



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 54800

Title: Post-transplant diabetes mellitus and preexisting liver disease - a bidirectional relationship affecting treatment and management

Reviewer's code: 00000663

Position: Peer Reviewer

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: Croatia

Manuscript submission date: 2020-02-22

Reviewer chosen by: Jin-Zhou Tang

Reviewer accepted review: 2020-03-27 15:58

Reviewer performed review: 2020-03-29 10:27

Review time: 1 Day and 18 Hours

| | |
|---------------------------------|---|
| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish |
| Language quality | <input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| Conclusion | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection |
| Re-review | <input type="checkbox"/> Yes <input type="checkbox"/> No |
| Peer-reviewer statements | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No |



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SPECIFIC COMMENTS TO AUTHORS

A well-detailed analysis of the intertwining relationship between diabetes and advanced liver disease in pre- and post-transplant patients. The authors dedicate most of their interest to NAFLD and post-NAFLD area, which is reasonable nowadays considering the importance and burden of disease. The references are generally up-to-date in a fast evolving area. I have only minor comments to increase interest and readability. • Although NAFLD takes the stage, there is scarce consideration to problems with HCV, no mention of the problems related to HB virus (mainly in post-transplanted patients) or in other less common diseases (e.g., hemochromatosis). A few lines might be included to expand these areas. • In particular, post-transplant weight gain remains a problem for most patients, and the reasons for it – and treatment, including psychological distress and post-survivor euphoria – might be more extensively dealt with. • There is no mention of the problems associated with pre-transplant bariatric surgery, an issue which might become crucial in next years, considering the role of bariatric surgery in curing and preventing diabetes. • The role of TZD in the management of liver disease should be extensively reconsidered (see and quote: Yen, Fu-Shun et al, Liver Int. 2020 Jan 21. doi: 10.1111/liv.14385.) • Figure. There is a lot of unused space and character is small. Consider redrawing



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 54800

Title: Post-transplant diabetes mellitus and preexisting liver disease - a bidirectional relationship affecting treatment and management

Reviewer’s code: 00058696

Position: Editor-in-Chief

Academic degree: MD

Professional title: Doctor, Professor

Reviewer’s Country/Territory: United States

Author’s Country/Territory: Croatia

Manuscript submission date: 2020-02-22

Reviewer chosen by: Jin-Zhou Tang

Reviewer accepted review: 2020-03-27 11:48

Reviewer performed review: 2020-03-30 20:59

Review time: 3 Days and 9 Hours

| | |
|---------------------------------|---|
| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish |
| Language quality | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| Conclusion | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection |
| Re-review | <input type="checkbox"/> Yes <input type="checkbox"/> No |
| Peer-reviewer statements | Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No |



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SPECIFIC COMMENTS TO AUTHORS

I have carefully read this new minireview. My major questions are summarized below:

1. There is no description of the methods used by the authors to obtain/collect/sort the information that they present herein. 2. Do the authors intend to describe only treatments that involve prescription medications in this minireview? If yes, then the Title should be changed and the authors could consider “affecting pharmacologic treatment” as the end of their Title. 3. This manuscript is presently difficult to read because the authors have not summarized important concepts that are being discussed in either Tables or Figures. 4. The authors should spell out more terms rather than use non-standard abbreviations. LT for liver transplantation should not be abbreviated (it usually means long term). IR to a gastrointestinal physician refers to “Interventional Radiology”, etc. 5. Please use a spell check in your word processing program. (see last sentence in Abstract: “patophysiology” should be pathophysiology and “oxydative” should be oxidative. 6. In “Non-alcoholic fatty liver disease (NAFLD)”, paragraph 4 starting with “Obesity and insulin resistance”: the authors state “it has been recognized that hepatic inflammation and fibrosis can exist without steatosis”; this sentence needs to be rewritten or clarified since every gastrointestinal physician knows that the authors could be referring to, for example, chronic Hepatitis C or chronic Hepatitis B. In this section, the authors provide no overview of the important information about treatment of NASH-induced cirrhosis in individuals with obesity by a joint Vertical Sleeve Gastrectomy-Liver Transplantation approach. 7. In “Diabetes mellitus and NAFLD - cardiovascular disease equivalents?”, in paragraph 2, the authors discuss an “intimate relationship”; are the authors referring to obesity-dependent or obesity-independent relationships? 8. In “Diabetes mellitus and liver cirrhosis”; sentence 1: the usual considered sequence is inflammation, necrosis, and



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fibrogenesis. In paragraph 2, the authors use the abbreviation NAFL but do they mean NAFLD? In the last paragraph of this section, the authors discuss “death rates are higher in cirrhotic patients with DM”. The authors should expand upon whether they are referring to controlled or to poorly controlled type 2 diabetes, since there is long-standing literature examining neutrophil function in the presence of chronic hyperglycemia. 9. In “T2DM treatment in the context of NAFLD, paragraph 2: “weight losing effect” should be weight losing effect and “ramdomized” should be randomized. The authors make no mention of the potential for weight loss programs as potential therapy (physicians have additional options available other than prescription medications). 10. In “GLP-1RA in the treatment of NAFLD”, paragraph 2, sentence 2: “achieving normalization of ALT”; this reference is from 2014. The more recent American College of Gastroenterology guidelines for “normal” levels of transaminases reduced the “normal” levels of ALT and so the authors should either consider the term reduction rather than “normalization” or provide information supporting declines in ALT levels to within the newer normal ALT range. In paragraph 4, the authors state that “it shows superiority over liraglutide in terms of weight loss”: the authors should either define the term “superiority”, or let the reader know that they are actually referring to a difference in weight loss of 2 to 3 lbs. (which is unlikely to be of any clinical significance for gastroenterologists treating individuals with NASH). 11. In “Post-transplant diabetes mellitus in LT patients”, in paragraph 2 there is a very long and very complex sentence; it might be better understood if the authors place a comma between “cardiovascular mortality” and “this therapeutic option has its merits”. In paragraph 4, the authors mention “are gastrointestinal (GI) [why is this abbreviation added here?] side effects”; authors please specify these GI side effects.