Reviewer’s report

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

Version: 0 Date: 15 Jun 2018

Reviewer: Armand Abergel

Reviewer's report:

The study of Fousekis et al. evaluates the frequency of liver, biliary and pancreatic diseases in patients with IBD.
This is a retrospective study conducted in a tertiary center from Greece

Major comments:
This is a retrospective study from a tertiary center and has the drawbacks of this kind of study: selection bias (tertiary center) and classification bias (quality of the data in a retrospective data)

There is no new information but there are interesting results about the epidemiology of drug induced liver and pancreatic injuries (DILI and DIPI). I think, you should give more details on these 2 populations and less on biliary diseases (see below)

To improve the quality of the manuscript, we need more information on the way the diagnosis was affirmed as drug induced injury is an exclusion diagnosis.

It is necessary to use standardized definitions. For example use the criteria of Aithal et al. (Clinical pharmacology & Therapeutics 2011) for DILI and Badalov et al. for DIPI (Clin Gastroenterol Hepatol 2007)

How did you evaluate the causality? Roussel Uclaf Causality Assessment Method for DILI?

Can you give a clear message to the readers: when do they have to stop for example azathioprine when ALT is increased? ALT > 3N or 5N?

Some studies have shown that DILI with azathioprine is cytolytic in roughly in one third of the patients, cholestatic 1/3, mixte 1/3. Did you observe a cholestatic injury?

DILI by AZA can be dose dependent or dose independent, did you observe the 2 types?

For steatosis, do you have information on BMI and the metabolic syndrome (waist size, lipids, glycemia, hypertension). Is steatosis nowadays associated with the activity of the disease or denutrition or metabolic syndrome?
How many patients had excessive consumption of alcohol?

Use also standardized epidemiological words as person-years when you give results of incidence

How do you explain the low number of PSC? When did your center started to use biliary MRI?

Minor comments:
Page 5, lane 23; several patients underwent imaging evaluation: how many? This is a selection bias. Then the frequency of biliary lithiasis has a very limited interest.

Page 6
lane 10: I think Table 1 does not add information
lane 16: The most "a word is missing" were males
lane 26: did you look for thrombophilia?

Page 7
Lane 8: this message is confusing as amylase should not be tested if the patient has no abdominal pain
Lane 18: what was the interval for sulfasalazine
Lane 21: You use ALT > 2 ULN, what are the percentage of patients with ALT > 3 ULN, 5 ULN and Hy's Law?
Lane 27: please say clearly that the patient received both drugs for 2 months and that azathioprine was started 6 months before methylprednisolone

Page 8
Lane 2: What was the value of HBVDNA and ALT in the second patient with reactivation?
Lane 24: associated instead of correlated

Page 9
Lane 3: in patients with PSC
Lane 8: did you observe common bile duct lithiasis?
Lane 15: can you comment on differential diagnosis of DIPI as autoimmune pancreatitis (IgG4) and familial pancreatitis? Other causes like duodenal inflammation……
Lane 18: viral hepatitis should move to lane 9
Lane 21: use the definitions of the EASL (2017 recommendations)

Page 10
Lane 18: same comments as page 7, lane 21

Page 13
Complete the last reference please

Page 16
The table does not add information

Pages 17 and 18
The title is too long
Page 21
% with ALT > 3N, ALT > 5N
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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