

COVID-19 SPECIAL FORUM - LETTER TO THE EDITOR

Impact of COVID-19 in patients with autoimmune bullous diseases: Report from an international registry

Dear Editor,

For autoimmune bullous diseases (AIBD) such as bullous pemphigoid (BP) and pemphigus an increased risk of COVID-19 infection and mortality was reported, with oral prednisolone (dose ≥ 10 mg/day) and treatment of rituximab being a risk factor.^{1,2} A population-based cohort study showed an increased COVID-19 associated mortality in patients with BP, but not in patients with pemphigus vulgaris.³ Here, we provide the findings of an international registry for health care providers about COVID-19 infection in patients with AIBD, reporting on timing and

clinical presentation of COVID-19 infection, AIBD disease activity and outcome.

For this international online registry (RECOVAB registry), dermatologists reported de-identified data of patients with AIBD after symptomatic COVID-19 infection for the period from June 2020 to December 2021 according to a predefined input mask. Diagnosis of COVID-19 was based on positive polymerase chain reaction test, symptoms and confirmative chest computer tomography scan, or detected anti-SARS-COV-2 antibodies. Included were 69 patients with a mean age of 63 years (19–94), 38 (55%) were female.

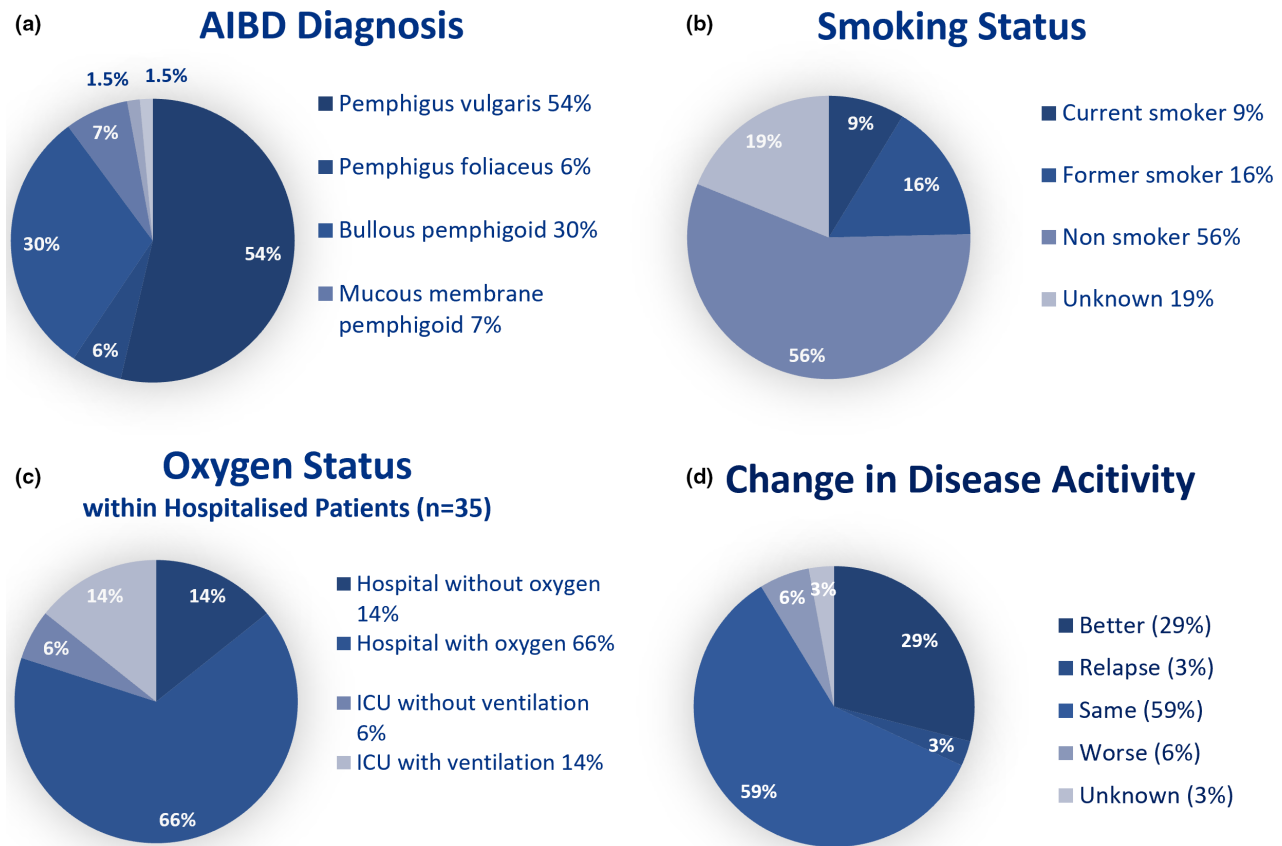


FIGURE 1 Summarized findings in patients with autoimmune bullous diseases (AIBD) and COVID-19 infection, reporting (a) AIBD diagnosis, (b) smoking status, (c) oxygen status within hospitalized patients, and (d) change in AIBD disease activity.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial License](https://creativecommons.org/licenses/by-nc/4.0/), which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2023 The Authors. *Journal of the European Academy of Dermatology and Venereology* published by John Wiley & Sons Ltd on behalf of European Academy of Dermatology and Venereology.

The distribution of AIBD diagnoses is depicted in [Figure 1a](#). Cases were reported by clinicians from Italy (33), Turkey (7), Czech Republic (6), Germany (6), Greece (6), the Netherlands (4), Serbia (3), United States (Iowa, 1), Israel (1), Spain (1) and the United Kingdom (1).

