Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Top 25 cited articles on Covid-19 and IBD: A bibliometric analysis

Ido Veisman\textsuperscript{a,b,*}, Noam Brakin Lederer\textsuperscript{b,c}, Offir Ukashi\textsuperscript{a,b,c}, Uri Kopylov\textsuperscript{a,b}, Eyal Klang\textsuperscript{b,d}

\textsuperscript{a} Department of Gastroenterology, Sheba medical center, Tel Hashomer, Israel
\textsuperscript{b} Faculty of Medicine, Tel-Aviv University, Israel
\textsuperscript{c} Department of Internal medicine A, Sheba medical center, Tel Hashomer, Israel
\textsuperscript{d} Sami Sagol AI Hub, ARC, Sheba Medical Center, Israel

Available online 21 May 2022

Abstract

Objectives: The use of citation analysis to identify the most cited Covid-19 and inflammatory bowel disease (IBD) manuscripts to provide an insight into the advances and knowledge accumulated regarding the pandemic in this subgroup of patients.

Methods: We've used a public application programming interface (API) U.S. National Center for Biotechnology Information (NCBI) to access the PubMed database. Data lock was performed on April 19, 2022. The API was used to retrieve all available IBD AND Covid-19 -related entries. For each retrieved entry, we've also obtained its citation count.

Results: The top 25 manuscripts were published between 2020 and 2021. The total citation count is 2051. The citation count of articles ranged from 41 to 313. The top 25 manuscripts were published in eight journals, while 16 were published in Gastroenterology and Gut. 36% of the most cited manuscripts reported clinical characteristics and patient outcomes, and 32% dealt with patient management. The most impactful manuscripts provided evidence that IBD patients are not at increased risk for severe morbidity or mortality from Covid-19 and that it is not advisable to discontinue the anti-inflammatory treatment for IBD during the pandemic. Two basic science studies demonstrated mechanistic insights for these observations. Studies that examined the immunogenic response of IBD patients treated with biologics were also part of the top-cited list.

Conclusions: Impactful scientific publications on Covid-19 in IBD patients provided reassurance and directed treatment at the time of this newly recognized severe disease.

© 2022 Elsevier Masson SAS. All rights reserved.

KEYWORDS
COVID-19; IBD

Abbreviations: TNF, tumor necrosis factor; COVID-19, Corona virus disease; IBD, inflammatory bowel disease; IG-IBD, Italian group for the study of IBD; AGA, American Gastroenterology Association; SARS, CoV-2- severe acute respiratory syndrome- Corona virus 2; ACE2, angiotensin I converting enzyme 2; TMPRSS2, transmembrane serine protease 2.

* Corresponding author.
E-mail address: ido.veisman@sheba.health.gov.il (I. Veisman).

https://doi.org/10.1016/j.clinre.2022.101959
2210-7401/© 2022 Elsevier Masson SAS. All rights reserved.
1. Introduction

From the beginning of the epidemic, research on Covid-19 had surged with an unprecedented number of publications. Since inflammatory bowel disease (IBD) treatment arsenal includes steroids, immunomodulators, and biologic therapies [1], at first, IBD patients were considered at high risk for SARS-CoV-2 infection and the development of a severe course of the disease [2]. Thus, extensive preliminary Covid-19 research examined various aspects of the disease in IBD patients.

Bibliometric citation analysis studies the scientific impact of manuscripts by analyzing the number of times they were cited in subsequent manuscripts. This study aims to present an analysis of the top 25 cited manuscripts that dealt with Covid-19 in patients with IBD.

2. Methods

We’ve used the public application programming interface (API) U.S. National Center for Biotechnology Information (NCBI) to access the PubMed database.

The PyMed Python package was used to query the PubMed API. The following data were extracted for each entry: PubMed unique article ID (PMID), title, publishing journal, abstract text, keywords (if any), and authors’ affiliations. The NCBI Entrez API was used to collect citation counts for the retrieved articles. Data lock was performed on April 19, 2022.

We retrieved all available IBD AND Covid-19-related entries. The search was conducted in entries’ titles, abstracts, and keywords using the terms “ulcerative colitis” OR “Crohn” OR “inflammatory bowel disease” for IBD, and “Covid-19” OR “COVID-19” OR “SARS-CoV-2” for Covid-19. We have limited the entries to studies published after January 1st, 2020.

Data retrieval, processing, and visualization were written in Python (Ver. 3.6.5, 64 bits).

A gastrointestinal expert (UK) and a gastrointestinal resident (IV) analyzed the retrieved studies in consensus.

