

Clinical implications of diabetes in chronic liver disease: diagnosis, outcomes and management. Current and future perspectives

Manuscript ID 72259

Dear Editors,

We deeply appreciate the revision made to our manuscript by reviewers and editors of the journal and appreciate the valuable comments of reviewers. We hereby wish to answer to the reviewers' comments point by point.

Modifications to the original text and added information are highlighted in yellow.

Reviewer number 1:

The review was well organized and written, especially the the current treatment measures and procedures were better summarized. If the author can enhance some related literature in 2021, the paper will be more ideal. 1) Hepatogenous diabetes: Diabetes is associated with poor short-term prognosis in patients with hepatitis B virus-related acute-on-chronic liver failure. *Hepatol Int.* 2021 Oct;15(5):1093-1102. 2) Mechanism: Is insulin the preferred treatment in persons with type 2 diabetes and liver cirrhosis? *BMC Gastroenterol.* 2021 Jun 12;21(1):263. Over time evaluation of glycaemic control in direct-acting antiviral-treated hepatitis C virus/diabetic individuals with chronic hepatitis or with cirrhosis. *Liver Int.* 2021 Sep;41(9):2059-2067. Dipeptidyl peptidase-4 inhibitors may accelerate cirrhosis decompensation in patients with diabetes and liver cirrhosis: a nationwide population-based cohort study in Taiwan. *Hepatol Int.* 2021 Feb;15(1):179-190 3) Treatment: Management of diabetes mellitus in patients with cirrhosis: An overview and joint statement. *Diabetes Metab.* 2021 Aug 4;47(5):101272. 4) Diagnosis--liver stiffness: Advanced Liver Fibrosis Is Common in Patients With Type 2 Diabetes Followed in the Outpatient Setting: The Need for Systematic Screening. *Diabetes Care.* 2021 Feb;44(2):399-406. High Prevalence of Advanced Liver Fibrosis Assessed by

Transient Elastography Among U.S. Adults With Type 2 Diabetes. *Diabetes Care*. 2021 Feb;44(2):519-525.

Answer : We deeply appreciate the reviewer's comments regarding our manuscript. We agree with the reviewer that the inclusion of publications made in 2021 could further enrich the text information. We have followed his/her suggestion by reviewing the list of proposed publications. After a careful analysis of the documents we have decided to incorporate 4 references considering them relevant based on the core topic of our text. We have also made a brief comment on its content in the text. The articles that we did not include in our manuscript did not provide more information than our text already contained.

Reviewer number 2:

The review "Clinical implications of diabetes in chronic liver disease: diagnosis, outcomes and management. Current and future perspectives". The title reflects the essence of the manuscript. The abstract summarizes and reflects the work described in the manuscript. Key words reflect the essence of the manuscript. The manuscript is devoted to the problem of the comorbidity of diabetes mellitus and liver cirrhosis. At the same time, diabetes is a risk factor for the development of liver cirrhosis, and cirrhosis is a diabetogenic disease. In recent years, research has intensified on various aspects of the association of the two pathologies. However, there is still not enough data, so this review is devoted to relevant topics. The review reflects data on epidemiology, pathophysiology, NAFLD and DM, HCV and DM, clinical manifestations of DM in LC, hepatogenous diabetes, complications, and management of DM in LC: lifestyle, diet, non-insulin agents, etc. At the end, it is concluded that based on the arguments presented in this review, it is time to classify LC-associated DM into T2DM and HD in order to standardize clinical research studies, which will make it possible to evaluate separately their impact on outcomes

of LC patients. It is also urgent to determine standardized therapeutic guidelines for these vulnerable patients. Moreover, difficult and difficult patients should be treated by a multidisciplinary team. The article analyzes data from 117 authoritative sources, the review is well illustrated - 3 figures and 5 tables. The manuscript is presented coherently, concisely; style and language are clear and accessible. Conclusion. Due to the high relevance of the presented review, well-written material, clarity of style and clearness of the data, this review can be recommended for publication without changes.

Answer: We deeply appreciate the reviewer's kindly favorable comments. We have done our best to get a good item. We are certain that it will be of interest to readers of the journal.