The reported mean duration of COVID-19 symptoms was 17.3 days (0–63), whilst the most common symptoms experienced were fatigue, fever, cough, myalgia and headaches. The smoking status of the patients is portrayed in [Figure 1b](#). During COVID-19 infection, 34 of 69 patients (49%) were treated at home, whilst 35 of 69 (50%) required hospitalization and diverse oxygen supplies ([Figure 1c](#)). The COVID-specific treatment administered at that time varied from corticosteroids (28%), hydroxychloroquine (17.4%), remdesivir (6%) and other medications (49%). [Table 1](#) summarizes the AIBD systemic treatment patients received before and after COVID-19 infection. Mean systemic corticosteroid dose was 15.4 mg/day ($n=50$). Rituximab was suspended from 16 (23%) to two (3%) patients. Respectively, the change in disease activity of AIBD before and after COVID-19 infection is shown in [Figure 1d](#).

A total of 58 patients (84%) recovered from COVID-19. Death occurred in nine patients (13%) with a mean age of 84.3 years; 6 of the 9 patients (67%) of them died during hospitalization for COVID-19 infection. The deceased group included 6 patients (67%) with BP and 3 (33%) with pemphigus. Those with BP also suffered from various comorbidities including dementia, chronic kidney disease, diabetes and being bedridden. Of deceased patients, 3 (33%) had active AIBD, while 6 (67%) were in complete remission on therapy.

Elevated COVID-19-associated mortality among patients with BP has previously reported in a population-based cohort study from 2020, while the use of systemic corticosteroids and immunosuppressive adjuvants did not predict worse COVID-19 outcomes.³ A systematic review of patients with AIBD and immunomodulating therapies did not reveal a higher rate of COVID-19 infection or more severe disease course.⁴ Being reported as a risk factor for mortality, treatment with rituximab was frequently suspended ([Table 1](#)).^{2,5} Other immunomodulatory treatments were mainly

continued to control disease activity, a recommendation still applicable during present COVID-19 outbreaks for patients not being vaccinated.⁶

This study is not without limitations. As a registry study, reporting bias with higher reporting of more severe or fatal cases cannot be excluded. Furthermore, the geographical distribution of reported patients was unbalanced.