3. Results

The top 25 most cited manuscripts are presented in Table 1. Most of the papers were published in 2020 (n=21), and only four were published in 2021. The total citation count is 2051. The citation count of articles ranged from 41 to 313. The top 25 manuscripts were published in eight journals, Gastroenterology (IF 22.68) published the highest number of top 25 papers (n=9 with 840 citations combined), followed by Gut (IF 22.05) with seven manuscripts and a total of 656 citations. Journal of Crohn’s and Colitis (IF 9.07), Alimentary Pharmacology & Therapeutics (IF 8.17), and The Lancet Gastroenterology & Hepatology (IF 18.48) had two papers in the top 25 manuscripts with a total citation count of 136, 131, 98 in accordance. In terms of content, 36% (n=9) of the most cited manuscripts reported clinical characteristics and patient outcomes, 32% (n=8) dealt with patient management. Four studies discussed pathophysiology, and three of the top 25 most cited manuscripts assessed the immunologic response post Covid-19 vaccination in IBD patients. One case report described a clinical course in treatment response in a Crohn’s disease patient.

Examination of the type of article demonstrated that 12 of the most cited manuscripts were clinical research (including clinical trials, case series, case reports, correspondence), 10 were non-clinical (including reviews, viewpoints, expert commentary, guidelines, recommendations from an international consensus meeting), two studies were basic science studies.

4. Discussion

From the first weeks of the Covid-19 pandemic, global medical research has focused on studying the various aspects of Covid-19 including disease evolution, transmission, detection, treatment, and prevention. The scientific community had responded promptly to the new disease, with a massive number of publications. Moreover, the open access policy that many journals have applied regarding Covid-19 publications contributed to the rapid distribution of new data and the exponential growth of publications [3]. One of the most significant challenges that arose with the pandemic outbreak involves the effect of Covid-19 on patients with an immune-mediated inflammatory condition such as IBD. In this bibliometric analysis, we present the topmost cited 25 papers that dealt with Covid-19 among IBD patients. These manuscripts, which were most influential regarding this subgroup of patients, were published in eight journals with 2051 citations. Gastroenterology and Gut contributed mostly to the top 25 most cited manuscripts with more than 60% of publications, consistent with the Bradford’s Law, first described in 1934, which state that the most essential journals in a particular field extract most of the citations [4]. Clinical characteristics, patient management, and outcomes are the most common topics in this top 25 most cited list.

The Covid-19 pandemic raised new challenges for IBD patients and their physicians. New dilemmas such as whether patients with IBD might be prone to severe Covid-19 infection and what will be the impact of immunosuppression and immunomodulation on the course of the disease and response to anti-Covid-19 vaccine.

The top 25 manuscripts listed here provided vital information about IBD in the Covid era, including reassuring information that patients with IBD are not at increased risk for severe morbidity or mortality from Covid-19 infection, as demonstrated in several of the top 25 cited manuscripts [5–9]. In addition, several studies provided crucial information about the safety of the common biologic therapies, including tumor necrosis alpha (TNF) inhibitors [9–11], and two studies suggest a pathophysiological explanation for this observation as demonstrating that IBD therapies are associated with lower levels of viral entry molecule ACE2 [12,13]. The anti-Covid-19 vaccination changed dramatically during the pandemic. However, concerns regarding the immunogenic response of IBD patients treated with an anti-inflammatory agent have been a major concern. Kennedy and
Table 1: Top 25 most cited manuscripts.

