COVID-19 BREAKTHROUGH INFECTIONS IN VACCINATED PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES AND CONTROLS – DATA FROM TWO PROSPECTIVE COHORT STUDIES

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ABSTRACT

Concerns have been raised regarding risks of COVID-19 break-through infections in vaccinated patients with immune-mediated inflammatory diseases (IMIDs) treated with immunosuppressants, but data on COVID-19 breakthrough infections in these patients are still scarce.

OBJECTIVES: The primary objective was to compare the incidence and severity of COVID-19 breakthrough infections with the SARS-CoV-2 delta variant between fully vaccinated IMID patients with immunosuppressants, and controls (IMID patients without immunosuppressants and healthy controls). The secondary objective was to explore determinants of breakthrough infections.

METHODS: In this study we pooled data collected from two large ongoing prospective multi-center cohort studies (Target-to-BI [T2BI] study and ARC study). Clinical data were collected between February and December 2021, using digital questionnaires, standardized electronic case record forms and medical files. Post-vaccination serum samples were analyzed for anti-RBD antibodies (T2BI study only) and anti-nucleocapsid antibodies to identify asymptomatic break-through infections (ARC study only). Logistic regression analyses were used to assess associations with the incidence of breakthrough infections. Multivariable models were adjusted for age, sex, cardiovascular disease, chronic pulmonary disease, obesity and vaccine type.

RESULTS: We included 3207 IMID patients with immunosuppressants and 1810 controls (985 IMID patients without immunosuppressants and 825 healthy controls). The incidence of COVID-19 breakthrough infections was comparable between patients with immunosuppressants (5%) and controls (5%). The absence of SARS-CoV-2 IgG antibodies after COVID-19 vaccination was independently associated with an increased incidence of breakthrough infections (P = 0.044). The proportion of asymptomatic COVID-19 breakthrough cases that were additionally identified serologically in the ARC cohort was comparable between IMID patients with immunosuppressants and controls; 68 (10%) of 695 patients vs. 64 (10%) of 647 controls. Hospitalization was required in 8 (5%) of 149 IMID patients with immunosuppressants and 5 (6%) of 86 controls with a COVID-19 breakthrough infection. Hospitalized cases were generally older, and had more comorbidities compared with non-hospitalized cases (Table 1). Hospitalization rates were significantly higher among IMID patients treated with anti-CD20 therapy compared to IMID patients using any other immunosuppressant (3 [23%] of 13 patients vs. 5 [4%] of 128 patients, P = 0.041; Table 1).

Table 1. Determinants of the severity of COVID-19 breakthrough infections.

Ambulatory care (n = 222) | Hospitalized (n = 13)
---|---
**Group - no. (%)**
IMID patients with immunosuppressants | 141 (64) | 14 (105)
IMID patients without immunosuppressants | 49 (22) | 3 (23)
Healthy controls | 32 (14) | 2 (15)
**Patient characteristics**
Age, years – mean (SD) | 51 (14) | 60 (11)
Female sex – no. (%) | 143 (64) | 4 (31)
**Comorbidities – no. (%)**
Cardiovascular disease | 17 (8) | 5 (39)
Chronic pulmonary disease | 17 (8) | 4 (31)
Diabetes | 15 (7) | 3 (23)
Obesity | 34 (15) | 5 (39)
**Immunosuppressants– no. (%)**
Anti-IL17i | 13 (6) | 3 (23)
Anti-CD20 therapy | 13 (6) | 3 (23)
Methotrexate | 36 (16) | 2 (15)
TNF inhibitor | 48 (22) | 2 (15)
Anti-CID20 therapy | 13 (6) | 3 (23)
Mycophenolate mofetil | 3 (1) | 0 (0)
S1P modulator | 3 (1) | 0 (0)
Other immunosuppressants | 7 (3) | 2 (15)

**Conclusion:** The incidence of COVID-19 breakthrough infections in IMID patients with immunosuppressants was comparable to controls, and infections were mostly mild. Anti-CD20 therapy might increase patients’ susceptibility to severe COVID-19 breakthrough infections, but traditional risk factors also continue to have a critical contribution to the disease course of COVID-19. Therefore, we argue that most patients with IMIDs should not necessarily be seen as a risk group for severe COVID-19, and that integrating other risk factors should become standard practice when discussing treatment options, COVID-19 vaccination, and adherence to infection prevention measures with patients.