 (0.4)***
Chronic liver disease	17 (1.2)	4 (2.2)	8 (1.1)	2 (2.2)	3 (0.7)
COPD	30 (2.1)	8 (4.4)	18 (2.5)	0 (0)	4 (0.9)**
Interstitial lung disease	52 (3.6)	35 (19.2)	15 (2.1)***	0 (0)***	2 (0.4)***
Coronary artery disease	31 (2.1)	11 (6.0)	16 (2.2)*	1 (1.1)	3 (0.7)***
Diabetes mellitus	83 (5.7)	32 (17.6)	34 (4.7)***	7 (7.9)*	10 (2.2)***
Dyslipidaemia	174 (12.0)	45 (24.7)	95 (13.3)***	7 (7.9)***	27 (5.9)***
HIV-AIDS	3 (0.2)	2 (1.1)	1 (0.1)	0 (0)	0 (0)
Hypertension	239 (16.5)	48 (26.4)	134 (18.7)*	16 (18.0)	41 (8.9)***
Stroke	15 (1.0)	4 (2.2)	9 (1.3)	2 (2.2)	0 (0) b
Mental health disorders	413 (28.5)	71 (39.0)	227 (31.7)*	29 (32.6)	86 (18.7)***
AID multimorbidity	270 (18.7)	62 (34.1)	174 (24.3)*	34 (38.2)	0 (0)
Immunosuppression received					
MTX	261 (18.0)	47 (25.8)	209 (29.2)	3 (3.4)***	–
MMF	97 (6.7)	44 (24.2)	52 (7.3)***	1 (1.1)***	–
AZA	69 (4.8)	14 (7.7)	52 (7.3)	3 (3.4)	–
HCQ	281 (19.4)	45 (24.7)	231 (32.3)	2 (2.2)***	–
SSZ	72 (5.0)	7 (3.8)	62 (8.7)	3 (3.4)	–
LEF	34 (2.3)	2 (1.1)	31 (4.3)*	1 (1.1)	–
Oral tacrolimus	13 (0.9)	5 (2.7)	6 (0.8)	1 (1.1)	–
CSA	19 (1.3)	4 (2.2)	13 (1.8)	0 (0)	–
IVIG	31 (2.1)	27 (14.8)	3 (0.4)***	0 (0)***	–
CYC	13 (0.9)	1 (0.5)	11 (1.5)	1 (1.1)	–
Rituximab	69 (4.8)	26 (14.3)	41 (5.7)***	1 (1.1)***	–
Anti-TNF agents	96 (6.6)	3 (1.6)	85 (11.9)***	6 (6.7)*	–
JAK inhibitors	22 (1.5)	2 (1.1)	19 (2.7)	1 (1.1)	–
Glucocorticoid (prednisone equivalent)					
No glucocorticoid	669 (46.2)	97 (53.3)	461 (64.4)***	73 (82.0)***	–
<10 mg a day	252 (17.4)	55 (30.2)	184 (25.7)	7 (7.9)	–
10–20 mg a day	73 (5.0)	15 (8.1)	51 (7.1)	5 (5.6)	–
>20 mg a day	29 (2.0)	15 (8.2)	14 (2.0)	0 (0)	–
Vaccines received					
Pfizer-BioNTech (BNT162b2)	660 (45.6)	98 (53.8)	317 (44.3)*	53 (59.6)	192 (41.7)*
Oxford-AstraZeneca (ChAdOx1 nCoV-19)	340 (23.5)	19 (10.4)	219 (30.6)***	17 (19.1)	85 (18.5)*
Moderna (mRNA 1273)	126 (8.7)	48 (26.4)	45 (6.3)***	8 (9.0)***	25 (5.4)***
Novovax (NVX-CoV2373)	1 (0.1)	0 (0)	0 (0)	0 (0)	1 (0.2)
Covishield (ChAdOx1 nCoV- 19)	43 (3.0)	1 (1.1)	11 (1.5)	3 (3.4)	28 (6.1)*
Covaxin (BBV152)	9 (0.6)	1 (0.5)	3 (0.4)	0 (0)	5 (1.1)
Sputnik (Gam-COVID-Vac)	24 (1.7)	0 (0)	5 (0.7)	0 (0)	19 (4.1)*
Sinopharm (BBIBP-CorV)	48 (3.3)	2 (1.1)	15 (2.1)	1 (1.1)	30 (6.5)**
Sinovac	90 (6.2)	6 (3.3)	40 (5.6)	5 (5.6)	39 (8.5)*
Other	106 (7.3)	7 (3.8)	61 (8.5)	2 (2.2)	36 (7.8)

