



Breakthrough SARS-CoV-2 infection and disease flares in patients with rheumatoid arthritis: result from COVAD e-survey study



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Background

- COVID-19 has been suggested as a **possible trigger of disease flares in patients with rheumatoid arthritis (RA)**. However, factors associated with disease flares remain unknown.
- This study aimed to **identify factors associated with breakthrough infection (BI) and disease flares in patients with RA following COVID-19**.

Methods

- We analysed data from RA patients who participated in the COVID-19 vaccination in autoimmune diseases (COVAD) study.
- Demographic data, patient-reported outcomes, comorbidities, pharmacologic treatment and details regarding disease flares were extracted from the COVAD database. Factors associated with disease flare-ups were determined by multivariate logistic regression analysis

Results

- The analysis comprised **1928 patients with RA** who participated in the COVAD study.
- Younger age, Caucasian ethnicity, comorbidities with obstructive chronic pulmonary disease and asthma** were associated with COVID-19 breakthrough infection.
- Moreover, **younger age** (odds ratio (OR): 0.98, 95% CI: 0.96 – 0.99, p<0.001 **ethnicity other than Asian, past history of tuberculosis** (OR: 3.80, 95% CI: 1.12 – 12.94, p=0.033), **treatment with methotrexate** (OR: 2.55, 95% CI: 1.56 – 4.17, p<0.001), **poor global physical health** (OR: 1.07, 95% CI: 1.00 –1.15, p=0.044) and **mental health** (OR: 0.91, 95% CI: 0.87 –0.95, p<0.001) were independent factors associated disease flares in patients with RA (Table 1).

Results

- Our study highlights the **impact of socio-demographic factors, clinical characteristics and mental health on disease flares in patients with RA**. These insights may help determine relevant strategies to proactively manage RA patients at risk of flares.

	Univariate			Multivariate		
	OR	95% CI	P value	OR	95% CI	P value
Age	0.98	(0.97-0.99)	<0.001**	0.98	(0.96-0.99)	<0.001**
Gender						
Female	Reference					
Male	0.76	(0.46-1.24)	0.268			
Ethnicity				Reference		
Asian	Reference					
Caucasian	3.73	(2.15-6.47)	<0.001**	4.33	(2.43-7.72)	<0.001**
African American/ African	4.13	(2.02-8.46)	<0.001**	3.64	(1.73-7.64)	0.001**
Hispanic	3.45	(1.78-6.66)	<0.001**	3.71	(1.88-7.34)	<0.001**
Native American/Indigenous/Pacific Islander	1.50	(0.19-12.01)	0.704	1.52	(0.18-12.60)	0.697
Mixed	2.87	(1.17-7.02)	0.021*	2.94	(1.18-7.34)	0.021*
Other	2.65	(1.16-6.09)	0.021*	2.83	(1.21-6.64)	0.017*
Comorbidities						
Asthma	1.49	(0.99-2.25)	0.057	1.21	(0.78-1.90)	0.394
Interstitial Lung Disease	1.89	(0.99-3.58)	0.053	2.01	(1.00-4.04)	0.051
Tuberculosis	3.41	(1.06-10.97)	0.040*	3.80	(1.12-12.94)	0.033*
Medication						
Glucocorticoid	1.98	(1.20-3.25)	0.007**	1.26	(0.71-2.23)	0.425
Methotrexate	2.80	(1.82-4.31)	<0.001**	2.55	(1.56-4.17)	<0.001**
Hydroxychloroquine	2.90	(1.44-5.84)	0.003**	1.78	(0.76-4.18)	0.186
Anti TNF agents [#]	3.72	(1.68-8.24)	0.001**	2.33	(0.94-5.77)	0.066
JAK inhibitors *	4.27	(1.27-14.29)	0.019*	2.93	(0.80-10.78)	0.106
PROMIS global physical health						
	1.07	(1.00-1.15)	0.044*	1.09	(1.00-1.18)	0.040*
PROMIS global mental health						
	0.91	(0.87-0.95)	<0.001**	0.91	(0.87-0.95)	<0.001**

Symptoms of COVID-19 infection

Fever
Fatigue
Muscle aches
Joint pains
Cough
Difficulty in breathing
Loss of smell
Loss of taste
Running nose
Nasal congestion
Throat pain
Chest pain
Diarrhoea
Headache
Oral ulcers
Nausea/vomiting
Abdominal pain
Skin rashes