| Rank | Title                                                                                                                                  | Journal                               | Year | Citations |
|------|----------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|------|-----------|
| 1    | 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 | 313       |
| 2    | Outcomes of COVID-19 in 79 patients with IBD in Italy: an IG-IBD study.                                                                 | Gut                                   | 2020 | 157       |
| 3    | British Society of Gastroenterology guidance for management of inflammatory bowel disease during the COVID-19 pandemic.                | Gut                                   | 2020 | 119       |
| 4    | AGA Clinical Practice Update on Management of Inflammatory Bowel Disease During the COVID-19 Pandemic: Expert Commentary. Management of Patients With Crohn's Disease and Ulcerative Colitis During the Coronavirus Disease-2019 Pandemic: Results of an International Meeting. | Gastroenterology                      | 2020 | 108       |
| 5    | COVID-19 and immunomodulation in IBD.                                                                                                   | Gut                                   | 2020 | 106       |
| 6    | Effect of IBD medications on COVID-19 outcomes: results from an international registry.                                                 | Gut                                   | 2020 | 102       |
| 7    | Are Patients with Inflammatory Bowel Disease at Increased Risk for Covid-19 Infection?                                                   | Journal of Crohn's & Colitis          | 2020 | 88        |
| 8    | 2019 novel coronavirus disease (COVID-19) in patients with inflammatory bowel diseases.                                                 | Alimentary Pharmacology & Therapeutics | 2020 | 84        |
| 9    | Uneventful Course in Patients With Inflammatory Bowel Disease During the Severe Acute Respiratory Syndrome Coronavirus 2 Outbreak in Northern Italy. | Gastroenterology                      | 2020 | 82        |
| 10   | Expression of SARS-CoV-2 Entry Molecules ACE2 and TMPRSS2 in the Gut of Patients With IBD.                                               | Inflammatory Bowel Diseases Gut       | 2020 | 77        |
| 11   | Infliximab is associated with attenuated immunogenicity to BNT162b2 and ChAdOx1 nCoV-19 SARS-CoV-2 vaccines in patients with IBD.         | Inflammatory Bowel Diseases Gut       | 2021 | 65        |
| 12   | Pediatric Crohn Disease and Multisystem Inflammatory Syndrome in Children (MIS-C) and COVID-19 Treated With Infliximab.                  | Journal of Pediatric Gastroenterology and Nutrition | 2020 | 59        |
| 13   | SARS-CoV-2 vaccination for patients with inflammatory bowel diseases: recommendations from an international consensus meeting.           | The Lancet. Gastroenterology & Hepatology | 2021 | 57        |
| 14   | Prevention of COVID-19 in patients with inflammatory bowel disease in Wuhan, China.                                                      | The Lancet. Gastroenterology          | 2020 | 55        |
| 15   | Gastrointestinal and hepatic manifestations of COVID-19: A comprehensive review.                                                          | World Journal of Gastroenterology    | 2020 | 54        |
| 16   | Baseline Disease Activity and Steroid Therapy Stratify Risk of COVID-19 in Patients With Inflammatory Bowel Disease.                    | Gastroenterology                      | 2020 | 52        |
| 17   | Anti-SARS-CoV-2 antibody responses are attenuated in patients with IBD treated with infliximab.                                           | Gut                                   | 2021 | 50        |
| 18   | Risk of Severe Coronavirus Disease 2019 in Patients With Inflammatory Bowel Disease in the United States: A Multicenter Research Network Study. | Gastroenterology                      | 2020 | 48        |
| 19   | Inflammatory Bowel Disease Care in the COVID-19 Pandemic Era: The Humanitas, Milan, Experience.                                           | Journal of Crohn's & Colitis          | 2020 | 48        |
| 20   | Endoscopy in inflammatory bowel diseases during the COVID-19 pandemic and post-pandemic period.                                           | The Lancet. Gastroenterology & Hepatology | 2020 | 47        |
| 21   | Characteristics and Prognosis of Patients With Inflammatory Bowel Disease During the SARS-CoV-2 Pandemic in the Basque Country (Spain). | Gastroenterology                      | 2020 | 44        |
| 22   | Review article: prevention, diagnosis and management of COVID-19 in the IBD patient.                                                      | Alimentary Pharmacology & Therapeutics | 2020 | 43        |
colleagues address this issue in two studies for the top 25 most cited list demonstrated that infliximab, but not vedolizumab, is associated with attenuated immunogenicity. However, vaccination after Covid-19 infection, or a second dose of vaccine, led to seroconversion in most patients [14,15]. In addition, it should be noted that few manuscripts in the top 25 most cited are guidelines and expert commentaries that addressed a variety of aspects of IBD in the pandemic period [16,17].

Conclusion

This study presents a concise bibliometric analysis of the most cited manuscripts on Covid-19 in IBD patients. Our study shows that the scientific community has been active in promoting research and understanding of the effect of the pandemic on IBD patients, including the determination of clinical guidelines and examination of the effects of anti-inflammatory medication on the course of Covid-19 infection immune response post-vaccination and pathophysiology aspects as well.

Author contributions

Conceptualization, I.V, U.K and E.K.; Methodology I.V and E. K.; Data Curation and analysis, E.K.; Writing — Original Draft Preparatation I.V, N.B.L and O.U.; Writing — Review & Editing, E.K.; All authors have approved the final draft submitted.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Study ethics and patient consent

This study was carried out in accordance with the ethical guidelines of the Declaration of Helsinki. The study was approved by the Sheba Medical Center ethics committee. Since this was a bibliometric analysis, no informed consent was obtained.

Data availability statement

Not applicable.

Declaration of Competing Interest

U.K.: speaker and advisory fees—Abbvie, Jannsen Takeda Medtronic; research support—Jannsen Takeda Medtronic. IV: consultation fees—Galmed. The remaining authors declare that there is no conflict of interest.

CRediT authorship contribution statement

Ido Veisman: Conceptualization, Methodology, Writing — original draft. Noam Brakin Lederer: Writing — original draft. Offir Ukashi: Conceptualization. Eyal Klang: Conceptualization, Methodology, Data curation, Writing — review & editing.