Comparisons between IIM *vs* individual groups (χ^2 for categorical variables, Mann–Whitney U for continuous variable).
* $P < 0.05$. ** $P < 0.005$. *** $P < 0.001$.
AIRDs: autoimmune rheumatic diseases; nrAIDs: non-rheumatic autoimmune diseases; BI: breakthrough infection; COPD: chronic obstructive pulmonary disease; HCs: healthy controls; IIMs: idiopathic inflammatory myopathies; JAK: Janus kinase.

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Table 2. Univariable Cox regression analysis of risk factors for COVID-19 breakthrough infection, severe breakthrough infection, and hospitalization in patients with idiopathic inflammatory myopathies

	Breakthrough infection				Severe BI				Hospitalization due to COVID-19			
	HR	95% CI		*P*	HR	95% CI		*P*	HR	95% CI		*P*
Age	0.98	0.97	0.98	<0.001	0.99	0.95	1.02	0.571	0.97	0.94	0.99	0.033
Female gender (ref male)	1.12	0.80	1.57	0.487	35.00	0.36	3334.7	0.126	2.79	0.82	9.4	0.098
Ethnicity												
White		Reference				Reference				Reference		
Non-white	1.57	1.13	2.18	0.007	2.31	0.84	6.37	0.105	3.52	1.55	8.00	0.003
Comorbidities												
Autoimmune multimorbidity	1.35	0.98	1.84	0.059	1.98	0.74	5.34	0.173	1.13	0.46	2.75	0.786
Any comorbidity	0.88	0.64	1.21	0.448	1.80	0.51	6.32	0.359	1.48	0.55	4.00	0.435
Mental health disorder	1.43	1.06	1.95	0.019	1.72	0.64	4.64	0.278	1.45	0.62	3.36	0.381
Country by HDI	1.18	0.95	1.47	0.125	1.50	0.86	2.61	0.153	1.54	0.99	2.40	0.053
First vaccine dose												
Adenovirus vector		Reference				Reference				Reference		
mRNA	0.97	0.60	1.57	0.927	1.84	0.24	14.0	0.553	1.36	0.32	5.85	0.673
Other	1.53	0.71	3.31	0.273	0.00	0.00	–[a]	0.983	0.00	0.00	–[a]	0.979
Number of vaccine doses												
Two		Reference				Reference				Reference		
Three	0.76	0.53	1.09	0.142	0.69	0.23	2.04	0.505	0.60	0.24	1.48	0.268
Four	2.13	1.27	3.58	0.004	0.00	0.00	–[a]	0.976	0.46	0.05	3.96	0.485
Immunosuppression												
MTX	1.31	0.93	1.85	0.112	1.75	0.60	5.04	0.300	1.71	0.70	4.16	0.236
MMF	1.50	1.06	2.13	0.020	2.14	0.74	6.17	0.157	2.56	1.08	6.04	0.032
AZA	0.90	0.51	1.59	0.730	0.75	0.09	5.72	0.781	1.14	0.26	4.94	0.853
HCQ	2.08	1.47	2.93	<0.001	1.45	0.41	5.13	0.561	0.96	0.28	3.25	0.951
SSZ	4.30	2.01	9.12	<0.001	0.04	0.00	–[a]	0.790	0.04	0.00	–[a]	0.751
LEF	0.80	0.11	5.74	0.828	0.04	0.00	–[a]	0.814	0.04	0.00	–[a]	0.778
Tacrolimus	1.56	0.64	3.80	0.325	3.74	0.49	28.4	0.202	5.23	1.22	22.4	0.026
CSA	1.03	0.38	2.79	0.944	0.04	0.00	–[a]	0.699	0.04	0.00	–[a]	0.631
IVIG	0.87	0.57	1.33	0.528	0.35	0.04	2.68	0.315	0.78	0.23	2.65	0.701
CYC	0.72	0.10	5.19	0.751	0.04	0.00	–[a]	0.811	0.04	0.00	–[a]	0.779
Rituximab	1.28	0.83	1.97	0.260	2.72	0.87	8.50	0.084	3.75	1.53	9.18	0.004
TNF inhibitors	1.49	0.47	4.66	0.494	0.04	0.00	–[a]	0.778	0.04	0.00	–[a]	0.737
JAK inhibitors	0.77	0.19	3.12	0.721	0.04	0.00	–[a]	0.739	0.04	0.00	–[a]	0.688
Any glucocorticoid dose	1.34	0.99	1.81	0.051	4.86	1.56	15.11	0.006	3.79	1.55	9.23	0.003