Require hospitalization

ICU
Oxygen
Advanced treatment

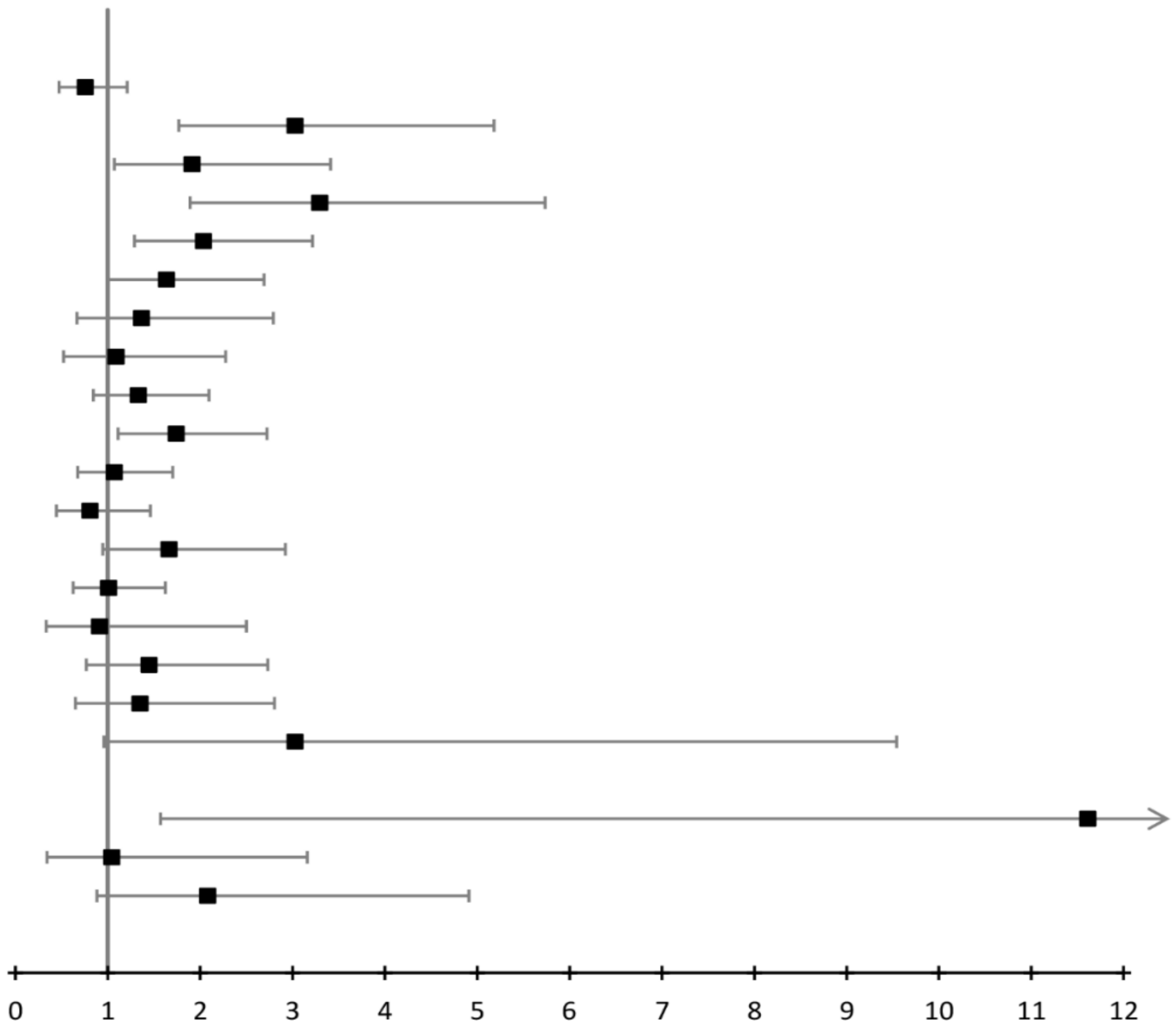


Table 1: Factors associated with disease flare in patients with RA after COVID breakthrough infections

By Logistic regression. *p<0.05, **p<0.01. [#]infliximab, adalimumab, certolizumab, golimumab, etanercept ^{*}tofacitinib, baricitinib, upadacitinib

Figure 1. Forest plots of symptoms of breakthrough infections and disease flare.