In summary, this international registry showed a rather stable disease activity in the majority of AIBD patients following COVID-19 infection. Increased risk of death appeared to be associated with diagnosis of BP and high age. In the eventuality of novel pandemic waves, a decrease in treatment with rituximab is advisable for patients not being vaccinated.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

JM, HR, SV, EA, PV, RB, SU, DS, HJ, LJ, AC, A Ponziani: none reported. A Patsatsi: consulting fees Abbvie, Argenx, Janssen, Pharmaserv –Lilly, Genesis Pharma, Novartis, Pfizer, UCB; payment or honoraria: Abbvie, Argenx, Janssen, Pharmaserv –Lilly, Genesis Pharma, Novartis, Pfizer, UCB, support for attending meetings; Abbvie, Janssen, Genesis Pharma, UCB. CG: none reported. GC: payment or honoraria: Lecture Cours management GmbH, Derma Live; Leadership, paid/unpaid role; board member german network systemic sclerosis, member AIBD study group EADV. MS, AM, GDZ, IS: none reported. JF: Grants/contracts: Regeneron (clinical trial site), Astra-Zeneca (clinical trial site); payments or lectures: Medical College of Winsconsin (lectures); Leadership, paid/unpaid role: Dermatology Foundation (president). JMM, MC, RM: none reported. ES: Grants/contracts paid to institution: UCB, Incyte, Biotest, ArgenX, Dompe, Euroimmun, Fresenius Medical Care, Bayer, Pharmaxis, Alpine Immune, CSL; consulting fees. Leo, Chugai, Almirall, Janssen, Sanofi; payment or honoraria for lectures. Bristol Meyer Squibbs, Sanofi; Patents planned, issued or pending: Euroimmun, Dompe; Participation in Data Safety Monitoring Board or Advisory Board: ArgenX, AstraZeneca, Sanofi; Leadership paid/unpaid role: EADV Task Force Autoimmune blistering diseases (chair). BH: none reported.

ETHICS STATEMENT

UMCG Ethics Review Board METc 2020/258 protocol reviewed and considered the research did not fall within the scope of the Medical Research Involving Human Subjects Act (WMO). No approval needed. Research complied with EU General Data Protection Regulation (GDPR).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.








Joost M. Meijer¹ 
 Hanan Rashid¹ 
 Styliani Vergadi¹

TABLE 1 Reported systemic treatment for AIBD before and after COVID-19 infection.

| Systemic treatment for AIBD | Before COVID-19 $n=69$ (%) | After COVID-19 $n=60^a$ (%) |
|-----------------------------|-------------------------------|--------------------------------|
| Corticosteroids | 50 (72.5) | 39 (65) |
| Azathioprine | 7 (10.1) | 6 (10) |
| Dapsone | 12 (17.4) | 9 (15) |
| Mycophenolate mofetil | 10 (14.5) | 8 (13.3) |
| Methotrexate | 3 (4.3) | 1 (1.7) |
| Rituximab | 16 (23.2) | 2 (3.3) |
| None | 12 (17.4) | 10 (16.7) |
| Unknown | 1 (1.5) | 1 (1.7) |

AIBD; autoimmune bullous diseases.

^a $n=60$ post-COVID-19 due to fatalities.

Emiliano Antiga² 
 Pamela Vezzoli³
 Riccardo Balestri⁴ 
 Aikaterini Patsatsi⁵ 
 Soner Uzun⁶
 Dusan Skiljevic⁷
 Hana Jedlickova⁸
 Lucia Janickova⁸
 Alberto Corrà²
 Alessandra Ponziani⁹ 
 Claudia Günther¹⁰
 Giuseppe Cianchini¹¹
 Matthias Schefzyk¹²
 Angelo Marzano¹³ 
 Giovanni Di Zenzo¹⁴
 Iakov Shimanovich¹⁵ 
 Janet Fairley¹⁶
 Jose M. Mascaró Jr¹⁷
 Marzia Caproni²
 Roberto Maglie²
 Enno Schmidt¹⁸ 
 Barbara Horváth¹

¹³*Dermatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, and Department of Pathophysiology and Transplantation, Università Degli Studi di Milano, Milan, Italy*

¹⁴*Molecular and Cell Biology Laboratory, IDI-IRCCS, Rome, Italy*

¹⁵*Department of Dermatology, University of Lübeck, Lübeck, Germany*

¹⁶*Department of Dermatology, University of Iowa, Iowa City, Iowa, USA*










¹⁷*Department of Dermatology, Universitat de Barcelona, Hospital Clínic de Barcelona, Barcelona, Spain*