Univariable Cox regression analysis performed.
[a] Those with wide CI (very high upper limits of 95% CI).
BI: breakthrough infection; HDI: Human Development Index; HR: hazard ratio; JAK: Janus kinase; severe BI: hospitalization due to COVID-19 or oxygen requirement or ICU/HDU admission or need for advanced treatment.

two, three or four vaccine doses did not differ significantly after adjusting for time from BI ($P = 0.705$). BIs across subtypes had differences in myalgia and arthralgia, which are insignificant clinically (Supplementary Table 2).

The second episode of COVID-19 BI

Two hundred and seventy-nine respondents (2.9%) experienced a second COVID-19 BI, and the characteristics were comparable among patients with IIMs, patients with other AIRDs, patients with nrAIDs, and HCs (Supplementary Table 3). However, a second BI in patients with IIMs had the longest symptom resolution time (IIMs = median 15 days, AIRDs = 10 days, nrAIDs = 12.5 days, and HCs = 7 days, $P = 0.006$). Treatment with antivirals or mAbs was also higher among patients with IIMs than in other groups (42.1%, AIRDs = 24.1%, nrAIDs = 16.7%, HCs = 10.5%, $P = 0.002$).

Discussion

In the present study, we analysed the characteristics and risk factors of COVID-19 BIs in a large and global sample of patients with IIMs. Our data showed that more than 1 in 10 patients with IIMs reported BIs after a median of 3.9 months post-vaccination. BIs were usually mild, although severe cases were more common in patients with IIMs than in patients with other AIRDs, patients with nrAIDs, and HCs. Glucocorticoid use was a risk factor for severe BIs, while having non-white ethnicity was a risk for all-cause hospitalization. Descriptive and quantitative analysis showed that the severity of BIs did not differ between the various IIM subtypes, or with the prior number of vaccines received. Although BIs have been described previously in patients with IIMs, our study explored the important aspect of the effect of multiple vaccine doses and of following advanced treatments for COVID. [2, 4, 7, 9–11, 22].

COVID-19 BIs are common in patients with AIRDs (5–30%) and occurred in 15.3% of the current study's participants [22, 23]. Reported BI cases are usually mild, as shown in our study, and they are increasing in frequency after the emergence of new SARS-CoV-2 variants, such as Omicron [7, 22, 23]. We found BIs occurred after a median of 3.9 months (percentiles 25th–75th = 2.0–5.9) following the second COVID-19 vaccine; this is consistent with the most recent ACR guidance for COVID-19 vaccination in patients with rheumatic diseases, which

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Table 3. Multivariable Cox regression analysis of risk factors for COVID-19 breakthrough infection, severe breakthrough infection, and hospitalization in patients with idiopathic inflammatory myopathies

