

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 63397

**Title:** Viral infections in Inflammatory Bowel Disease: tips and tricks for correct management

**Reviewer's code:** 01429233

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-01-28

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-01-29 02:24

**Reviewer performed review:** 2021-01-29 03:45

**Review time:** 1 Hour

|                                 |   |
|---------------------------------|---|
| <b>Scientific quality</b>       | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>         | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>               | <input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Re-review</b>                | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |
| <b>Peer-reviewer statements</b> | Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous<br>Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |



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#### **SPECIFIC COMMENTS TO AUTHORS**

In this review manuscript, the authors have focused on the vulnerability of patients with IBD to multiple, but known infectious micro-organisms. The topic has been most thoroughly and broadly highlighted. Further, given that currently, the Covid-19 pandemic is a serious concern, especially for IBD patients who may receive immunosuppressive medications, publication of this manuscript could not have been at a better time. With this background in mind, I had no hesitation to recommend publication of this manuscript. Authors, please allow me to advise you that minor language editing by a native academic should benefit the overall impact of your manuscript.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 63397

**Title:** Viral infections in Inflammatory Bowel Disease: tips and tricks for correct management

**Reviewer's code:** 04088775

**Position:** Editorial Board

**Academic degree:** BMed, FRACP, PhD

**Professional title:** Doctor, Staff Physician

**Reviewer's Country/Territory:** Australia

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-01-28

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-02-02 22:05

**Reviewer performed review:** 2021-02-02 22:52

**Review time:** 1 Hour

|                                 |   |
|---------------------------------|---|
| <b>Scientific quality</b>       | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>         | <input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing<br><input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>               | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Re-review</b>                | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No   |
| <b>Peer-reviewer statements</b> | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous<br>Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |

## **SPECIFIC COMMENTS TO AUTHORS**

The authors have performed a review of well-known viral infections that can occur with inflammatory bowel disease and suggestions on how to diagnose and manage these infections. There is a lot of information presented in the text which makes the article informative but does make it difficult to follow the structure in some sections. There are some important practical points that treating clinicians need to know with these viruses and it mainly relates to when they should be considered, how the symptoms may differ from normal in an IBD/ immunosuppressed patient, whether vaccination or prophylaxis is needed (and should be given in someone on immunosuppression) and how to treat the infection. If each section is broken up with sub-headings to discuss these issues it may assist readers in better understanding the presented information. I have the following suggestions: 1. For the general approach to infections section, it may be more clinically relevant to break up investigations based on the symptoms present or provide a list of viruses to consider in different situations and then either provide a suggested algorithm or table. 2. For the hepatitis A section, information on symptoms it will cause in an IBD patient is important 3. For the 'core tips' section, a summary of key points identified by the article should be provided rather than a general overview of the article. Page 4, line 2 – 'ad' should be 'and' Page 4, line 3 – 'flair' should be 'flare' Page 4, line 7 – 'microbioma' should be 'microbiota' Page 5, line 21 – '40% due to viral pathogens' should be '40% are due to viral pathogens' Page 7, line 17 – 'and more especially CMV' – remove 'more' Page 10, line 5 – 'loss' should be 'lose'

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 63397

**Title:** Viral infections in Inflammatory Bowel Disease: tips and tricks for correct management

**Reviewer's code:** 03656360

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-01-28

**Reviewer chosen by:** Jin-Lei Wang

**Reviewer accepted review:** 2021-02-01 06:07

**Reviewer performed review:** 2021-02-05 07:41

**Review time:** 4 Days and 1 Hour

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|---------------------------------|---|
| <b>Scientific quality</b>       | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>         | <input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>               | <input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Re-review</b>                | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No   |
| <b>Peer-reviewer statements</b> | Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous<br>Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |



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## **SPECIFIC COMMENTS TO AUTHORS**

Viral infections in Inflammatory Bowel Disease: tips and tricks for correct management

