Name of journal: World Journal of Clinical Cases
Manuscript NO: 84753
Title: Menstrual cycle abnormalities in women with inflammatory bowel disease and effects of biological therapy on gynecological pathology
Provenance and peer review: Invited Manuscript; Externally peer reviewed
Peer-review model: Single blind
Reviewer’s code: 03537165
Position: Editorial Board
Academic degree: PhD
Professional title: Associate Professor
Reviewer’s Country/Territory: Croatia
Author’s Country/Territory: Lithuania
Manuscript submission date: 2023-03-27
Reviewer chosen by: AI Technique
Reviewer accepted review: 2023-04-24 05:04
Reviewer performed review: 2023-05-04 04:56
Review time: 9 Days and 23 Hours

Scientific quality
[ ] Grade A: Excellent [ ] Grade B: Very good [ Y] Grade C: Good
[ ] Grade D: Fair [ ] Grade E: Do not publish

Novelty of this manuscript
[ ] Grade A: Excellent [ Y] Grade B: Good [ ] Grade C: Fair
[ ] Grade D: No novelty

Creativity or innovation of this manuscript
[ ] Grade A: Excellent [ Y] Grade B: Good [ ] Grade C: Fair
[ ] Grade D: No creativity or innovation
### Scientific significance of the conclusion in this manuscript

- [ ] Grade A: Excellent
- [Y] Grade B: Good
- [ ] Grade C: Fair
- [ ] Grade D: No scientific significance

### Language quality

- [ ] Grade A: Priority publishing
- [Y] Grade B: Minor language polishing
- [ ] Grade C: A great deal of language polishing
- [ ] Grade D: Rejection

### Conclusion

- [ ] Accept (High priority)
- [ ] Accept (General priority)
- [Y] Minor revision
- [ ] Major revision
- [ ] Rejection

### Re-review

- [Y] Yes
- [ ] No

### Peer-reviewer statements

- Peer-Review: [ ] Anonymous
- [Y] Onymous
- Conflicts-of-Interest: [ ] Yes
- [Y] No

### SPECIFIC COMMENTS TO AUTHORS

Review - 84753: The review paper evaluates the gynecological disorders in inflammatory bowel disease with special emphasis on effects of anti-TNF therapy and menstrual abnormalities. Could authors comment whether studies evaluated the effects of severity or response to anti-TNF therapy on the menstrual abnormalities. Are the menstrual abnormalities more related to the severity of the IBD or negative or positive effects of anti TNF? The title, abstract, manuscript organization, discussion, tables and references are appropriate. Language requires minor polishing to achieve precision, clarity and grammatical correctness.
# PEER-REVIEW REPORT

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**Provenance and peer review:** Invited Manuscript; Externally peer reviewed  
**Peer-review model:** Single blind  
**Reviewer’s code:** 04091850  
**Position:** Editorial Board  
**Academic degree:** DSc, MD, PhD  
**Professional title:** Chief Doctor, Professor  
**Reviewer’s Country/Territory:** Denmark  
**Author’s Country/Territory:** Lithuania  
**Manuscript submission date:** 2023-03-27  
**Reviewer chosen by:** Geng-Long Liu  
**Reviewer accepted review:** 2023-05-19 06:14  
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**Review time:** 9 Days and 2 Hours

<table>
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<th>Scientific quality</th>
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SPECIFIC COMMENTS TO AUTHORS
Since inflammatory bowel diseases affect women of reproductive age it is of interest to investigate the impact of the diseases and their treatment on various aspects of gynecology issues presenting a review on the matter The authors of the present manuscript attempt to do so. However much of the data presented is based on case stories and results of animal studies where it could be questioned whether the data is relevant for the females suffering from IBD as a group. Title: A bit "broad". It is stated that the manuscript deals with "gynecological manifestations" but mainly disturbances in menstrual cycle and ovarian capacity are described. Introduction: I think a short description of fertility problems in women with IBD with major references of interest is necessary to frame why it is of interest to dig deeper into gynecological manifestations is needed. Besides there is a lack of references to underline the major statements in the two first sections of the introduction. It is mentioned that several studies have provided new information regarding benefit of biological therapy but these studies are animal studies which should be noted. Methods: There is a lot of focus on adalimumab in the manuscript. This could reflect that data are lacking on other treatments but I would
suggest that the search is including other therapies as well (TNFalpha blocking agents as a group; Vedolizumab, Ustekinumab, 5-ASAs, steroids, immunomodulators, small molecules). Should no data on some of these drugs not be available this should be noted.

Table 2 and 3: No need to use space on providing tables describing few animal studies and case reports. The tables should be omitted. IBD and menstrual cycle: A study regarding 662 female patients with IBD undergoing surgery is cited. However it is not discussed whether the results presented is related to IBD or to the surgery. This is of importance since the study by Saha et al produced contradictory results. The reason for that might well be that the populations described in the two papers differs in many aspects. Adalimumab and gynecologic manifestations: Adalimumab is a TNFalpha blocking agent and the section should be named "TNFalpha blocking agents and gynecological manifestations". If data is not available regarding effects of other therapies than TNFalpha blockers this should be mentioned in the manuscript. Lymphoma is listed as a primary side effects of adalimumab. This is no true. It is debated as to whether TNFalpha blockers seldomly can lead to development of lymphomas but anyhow it is not a primary side effect of the drug. The effects of adalimumab on ovarian ischemia: For practical purposes all the data given in this section on the possible effects of adalimumab on ovarian ischemia is based on animal experiments and the presented hypothesis that TNFalpha blockers may be used to prevent ischemia in women is simply too speculative based on very limited evidence. I don’t think this section should be included. The sections describing the possible effects of adalimumab and other TNFalpha blockers on endometriosis should be combined. It should be clearly noted that there is a profound lack of knowledge on the matter and that most data comes from animal experiments and that besides the cited study on infliximab no human studies specifically addressing the issue is available. As the manuscript cannot be recommended for publication but it could be reconsidered if the authors would make changes
according to the suggestions og widen the search to include more drugs used in the treatment of IBD