	Breakthrough infection			Severe BI			Hospitalization due to COVID-19		
	HR	95% CI		HR	95% CI		HR	95% CI	
Age	**0.98***	**0.97***	**0.99***	1.00	0.96	1.03	0.99	0.96	1.02
Female gender	0.77	0.53	1.11	–	–	–	1.65	0.47	5.82
Ethnicity	–	–	–	–	–	–	–	–	–
White		Reference			Reference			Reference	
Non-white	1.17	0.80	1.71	–	–	–	**2.61**	**1.03**	**6.59**
Comorbidities									
Autoimmune multimorbidity	1.11	0.79	1.56	1.76	0.62	4.95	–	–	–
Mental health disorder	1.20	0.87	1.65	–	–	–	–	–	–
Immunosuppression									
MTX	1.07	0.73	1.56	–	–	–	–	–	–
MMF	1.34	0.91	1.96	1.47	0.46	4.64	1.60	0.62	4.16
HCQ	**1.81***	**1.24***	**2.64***	–	–	–	–	–	–
SSZ	**3.79***	**1.69***	**8.42***	–	–	–	–	–	–
Tacrolimus	–	–	–	–	–	–	1.82	0.38	8.73
Rituximab	–	–	–	1.67	0.48	5.73	1.87	0.69	5.08
Any glucocorticoid dose	0.98	0.71	1.36	**3.61***	**1.09***	**11.8***	2.34	0.90	6.08

Cox regression analysis adjusted for age, gender, ethnicity, and other covariates significant in univariable analysis (or $P < 0.2$), and eliminating those with a wide CI was used. Some covariates, like number of vaccine doses, country by HDI, that did not follow the proportional hazards assumption were eliminated from the model.

* $P < 0.05$ was considered significant (indicated in bold typeface).

BI: breakthrough infection; HDI: Human Development Index; HR: hazard ratio; JAK: Janus kinase; severe BI: hospitalization due to COVID-19 or oxygen requirement or ICU/HDU admission or need for advanced treatment.

Table 4. Comparison of COVID-19 breakthrough infections symptoms and severity among participants

	IIMs ($n = 182$)	AIRDs ($n = 716$)	nrAIDs ($n = 89$)	HCs ($n = 460$)	P^a
Median symptoms resolution time, days (25th–75th)	12 (7–24)	11 (6–20)	8 (4–15.5)*	7 (4–14)***	<0.001
Any symptoms	179 (98.4)	687 (96.0)	84 (94.4)	434 (94.3)	0.135
Fever	90 (49.5)	366 (51.1)	40 (44.9)	214 (46.5)	0.390
Fatigue	116 (63.7)	453 (63.3)	49 (55.1)	272 (59.1)	0.263
Muscle aches	86 (47.3)	335 (46.8)	39 (43.8)	233 (50.7)	0.498
Joint pains	51 (28.0)	291 (40.6)	21 (21.3)	119 (25.9)	<0.001
Cough	123 (67.6)	423 (59.1)	42 (47.2)	235 (51.1)	<0.001
Difficulty breathing	35 (19.2)	152 (21.2)	14 (15.7)	55 (12.0)	<0.001
Loss of smell	32 (17.6)	161 (22.5)	20 (22.5)	102 (22.2)	0.540
Loss of taste	38 (21.0)	150 (21.0)	14 (15.7)	82 (17.8)	0.427
Running nose	87 (47.8)	320 (44.7)	35 (39.3)	170 (37.0)	0.022
Congestion	74 (40.7)	249 (34.8)	25 (28.1)	148 (32.2)	0.123
Throat pain/scratchiness	89 (48.9)	363 (50.7)	45 (50.6)	209 (45.0)	0.285
Chest pain	20 (11.0)	111 (15.5)	5 (5.6)	41 (8.9)	0.001
Diarrhoea	29 (15.9)	114 (16.0)	8 (9.0)	62 (13.5)	0.269
Headache	77 (42.3)	335 (46.8)	27 (30.3)	170 (37.0)	<0.001
Oral ulcers	6 (3.3)	27 (3.8)	2 (2.2)	8 (1.7)	0.237
Nausea/vomiting	22 (12.1)	86 (12.0)	2 (2.2)	29 (6.3)	<0.001
Abdominal pain	12 (6.6)	72 (10.1)	4 (4.5)	27 (5.9)	0.030
Skin rashes	6 (3.3)	27 (3.8)	2 (2.2)	8 (1.7)	0.237
Outcomes					
All-cause hospitalization	14 (7.7)	33 (4.6)	1 (1.1)	7 (1.5)	<0.001
ICU care or other HDU	4 (2.2)	4 (0.6)	0 (0)	0 (0)	0.007
Oxygen requirement	11 (6.0)	13 (1.8)	2 (2.2)	4 (0.9)	<0.001
Advanced treatment for COVID-19 infection	62 (34.1)	185 (25.8)	13 (14.6)	59 (12.8)	<0.001

