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ORIGINAL ARTICLE

Top 25 cited articles on Covid-19 and IBD: A bibliometric analysis

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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.

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.

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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.	Gastroenterology	2020	110
5	Management of Patients With Crohn's Disease and Ulcerative Colitis During the Coronavirus Disease-2019 Pandemic: Results of an International Meeting.	Gastroenterology	2020	108
6	COVID-19 and immunomodulation in IBD.	Gut	2020	106
7	Effect of IBD medications on COVID-19 outcomes: results from an international registry.	Gut	2020	102
8	Are Patients with Inflammatory Bowel Disease at Increased Risk for Covid-19 Infection?	Journal of Crohn's & Colitis	2020	88
9	2019 novel coronavirus disease (COVID-19) in patients with inflammatory bowel diseases.	Alimentary Pharmacology & Therapeutics	2020	84
10	Uneventful Course in Patients With Inflammatory Bowel Disease During the Severe Acute Respiratory Syndrome Coronavirus 2 Outbreak in Northern Italy.	Gastroenterology	2020	82
11	Expression of SARS-CoV-2 Entry Molecules ACE2 and TMPRSS2 in the Gut of Patients With IBD.	Inflammatory Bowel Diseases	2020	77
12	Infliximab is associated with attenuated immunogenicity to BNT162b2 and ChAdOx1 nCoV-19 SARS-CoV-2 vaccines in patients with IBD.	Gut	2021	65
13	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
14	SARS-CoV-2 vaccination for patients with inflammatory bowel diseases: recommendations from an international consensus meeting.	Gut	2021	57
15	Prevention of COVID-19 in patients with inflammatory bowel disease in Wuhan, China.	The Lancet. Gastroenterology & Hepatology	2020	55
16	Gastrointestinal and hepatic manifestations of COVID-19: A comprehensive review.	World Journal of Gastroenterology	2020	54
17	Baseline Disease Activity and Steroid Therapy Stratify Risk of COVID-19 in Patients With Inflammatory Bowel Disease.	Gastroenterology	2020	52
18	Anti-SARS-CoV-2 antibody responses are attenuated in patients with IBD treated with infliximab.	Gut	2021	50
19	Risk of Severe Coronavirus Disease 2019 in Patients With Inflammatory Bowel Disease in the United States: A Multicenter Research Network Study.	Gastroenterology	2020	48
20	Inflammatory Bowel Disease Care in the COVID-19 Pandemic Era: The Humanitas, Milan, Experience.	Journal of Crohn's & Colitis	2020	48
21	Endoscopy in inflammatory bowel diseases during the COVID-19 pandemic and post-pandemic period.	The Lancet. Gastroenterology & Hepatology	2020	47
22	Characteristics and Prognosis of Patients With Inflammatory Bowel Disease During the SARS-CoV-2 Pandemic in the Basque Country (Spain).	Gastroenterology	2020	44
23	Review article: prevention, diagnosis and management of COVID-19 in the IBD patient.	Alimentary Pharmacology & Therapeutics	2020	43

Table 1 (*Continued*)

Rank	Title	Journal	Year	citations
24	Serologic Response to Messenger RNA Coronavirus Disease 2019 Vaccines in Inflammatory Bowel Disease Patients Receiving Biologic Therapies.	Gastroenterology	2021	42
25	Intestinal Inflammation Modulates the Expression of ACE2 and TMPRSS2 and Potentially Overlaps With the Pathogenesis of SARS-CoV-2-related Disease.	Gastroenterology	2020	41

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 Preparation I.V, N.B.L and O.U.; Writing – Review & Editing, E.K.; All authors have approved the final draft submitted.

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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:** Writing – original draft. **Uri Kopylov:** Conceptualization. **Eyal Klang:** Conceptualization, Methodology, Data curation, Writing – review & editing.

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