

We would like to thank the reviewer for their detailed comments and suggestions for the manuscript. We believe that the comments have identified important areas which required improvement. After completion of the suggested edits, the revised manuscript has benefitted from an improvement in the overall presentation and clarity.

Below, you will find a point by point description of how each comment was addressed in the manuscript: original reviewer comments in regular typeface, responses in boldface.

Reviewer 1

Pancreatitis is an important problem in IBD patients. Sometimes it is difficult to differentiate the etiology of pancreatitis (IgG4 AIP or extraintestinal manifestation). Serum IgG4 levels are not always helpful. It is better to add a table for differential diagnosis of drug induced, extraintestinal manifestation or AIP. Generally this is well written paper. also meselamine is another rare cause of pancreatitis. If drug induced pancreatitis occurred. These drugs must not use for treatment again.

- we have added a table (Table 1) for the differential diagnosis between AIP, Drug-induced pancreatitis and Idiopathic IBD-associated pancreatitis, as suggested.

- “Drug-induced pancreatitis” section has been extended.

Reviewer 2

The minireview of Antonini et al. discusses an important aspect of IBD, namely the presence of pancreatitis in IBD patients. The review is well written, however, some points need revision: - in case of drug-induced pancreatitis, it is important to underline that pancreatitis may develop anytime during the treatment not just at the beginning.

- we highlighted this concept in the key issues: “However drug-induced pancreatitis could develop any time during the course of the treatment and it is not always easy to establish a direct correlation between resolution of symptoms and drug withdrawal. Re-challenge test may be attempted in some cases of mild pancreatitis, as defined according to the CT severity index”

- in case of asymptomatic hyperenzymemia it is important to mention that in case of absent urinary amylase the source of elevated amylase is the salivary glands (hyperamylasemia, affecting 1-2% of the population). The elevated lipase is a question of debate. Lipase is known to be pancreatitis-specific, but sometimes it can be found elevated without any symptoms.

- we have added this sentences in the text: “Moreover, it must be considered that in case of absent urinary amylase the source of elevated amylase could be the salivary glands. Even lipase, that is known to be pancreatitis-specific, sometimes can be found elevated without any symptoms.”

- In the Pathophysiology section, AIP and IBD-associated pancreatitides are confusely presented. The authors should define exactly the diagnostic criteria of type I. and II. autoimmune pancreatitides, from which type II. usually associated with IBD (especially with Crohn's disease), while type I. overlaps several autoimmune disorders, but usually not with IBD. Type I and II. AIP belongs the IgG4-related diseases. Also, IBD-associated pancreatitides must be other than AIP. (like drug-induced, or caused by IBD-associated mesenterial vasculitis. This latter also need discussion).

We have added in the “Pathophysiology” section:

- a presentation of autoimmune pancreatitis (AIP). Moreover a table is added (Table 1) for the differential diagnosis between AIP, Drug-induced pancreatitis and Idiopathic IBD-associated pancreatitis.

- a comment on mesenteric vasculitis: “Finally, a possible coexistence of IBD with other autoimmune condition, like lupus mesenteric vasculitis, should be considered in case of pancreatitis, since IBD predominantly affects gastrointestinal tract, while lupus mesenteric vasculitis may also present extraintestinal involvement such as pancreatitis.”

After major revision, I suggest to accept the manuscript for publication

Reviewer 3

This review is well-written. Several points should be added. Treatment of pancreatitis should be described, including infliximab for idiopathic pancreatitis with IBD.

- we have added in the text: “In most cases, AP in IBD patients are mild. The management should be the same of that in the general population, and involves supportive care with fluid therapy, electrolyte replacement, pain control, and nutritional support. Treatment of active IBD in a patient with AP could be challenging because most of the drugs used for IBD (including total parenteral nutrition) can result in exacerbation of pancreatitis. A case of successful use of Infliximab for the treatment of idiopathic AP in a young male patient with a severe active Crohn’s disease has been reported”.

Pediatric aspects of pancreatitis and anatomical abnormalities of biliary and pancreatic ducts should be added.

- we have added specific pediatric aspect in the “Introduction” section. Moreover, in the review there are sentences regarding both adults than children. Duct system abnormality in IBD is explained in the manuscript.