Data are expressed as median (25th–75th percentiles) or frequency (%).

[a] Kruskal Wallis for continuous variables and χ^2 for categorical variables. $P < 0.0125$ is significant after Bonferroni correction.

* $P < 0.05$. ** $P < 0.005$. *** $P < 0.001$ by Dunn–Bonferroni *post hoc* test comparing IIM *vs* the particular group.

Advanced treatment: antiviral or monoclonal antibodies; AIRDs: autoimmune rheumatic diseases; nrAIDs: non-rheumatic autoimmune diseases; HCs: healthy controls; HDU: high-dependency unit; ICU: intensive care unit; IIMs: idiopathic inflammatory myopathies; IQR: interquartile range; PROMIS: Patient Reported Outcomes Measurement Information System.

recommends a booster shot 3–4 months after completion of the primary vaccine series [24]. However, the timing for a booster dose is a complex matter that may vary according to the approach of the local authorities, the previous vaccine received, immunosuppression status, and the emergence of new variants [24, 25].

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We found that HCQ use was associated with higher risk of BIs, unlike the findings in previous studies. While our study was not designed to study the effect of immunosuppression on COVID-19, we cannot fully discount the possibility of disease heterogeneity, alongside a global sample of patients that may result in varied prescription practices, accounting for differences in our results from those of other groups [12]. In addition, this is the largest series of patients with IIMs for whom data on BIs have been published to date. IIMs are known to exhibit an active IFN axis, which may influence viral clearance in these patients [13]. Our group has previously reported that BIs were less common in patients with IIMs, albeit the BIs are more severe when testing positive for COVID-19 [4].

We also found an increased risk of severe COVID-19 among patients with IIMs on glucocorticoids, drugs well known for being associated with unfavourable outcomes among patients with autoimmune diseases and SARS-CoV-2 infection [6, 26, 27]. Finally, having non-white ethnicity was a risk factor for all-cause hospitalization, which may be explained by inequity in access to health-care services and socio-economic disparity of ethnic minorities, though we did not assess these other covariates [28]. Non-white ethnicity has also been described as a risk factor for severe COVID-19 in patients with neuromuscular diseases, including IIMs [29].

All-cause hospitalization related to BIs was more common in patients with IIMs compared with patients with other AIRDs, patients with nrAIDs, and HCs, consistent with previous data [4]. This may be explained by the increased susceptibility of patients with IIMs to infections, owing to the frequent need for immunosuppression, multi-organ particularly pulmonary disease sequelae [30], and underlying activation of IFN pathways that may give rise to deleterious virus–host interactions [13]. On the contrary, a recent registry-based cohort analysis found COVID-19 outcomes to be more favourable in patients with DM than HCs, though the cohort had a considerably distinct ethnicity and comorbidity profile compared with ours [31]. A global registry study did not find any specific rheumatic disease to be a risk factor for COVID-19 hospitalization in people with rheumatic diseases, although patients with IIMs were not included as a covariate in the multivariable regression model used in that study [32].