The mortality of Inflammatory Bowel Disease increased in the past decade. Asain is 1.4/ diagnosis standard of Inflammatory Bowel Disease change from 2001 ChengDu to 2012 GuangZhou. This vast IBD population treated with immune-modifying therapies, is at increased risk of severe infections, including opportunistic infections sustained by viral, bacterial, parasitic, and fungal agents. A recent population-based study of patients with IBD[18] found among opportunistic infections 40% due to viral pathogens. During a 5-y follow-up, combination therapy (anti-TNF + thiopurine) was associated with an increased risk of opportunistic viral infections compared with anti-TNF monotherapy (1.3% vs. 0.7%); HCV infection is confirmed, patients should be treated according to the HCV clinical practice guidelines. Recognized risk factors were treatment with 2 or more immunomodulators for a long period of time, presence of HBV DNA and avoidance of antiviral prophylaxis. TNF- $\alpha$  and related cytokines are important in regulating hepatitis B replication and anti-TNF treatments confer a high risk of HBV reactivation. A special attention must be paid to patients receiving corticosteroids, thiopurine, or combination therapy with thiopurines and anti-TNF agents because they are more prone to contract opportunistic viral infections, in particular HSV, VZV, CMV, and EBV.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 63397

**Title:** Viral infections in Inflammatory Bowel Disease: tips and tricks for correct management

**Reviewer's code:** 02548913

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-01-28

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-01-29 14:20

**Reviewer performed review:** 2021-02-15 14:04

**Review time:** 16 Days and 23 Hours

|                                 |   |
|---------------------------------|---|
| <b>Scientific quality</b>       | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>         | <input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>               | <input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Re-review</b>                | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No   |
| <b>Peer-reviewer statements</b> | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous<br>Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |

#### **SPECIFIC COMMENTS TO AUTHORS**

Comments to the author The authors reviewed viral infections in patients with inflammatory bowel disease. This problem is very important. Please consider adding the following matters. Influenza section IBD patients treated with anti-tumor necrosis factor may have weak antibody production after inactivated non-live trivalent influenza vaccination (Inflamm Bowel Dis. 2020 Mar 4;26(4):593-602.) SARS-CoV-2 or conclusion section In several studies of IBD patients with COVID-19, a trend towards adverse outcome with concomitant corticosteroids was reported (Gut. 2020;69:1213 etc.). It is difficult to conclude on their benefit and risk as they have many selection bias, as corticosteroids are likely to be given to patients with severe disease, there is heterogeneity in the type, dose and duration of their use. There are data suggesting that doses of prednisolone above 20 mg are associated with increased risk of bacterial and viral infections in IBD. (J Crohns Colitis. 2020;14:1316-29.etc). It seems prudent to minimize the use of systemic steroids, think of alternatives to steroids and, if used, taper to the lowest possible dose quickly. As a matter of course, long-term steroids are contraindicated to avoid the risk of viral infection (There are many other harmful effects). Therefore, this need be specified somewhere.



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 63397

**Title:** Viral infections in Inflammatory Bowel Disease: tips and tricks for correct management

**Reviewer's code:** 04088775

**Position:** Editorial Board

**Academic degree:** BMed, FRACP, PhD

**Professional title:** Doctor, Staff Physician

**Reviewer's Country/Territory:** Australia

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-01-28

**Reviewer chosen by:** Ze-Mao Gong

**Reviewer accepted review:** 2021-04-03 03:38

**Reviewer performed review:** 2021-04-03 04:04

**Review time:** 1 Hour

|                                 |   |
|---------------------------------|---|
| <b>Scientific quality</b>       | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good<br><input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish            |
| <b>Language quality</b>         | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing<br><input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| <b>Conclusion</b>               | <input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority)<br><input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection             |
| <b>Peer-reviewer statements</b> | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous<br>Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |

## SPECIFIC COMMENTS TO AUTHORS



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The authors have addressed all the reviewers' comments.