Acknowledgments

Not applicable.

References

[1] Bernstein CN. Treatment of IBD: where we are and where we are going. Am J Gastroenterol Jan 2015;110(1):114–26. doi: 10.1038/ajg.2014.357.
[2] Fagni F, Simon D, Tascilar K, et al. COVID-19 and immune-mediated inflammatory diseases: effect of disease and treatment on COVID-19 outcomes and vaccine responses. Lancet Rheumatol Oct 2021;3(10):e724–36. doi: 10.1016/S2665-9913(21)00247-2.
[3] ElHawary H, Salimi A, Diab N, Smith L. Bibliometric analysis of early COVID-19 research: the top 50 cited papers. Infect Dis (Auckl) 2020;13:1178633720962935. doi: 10.1177/1178633720962935.
[4] SC B. Sources of information on specific subjects. Engineering 1934:85 6.
[5] Taxonera C, Sagastagoitia I, Alba C, Mañas N, Olivares D, Rey E. 2019 novel coronavirus disease (COVID-19) in patients with inflammatory bowel diseases. Aliment Pharmacol Ther 2020;52 (2):276–83 07. doi: 10.1111/apt.15804.
[6] Monteleone G, Ardizzone S. Are patients with inflammatory bowel disease at increased risk for covid-19 infection? J Crohns Colitis Sep 16 2020;14(9):1334–6. doi: 10.1093/ecco-jcc/jjaa061.
[7] Singh S, Khan A, Chowdhry M, Bilal M, Kochhar GS, Clarke K. Risk of severe coronavirus disease 2019 in patients with inflammatory bowel disease in the United States: A multicenter research network study. Gastroenterology Oct 2020;159 (4):1575–8 e4. doi: 10.1053/j.gastro.2020.06.003.
[8] Rodríguez-Lago I, Ramírez de la Piscina P, Elorza A, Merino O, Ortiz de Zárate J, Cabriada JL. Characteristics and prognosis of patients with inflammatory bowel disease during the SARS-CoV-2 pandemic in the Basque Country (Spain). Gastroenterology Aug 2020;159(2):781-3. doi: 10.1053/j.gastro.2020.04.043.

[9] Lukin DJ, Kumar A, Hajifathalian K, et al. Baseline disease activity and steroid therapy stratify risk of COVID-19 in patients with inflammatory bowel disease. Gastroenterology Oct 2020;159(4):1541-4 e2. doi: 10.1053/j.gastro.2020.05.066.

[10] 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 disease: results from an international registry. Gastroenterology 2020;159(2):481-91 08e3. doi: 10.1053/j.gastro.2020.05.032.

[11] Neurath MF. COVID-19 and immunomodulation in IBD. Gut 2020;69(7):1335-42 07. doi: 10.1136/gutjnl-2020-321269.

[12] Burgueno JF, Reich A, Hazime H, et al. Expression of SARS-CoV-2 entry molecules ACE2 and TMPRSS2 in the gut of patients with IBD. Inflamm Bowel Dis 05 12 2020;26(6):797-808. doi: 10.1093/ibd/izaa085.

[13] Suárez-Farrónas M, Tokuyama M, Wei G, et al. Intestinal inflammation modulates the expression of ACE2 and TMPRSS2 and potentially overlaps with the pathogenesis of SARS-CoV-2-related disease. Gastroenterology 2021;160(1):287-301 01e20. doi: 10.1053/j.gastro.2020.09.029.

[14] Kennedy NA, Goodhand JR, Bewshea C, et al. Anti-SARS-CoV-2 antibody responses are attenuated in patients with IBD treated with infliximab. Gut 2021;70(5):865-75 05. doi: 10.1136/gutjnl-2021-324388.

[15] Kennedy NA, Lin S, Goodhand JR, et al. Infliximab is associated with attenuated immunogenicity to BNT162b2 and ChAdOx1 nCoV-19 SARS-CoV-2 vaccines in patients with IBD. Gut 2021;70(10):1884-93 10. doi: 10.1136/gutjnl-2021-324789.

[16] Kennedy NA, Jones GR, Lamb CA, et al. British Society of Gastroenterology guidance for management of inflammatory bowel disease during the COVID-19 pandemic. Gut 2020;69(6):984-90 06. doi: 10.1136/gutjnl-2020-321244.

[17] Rubin DT, Feuerstein JD, Wang AY, Cohen RD. AGA clinical practice update on management of inflammatory bowel disease during the COVID-19 pandemic: expert commentary. Gastroenterology Jul 2020;159(1):350-7. doi: 10.1053/j.gastro.2020.04.012.