The large sample size of our study enabled us to meaningfully compare BIs in various subtypes of IIMs, an aspect not explored in previous studies [6, 31]. We found that while the severity of BIs did not, reassuringly, differ, there were subtle differences in the incidence of myalgia and joint pain, which may possibly be attributed to the exacerbation of distinct underlying disease processes in the different subtypes by COVID-19, manifesting as varied symptom profiles [33]. With our large sample, we could also analyse both descriptively and quantitatively the characteristics of the second BI, which had longer symptoms and required more treatment with antiviral or mAbs in patients with IIMs than in other groups. Though less severe than the first episode of a BI, these findings emphasize that patients with IIMs are more vulnerable to severe COVID-19 BIs than patients with other AIDRs, patients with nrAIDs, and HCs.

Our study has limitations. Whether COVID-19 first infection or BI was not confirmed specifically by RT-PCR, although a positive diagnostic test was required to confirm COVID-19 infection. We did not assess the effect of educational level, income, hybrid immunity (immunity due to both COVID-19 infection and vaccination), or specific SARS-CoV-2 variants of concern on the risk of developing BIs or all-cause hospitalization. Although we did not collect data about virus sequencing and genotyping from our participants, the main variants of concern circulating during the study were Delta, Omicron BA.1 and Omicron BA.5 [34]. Additionally, patients who received the primary series with a single vaccine dose were excluded from the analysis to facilitate the interpretation and analysis of data on subsequent vaccine doses, although they represented only a small percentage of the available sample. We are also prone to recall and report bias associated with self-reported surveys of this nature, though we tried to minimize this through the inclusion of controls and analysis of stratified subsets. Additionally, the multivariable regression model included some variables with small numbers (like the medication SSZ) giving some significant results which needs to be interpreted with caution. Disease activity or flares were not assessed as outcomes of interest following BIs, although recent studies from our group have shown that disease flares following vaccination occur in 11.3% and are mild among patients with AIRDs [35], while 30.4% of patients with IIMs reported a flare following COVID-19 infection [36].

We analysed COVID-19 BIs in a large ethnically and geographically diverse sample of IIMs and explored understudied aspects, including the role of multiple vaccinations and IIM subtypes. In the current landscape of booster doses, the results still hold significance, since they address various crucial facets of the COVID-19 vaccination. Patients with IIMs required more supplemental oxygen therapy, intensive care unit admission, advanced treatment with antiviral or monoclonal antibodies, and had more all-cause hospitalization than their counterparts. Therefore, they can be considered a vulnerable subgroup for severe BIs. Future prospective studies with longer follow-ups are needed to better elucidate clinical and demographic factors associated with COVID-19 BIs and unfavourable outcomes among vaccinated patients with IIMs.

Supplementary material

Supplementary material is available at *Rheumatology* online.

Data availability

The datasets generated and/or analysed during the current study are not publicly available but are available from the corresponding author upon reasonable request.

Contribution statement

L.G., S.S.A., P.S. and N.R contributed to conceptualization of the study. All authors contributed to data curation and to reviewing and editing of the manuscript. S.S.A., P.S. and L.G. wrote the original draft of the manuscript. Formal analysis was undertaken by N.R. Investigation was undertaken by L. G., S.S.A., P.S. and N.R. The methodology was designed by L.G., V.A. and N.R. The software was used by L.G. Validation was undertaken by V.A., R.A., J.B.L. and H.C. Visualization was carried out by R.A, V.A. and L.G.

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References

1. Korang SK, von Rohden E, Veroniki AA *et al.* Vaccines to prevent COVID-19: a living systematic review with Trial Sequential