¹⁸*Department of Dermatology and Lübeck Institute of Experimental Dermatology (LIED), University of Lübeck, Lübeck, Germany*

Correspondence

Joost M. Meijer, Department of Dermatology, University Medical Center Groningen, Hanzeplein 1, 9700 RB Groningen, the Netherlands.
 Email: j.m.meijer@umcg.nl

ORCID

Joost M. Meijer  <https://orcid.org/0000-0001-7654-3528>
 Hanan Rashid  <https://orcid.org/0000-0002-9725-5207>
 Emiliano Antiga  <https://orcid.org/0000-0001-7787-4433>
 Riccardo Balestri  <https://orcid.org/0000-0002-0885-054X>
 Aikaterini Patsatsi  <https://orcid.org/0000-0001-9616-2001>
 Alessandra Ponziani  <https://orcid.org/0000-0001-8008-9399>
 Angelo Marzano  <https://orcid.org/0000-0002-8160-4169>
 Iakov Shimanovich  <https://orcid.org/0000-0002-7549-2682>
 Enno Schmidt  <https://orcid.org/0000-0002-1206-8913>

REFERENCES

- Carugno A, Sena P, Raponi F, Robustelli Test E, Vezzoli P. Patients with bullous skin disease in a high-epidemic COVID-19 area, Bergamo. *Italy Br J Dermatol.* 2020;183(3):589–91.
- Joly P, Gillibert A, Bohelay G, Aouar K, Ingen-Housz-Oro S, Bedane C, et al. Incidence and severity of COVID-19 in patients with autoimmune blistering skin diseases: a nationwide study. *J Am Acad Dermatol.* 2022;86(2):494–7.
- Kridin K, Schonmann Y, Weinstein O, Schmidt E, Ludwig RJ, Cohen AD. The risk of COVID-19 in patients with bullous pemphigoid and pemphigus: a population-based cohort study. *J Am Acad Dermatol.* 2021;85(1):79–87.
- Kasperkiewicz M. COVID-19 outbreak and autoimmune bullous diseases: a systematic review of published cases. *J Am Acad Dermatol.* 2021;84(2):563–8.
- Mahmoudi H, Farid AS, Nili A, Dayani D, Tavakolpour S, Soori T, et al. Characteristics and outcomes of COVID-19 in patients with autoimmune bullous diseases: a retrospective cohort study. *J Am Acad Dermatol.* 2021;84(4):1098–100.
- Kasperkiewicz M, Schmidt E, Amagai M, Fairley JA, Joly P, Murrell DF, et al. Updated international expert recommendations for the management of autoimmune bullous diseases during the COVID-19 pandemic. *J Eur Acad Dermatol Venereol.* 2021;35:e412–4.

¹*Department of Dermatology, UMCG Center of Expertise for Blistering Diseases, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands*

²*Section of Dermatology, Department of Health Sciences, University of Florence, Florence, Italy*

³*Dermatology Unit, ASST Papa Giovanni XXIII Hospital, Bergamo, Italy*

⁴*Division of Dermatology, Outpatient Consultation for Rare Diseases, Trento, Italy*

⁵*Faculty of Medicine, Papageorgiou General Hospital, 2nd Dermatology Department, Autoimmune Skin and Bullous Diseases Unit, Aristotle University, Thessaloniki, Greece*

⁶*Faculty of Medicine, Department of Dermatology, Akdeniz University, Antalya, Turkey*

⁷*Faculty of Medicine, Department of Dermatovenereology and Clinic of Dermatovenereology, University Clinical Center of Serbia, University of Belgrade, Belgrade, Serbia*

⁸*I. Department of Dermatovenereology, St. Anna Hospital, Masaryk University, Brno, Czech Republic*

⁹*Dermatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*

¹⁰*Department of Dermatology, Technical University Dresden, University Hospital, Dresden, Germany*

¹¹*Department of Dermatology, Ospedale classificato Cristo Re, Rome, Italy*

¹²*Department of Dermatology and Allergology, Hannover Medical School, Hannover, Germany*