

Digestive disease center. Inflammatory bowel disease program

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Response letter.

Dear Editor,

With this letter we wish to reply, point by point, to the issues and concerns raised by the reviewers regarding our manuscript entitled "Hepatobiliary manifestations in Inflammatory bowel disease: A practical approach".

We thank you for the meticulous comments that will help us to improve our work

Reviewer #1:

- 1. We improved the grammatical mistakes.
- 2. We added more information about Primary Sclerosing Cholangitis and IBD prognosis and complications.
- 3. Autoimmune Sclerosing Cholangitis in pediatric IBD patients' entity was included
- 4. We described the types of Auto immune Hepatitis and the IBD association with AIH type 1.
- 5. We provide a table with the most frequently types of Hepatobiliary manifestations classified from the type of liver patter presentation.
- 6. In the stepwise approach, abnormal liver test in IBD we decided to repeat liver test function every 1-2 months in mild/moderate aminotransferases elevation(< 3 ULN).

Reviewer #2:.

1. We added also dermatological complications since they are even more frequent than others comorbidities.

2. In this sentence "The autoimmune disease that is most frequently associated with IBD is primary sclerosing cholangitis (PSC), followed by autoimmune hepatitis (AIH) and overlap syndromes; we added and "others" and later on we discussed the neutrophilic cholangitis disease although is

not so frequently.

- 3. We didn't include neutrophilic cholangitis, because there is no association with inflammatory bowel disease.
- 4. In the chapter of Non-Alcoholic Fatty Liver Disease (NAFLD) it is already described the different aetiologies of NAFLD and we added IBD drug **related.**

Reviewer #3:

- **1**. We added information about hepatotoxicity of thiopurines, methotrexate, corticosteroids and 5-ASA.
- 2. Information about hepatitis C and IBD was added.
- 3. Information about IgG4-cholangiopathy and IBD was included.

Reviewer #4:

- We added some suggestion about hepatobiliary complications previously omitted.
 Cholangiocarcinoma, HCC, portal hypertension and liver malignancies
 risks cholangiocarcinoma and hepatocellular carcinoma.
- 2. We modified the incorrect of alkaline phosphatase is not AF but ALP (Alkaline Phosphatase)
- 3. We modified abbreviations (p.10 BMI , p.11 HTN, p.13 FA, Fig.1 ALF, Table 1 TPMT)

Re-reviewer:

As the reviewers' requirements have been addressed, the manuscript can be published

Thanks for your comments.

Hopefully the manuscript has improved according to your suggestions.

Kind regards,

Paulina Nuñez F MD

On behalf of all co-authors

Rodrigo Quera, Lorena Castro, Diego Jara, Gabriel Mezzano and Fabiola Castro,