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Analysis and network meta-analysis of randomized clinical trials. PLoS ONE 2022;17:e0260733.
2. Lee CJ, Woo W, Kim AY *et al.* Clinical manifestations of COVID-19 breakthrough infections: a systematic review and meta-analysis. J Med Virol 2022;94:4234–45.
3. Gopinath S, Ishak A, Dhawan N *et al.* Characteristics of COVID-19 breakthrough infections among vaccinated individuals and associated risk factors: a systematic review. Trop Med Infect Dis 2022;7:81.
4. Hoff LS, Ravichandran N, Shinjo SK *et al.*; COVAD Study Group. COVID-19 severity and vaccine breakthrough infections in idiopathic inflammatory myopathies, other systemic autoimmune and inflammatory diseases, and healthy controls: a multicenter cross-sectional study from the COVID-19 Vaccination in Autoimmune Diseases (COVAD) survey. Rheumatol Int 2023;43:47–58.
5. Xu C, Yi Z, Cai R *et al.* Clinical outcomes of COVID-19 in patients with rheumatic diseases: a systematic review and meta-analysis of global data. Autoimmun Rev 2021;20:102778.
6. Yeoh SA, Gianfrancesco M, Lawson-Tovey S *et al.*; COVID-19 Global Rheumatology Alliance. Factors associated with severe COVID-19 in people with idiopathic inflammatory myopathy: results from the COVID-19 Global Rheumatology Alliance physician-reported registry. RMD Open 2022;8:e002508.
7. Liew J, Gianfrancesco M, Harrison C *et al.* SARS-CoV-2 breakthrough infections among vaccinated individuals with rheumatic disease: results from the COVID-19 Global Rheumatology Alliance provider registry. RMD Open 2022;8:e002187.
8. Stouten V, Hubin P, Haarhuis F *et al.* Incidence and risk factors of COVID-19 vaccine breakthrough infections: a prospective cohort study in Belgium. Viruses 2022;14:802.
9. Patel NJ, Wang X, Fu X *et al.* Factors associated with COVID-19 breakthrough infection among vaccinated patients with rheumatic diseases: a cohort study. Semin Arthritis Rheum 2023;58:152108.
10. Cook C, Patel NJ, D'Silva KM *et al.* Clinical characteristics and outcomes of COVID-19 breakthrough infections among vaccinated patients with systemic autoimmune rheumatic diseases. Ann Rheum Dis 2022;81:289–91.
11. Di Fusco M, Moran MM, Cane A *et al.* Evaluation of COVID-19 vaccine breakthrough infections among immunocompromised patients fully vaccinated with BNT162b2. J Med Econ 2021;24:1248–60.
12. Mehta P, Rathore U, Naveen R *et al.* Prevalent drug usage practices in adults and children with idiopathic inflammatory myopathies: registry-based analysis from the MyoCite cohort. J Clin Rheumatol 2022;28:89–96.
13. Bolko L, Jiang W, Tawara N *et al.* The role of interferons type I, II and III in myositis: a review. Brain Pathol 2021;31:e12955.
14. Fazal ZZ, Sen P, Joshi M *et al.*; COVAD Study Group. COVAD survey 2 long-term outcomes: unmet need and protocol. Rheumatol Int 2022;42:2151–8.
15. Indian Council of Medical Research. National Guidelines for Ethics Committees Reviewing Biomedical & Health Research during COVID-19 Pandemic. 2020. https://www.icmr.gov.in/pdf/covid/techdoc/EC_Guidance_COVID19_06052020.pdf (28 November 2023, date last assessed).
16. Gaur PS, Zimba O, Agarwal V, Gupta L. Reporting survey based studies—a primer for authors. J Korean Med Sci 2020;35:e398.
17. Eysenbach G. Improving the quality of web surveys: the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). J Med Internet Res 2004;6:e34.
18. Sen P, Gupta L, Lilleker JB *et al.*; COVAD Study Group. COVID-19 vaccination in autoimmune disease (COVAD) survey protocol. Rheumatol Int 2022;42:23–9.
19. CDC COVID-19 Vaccine Breakthrough Case Investigations Team. COVID-19 vaccine breakthrough infections reported to CDC – United States, January 1–April 30, 2021. MMWR Morb Mortal Wkly Rep 2021;70:792–3.
