Author’s response to reviews

Title: Hepatobiliary and Pancreatic Manifestations in Inflammatory Bowel Diseases: A Referral Center Study

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Author’s response to reviews:

My colleagues — co-authors and I sincerely hope that you will deem it appropriate for publication in BMC Gastroenterology.

We would like to thank the Reviewers for their useful comments.

A great emphasis has been placed on the revision of the manuscript, following the instructions/comments posed by the Reviewers.

The responses to the Reviewers are presented in details as follows:

Responses to reviewer and Editor

Comments:
Some points should be improved:
1) Page 3, lane 9: the most frequent hepatic, biliary and pancreatic finding were respectively fatty liver, cholelithiasis and acute pancreatitis.

lane 9: It is difficult to clearly know how the percentages are calculated. I think it could be useful to add every time the numerator, the denominator and the percentage. Example: 55% (120/220). You have to tell maybe in the methods that the calculation method tend to surestimate the frequency of the events.

lane 12: For example in the abstract 5.3% of them had positive hepatitis B. Add in parenthesis: 12/225. I am not sure that the precision 5.3% is necessary. 5% is enough (12/225)

2) lane 15: 24 patients had drug related side effects. The 2 cases with hyperamylasemia, are not side effects. The 2 patients with SULFASALAZINE cannot be imputed to sulfasalazine after 1.5 to 5 years. Then we are left with 21 patients with DILI and 3 with DIPI.

3) Page 3, lane 17: it is very difficult to diagnose exacerbation of hepatitis C as ALT fluctuates in CHC. Plase replace by one case of chronic hepatitis

4) lane 19. replace some kind by an

5) Page 3, lane 21: replace innocent by benign

6) Page 4, lane 21: replace not a rare by common

7) Page 4, lane 25, remove cumulative

8) Page 5, lane 8: I will add autoimmune pancreatitis in the differential diagnosis

9) Page 5, lane 20: only 30% have typical histology. I will remove typical.

10) Page 6, lane 19: revealed abnormal findings

11) lane 26 : remove in patients

remove information on sulfasalazine unless you have good arguments for keeping it

12) Page 7, lane 2: patient with primary

13) Page 7, lane 5. The most common pancreatic manifestation. What was the etiology for the fourth patient?

14) Page 7, lane 28. four patients with ALT > 3 ULN and not one.

15) Page 9, lane 5: of our study

16) lane 14: with a highest number of males having cholelithiasis

17) lane 17: concerning PSC

18) lane 19: our retrospective

19) Page 10, lane 7: mesalazine
20) lane 7: The delay between drug introduction and acute pancreatitis was similar....

21) lane 9: should include DIPI, biliary pancreatitis, auto-immune pancreatitis and duodenal involvement.

22) lane 12: of their immunization for hepatitis

23) lane 21: the low proportion

24) Page 11, lanes 18 to 20: it is a result and should be included in the results section

25) lane 21: ULN

26) lane 22: may be better tolerated

27) Page 12, lane 1: In our study, one out of four....

28) A descriptive Table is necessary and can replace the Table 2
Columns: Whole population, UC, Crohn
Lanes: age sex, severity, localization, frequency of the extra-intestinal manifestations.....

29) Table 3: I think sulfasalazine should be removed unless you have very good reasons to think that it is responsible of DILI

Response:

On comment 1: We followed your instructions and we added on page 3, lane 9 “pancreas in 55% of examined patients (120/220)” and on page 3, lane 10 and 11 “were fatty liver (20%, 44/220), cholelithiasis (14.5%, 32/220) and acute pancreatitis (0.6%, 4/602)”. On page 3 lane, we changed “5.3%” to “5% (12/225)”.

On comment 2: We removed “and 2 cases with elevated amylase”. In addition, we followed your instructions and we reduced the number of patients with DILI and the number of patients with drug side effects, on page 3 lane 15 “, 24 patients had drug-related side” and on page 3 lane 16 “21 cases”.

On comment 3: we changed “one case of exacerbation of HCV infection” to “one case of chronic hepatitis C”.

On comment 4: It was done.

On comment 5: It was done.

On comment 6: It was done.

On comment 7: It was done.

On comment 8: On page 5, lane 8 we added “and autoimmune pancreatitis”.
On comment 9: We removed “typical”.

On comment 10: We changed “revealed findings” to revealed abnormal findings”.

On comment 11: We removed the information on sulfasalazine.

On comment 12: On page 7, lane 2, we added “with”.

On comment 13: On page 7 lane 5, we added “while in one case, the cause was gallstones.”.

On comment 14: On page 8 lane 3, we changed “one patient” to “four patients”.

On comment 15: It was done.

On comment 16: On page 9 lane 17-18, we changed “with the males with cholelithiasis being more than the females” to “with a highest number of males having cholelithiasis”.

On comment 17: It was done.

On comment 18: It was done.

On comment 19: It was done.

On comment 20: On page 10 lane 10, we changed “The manifestation time of acute pancreatitis after drug administration is similar” to “The delay between drug introduction and acute pancreatitis was similar”.

On comment 21: On page 10 lane 12, we added DIPI, biliary pancreatitis.

On comment 22: On page 10 lane 15, we added “immunization”

On comment 23: On page 10 lane 24, we changed “the poor proportion” to “the low proportion”.

On comment 24: We followed your instructions and transported “according to R factor for liver injury, in 8 of the 9 AZA-hepatotoxicity cases hepatotoxicity liver injury was observed (R>5) and in only one case the cause of liver injury was mixed (R: 2-5)” from page 11 lanes 18-20 to page 7 lanes 27-28 (results section).

On comment 25: It was done.

On comment 26: On page 11 lane 25, we changed “may be tolerated” better to “may be better tolerated”.

On comment 27: It was done.

On comment 28: We followed your instructions and we added four extra lanes on 2 Table (sex, Age at diagnosis of disease, Localization at diagnosis and severity at diagnosis according to Mayo score and CDAI score).
On comment 29: On Table 3, we removed information on sulfasalazine.

We hope that the revised manuscript will vouch for a position among other relative studies already published in your Journal. Once more we would like to thank the Section Editor and their reviewers for their fruitful comments and their important contribution.

This work is part of thesis of the first author Dr Fotios Fousekis, who tried hard and gave a lot of effort and energy to gather the data and draft the initial manuscript.

On behalf of the co-authors with my great appreciation

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