

ANSWERING REVIEWERS



January 4th, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6872-edited.doc).

Title: Focus on Alcoholic Liver Disease: from nosography to treatment

Author: Letiția Adela Maria Streba, Cristin Constantin Vere, Costin Teodor Streba, Marius Eugen Ciurea

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6872

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) 00722706

Reviewer comment:

A well written work, even for non-experts in liver pathology.

Thank you for your comment! We are glad this paper served its purpose, as we believe a Topic Highlight should be as clear for a general practitioner as for an expert in the field of hepatology.

(2) 02539873

Reviewer comments:

GENERAL COMMENTS

The manuscript represents a very brief review of literature describing different aspects of alcoholic liver disease (ALD). It highlights a wide spectrum of issues, which are relevant for the disease epidemiology, its global burden, pathogenesis, and treatment, which focused researchers' attention during the last decade. It is a pity that many vital issues are not discussed in details, but I understand that the main goal of the manuscript, as a Topic Highlight, was only to signal a need of ALD update coming from recent reports of the world literature.

Thank you for your comments. Indeed, the purpose of this Topic Highlight was to briefly acknowledge some of the major points and controversies in recent literature concerning ALD, while addressing a broad audience and signaling the need for an update.

SPECIFIC COMMENTS

Page 5-

• Having described risky alcohol intake, the Authors should mention that according to the present knowledge there is no safe minimum for beverages containing ethanol;

Thank you for your suggestion. The point has been addressed and a revision has been made according to the suggestions of the reviewer.

• "The most important environmental risk factors of ALD development are (...) type of alcoholic beverage..."??? - Whether the type of alcoholic drink consumed influences the risk of ALD is still unclear;

Thank you for pointing this out. We have now altered the text to better reflect the uncertainty of this correlation, as well as adding the data required for justifying our statements. All references supporting the ideas were inserted and properly cited.

- *Higher susceptibility to ethanol toxicity observed in females is not associated only with sex hormones. Other factors are important as well. Please indicate them e.g. gastric metabolism, gastric and hepatic dehydrogenases, body composition;*

Thank you for your suggestions, we have made the necessary additions as per your recommendation and highlighted them in the manuscript body. All references were properly cited.

- *"The pathogenesis of ALD involves many simultaneous pathways, dependent on disease stage [30]."- what do you mean by dependent on disease stage ?*

Thank you for your remark. To avoid all misunderstandings, we have eliminated the statement from the text. The main idea is clearly explained by the remaining paragraphs, without the use of any debatable phrasing.

Page 6-

- *"Increased of gamma glutamyltransferase (GGT) level indicate heavy alcohol use and liver injury [4,30]."* Rather may indicate, because it is not specific;

Thank you for your suggestion, we have now revised the text accordingly.

- *Novel prognostic scoring systems are now available to grade the severity of AH and assess its prognosis as early in the disease course as possible. Although the Discriminant Function is the most established and widely used in clinical trials, it lacks specificity and (together with Child- Turcote- Pugh score) is the oldest one. More recent systems i.e. Model for End-stage Liver Disease (MELD), the Glasgow Alcoholic Hepatitis Score (GASH), Age, bilirubin, INR and creatinine (ABIC), and the Lille score have been introduced to identify severe AH with greater accuracy. Authors should address this issue.*

Thank you for this suggestion, we found it most useful. Revision has been made according to the suggestions of the reviewer. Therefore, we considered it was necessary to introduce a new chapter ("Prognostic scoring systems in alcoholic hepatitis") in our manuscript. Additionally, we have added a table with prognostic scoring systems in alcoholic hepatitis. We have of course added all necessary references and properly cited them in text.

Page 7-

- *The goal of ALD therapy is to diminish steatosis?*

Thank you for pointing it out. Revision has been made according to the suggestions of the reviewer by eliminating the wrong statement from the text.

- *In the treatment of ALD, not only vitamin administration is required, but first of all protein supplementation is essential for nutritional support. The role of antioxidants has not been proven effective ("controversial" seems not to be appropriate word in this context).*

Thank you for your suggestion! Revision has been made according to the suggestions of the reviewer. We have added two statements, along with the necessary references properly cited.

Page 9

- *Please, be consistent in presenting page numbers in references, correct and unify them. : e.g. 2. Am J Gastroenterol. 2010; 105(8):1782-1787. and 3. Lancet 2009; 373:2223-33.*

- *In addition following references should be corrected: 19, 30, 55, 57, 59, 61, 62.*

Thank you for your remark. References and typesetting were corrected, along with introducing a number of references when we covered all previous points. Style should now be consistent through the manuscript.

Minor language polishing is required

Thank you for pointing out several minor language mistakes. We have thoroughly revised the

grammar and phrasing and with the expert help of a native English speaker have eliminated the minor mistakes that were made.

Conclusion:

The manuscript should be revised according to above presented hints and may be reconsidered after minor changes.

Thank you for your comments, we found them extremely useful when revising our manuscript. Hopefully we have addressed all the points raised in a satisfactory manner and the manuscript has now reached the necessary level for publication. Please find all our revisions marked in the submitted manuscript.

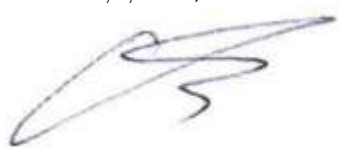
3 References and typesetting were corrected according to the editorial suggestions.

All editorial concerns were addressed:

- We accepted the Running Title presented in the edited manuscript: *Focus on Alcoholic Liver Disease*
- We have added the telephone and fax numbers according to editorial requirements
- We have written a Core Tip and inserted it in the manuscript file
- We have unified the style of all references and added the PubMed accession numbers as well as the DOIs, where available.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



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