20. Cella D, Lai JS, Jensen SE *et al.* PROMIS Fatigue Item Bank had clinical validity across diverse chronic conditions. J Clin Epidemiol 2016;73:128–34.
21. PROMIS Health Organization (PHO). PROMIS® Item Bank v1.0 –Fatigue – Short Form 4a. [update 2018, July 10]. https://heal.nih.gov/files/CDEs/2023-07/promis-short-form-4a-fatigue-crf.pdf (21 April 2023, date last accessed).
22. Stalman EW, Wieske L, van Dam KPJ *et al.*; T2B! Immunity against SARS-CoV-2 Study Group. Breakthrough infections with the SARS-CoV-2 omicron (B.1.1.529) variant in patients with immune-mediated inflammatory diseases. Ann Rheum Dis 2022;81:1757–66.
23. Boekel L, Stalman EW, Wieske L *et al.*; T2B! Immunity against SARS-CoV-2 Study Group. Breakthrough SARS-CoV-2 infections with the delta (B.1.617.2) variant in vaccinated patients with immune-mediated inflammatory diseases using immunosuppressants: a substudy of two prospective cohort studies. Lancet Rheumatol 2022;4:e417–29.
24. Curtis JR, Johnson SR, Anthony DD *et al.* American college of rheumatology guidance for COVID-19 vaccination in patients with rheumatic and musculoskeletal diseases: version 5. Arthritis Rheumatol 2023;75:E1–16.
25. Landewé RBM, Kroon FPB, Alunno A *et al.* EULAR recommendations for the management and vaccination of people with rheumatic and musculoskeletal diseases in the context of SARS-CoV-2: the November 2021 update. Ann Rheum Dis 2022;81:1628–39.
26. Strangfeld A, Schäfer M, Gianfrancesco MA *et al.*; COVID-19 Global Rheumatology Alliance. Factors associated with COVID-19–related death in people with rheumatic diseases: results from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis 2021;80:930–42.
27. Brenner EJ, Ungaro RC, Gearry RB *et al.* Corticosteroids, but not TNF antagonists, are associated with adverse COVID-19 outcomes in patients with inflammatory bowel diseases: results from an international registry. Gastroenterology 2020;159:481–91.e3.
28. Gianfrancesco MA, Leykina LA, Izadi Z *et al.*; COVID-19 Global Rheumatology Alliance. Association of race and ethnicity with COVID-19 outcomes in rheumatic disease: data from the COVID-19 Global Rheumatology Alliance Physician Registry. Arthritis Rheumatol 2021;73:374–80.
29. Pizzamiglio C, Pitceathly RDS, Lunn MP *et al.*; Neuromuscular Diseases and COVID-19 Study Group. Factors associated with the severity of COVID-19 outcomes in people with neuromuscular diseases: data from the International Neuromuscular COVID-19 Registry. Eur J Neurol 2023;30:399–412.
30. Marie I, Ménard JF, Hachulla E *et al.* Infectious complications in polymyositis and dermatomyositis: a series of 279 patients. Semin Arthritis Rheum 2011;41:48–60.
31. Pakhchanian H, Khan H, Raiker R *et al.* COVID-19 outcomes in patients with dermatomyositis: a registry-based cohort analysis. Semin Arthritis Rheum 2022;56:152034.
32. Gianfrancesco M, Hyrich KL, Al-Adely S *et al.* Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis 2020;79:859–66.
33. Conticini E, d'Alessandro M, Grazzini S *et al.* Relapses of idiopathic inflammatory myopathies after vaccination against COVID-19: a real-life multicenter Italian study. Intern Emerg Med 2022;17:1921–8.
34. SARS-CoV-2 sequences by variant. Our World in Data. https://ourworldindata.org/grapher/covid-variants-bar (21 April 2023, date last accessed).
35. Jagtap K, Naveen R, Day J *et al.*; COVAD Study Group. Flares in autoimmune rheumatic diseases in the post-COVID-19 vaccination period—a cross-sequential study based on COVAD surveys. Rheumatology (Oxford) 2023;62:3838–48.
36. Ali SS, Naveen R, Sen P *et al.*; COVAD Study Group. Flares after COVID-19 infection in patients with idiopathic inflammatory myopathies: results from the COVAD study. Rheumatology (Oxford) 2023;62:e263–8.

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