

**INVITED REVIEW ID 00188507**

Editor in Chief, *World Journal of Gastroenterology*

Lian-Sheng Ma, President and Company Editor-in-Chief

Feb 16, 2015

Dear Editors and Reviewers,

Thank you and the reviewers for a thorough review of our manuscript entitled “**Advances in understanding and treating liver diseases during pregnancy: Review**” (Manuscript number 16529, **INVITED REVIEW ID 00188507**) by Hiroyuki Abe, Hirokazu Kawai, Hiroteru Kamimura, Yuji Kobayashi, Minoru Nomoto, Yutaka Aoyagi, Shuji Terai, and myself. The thoughtful comments from the reviewers are greatly appreciated. In preparing for revision, we have carefully studied reviewers’ comments and incorporated many of their suggestions into the revised manuscript. For your convenience, we have highlighted the changes made in blue. We hope this revised manuscript is now acceptable for publication in *World Journal of Gastroenterology*.

We declare that this work is original, the manuscript is not under consideration by other journals. All authors approved the contents submitted. We look forward to hearing from you at your earliest convenience.

Thank you for your consideration.

Sincerely yours,

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Dear Reviewers:

Thank you very much for your thoughtful comments and suggestions. In preparing the revision, we have carefully studied your comments and incorporated many of your suggestions into the revised manuscript. The following are our point-by-point responses to your comments/concerns. For your convenience, we have highlighted the changes made in blue.

**Title: Advances in understanding and treating liver diseases during pregnancy: Review** (Author ID 00188507)

**Author:** Kenya Kamimura, Hiroyuki Abe, Hirokazu Kawai, Hiroteru Kamimura, Yuji Kobayashi, Minoru Nomoto, Yutaka Aoyagi, Shuji Terai

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 16529

**Editor**

*Based on the reviewers' comments, your manuscript may be accepted for publication if the suggested revisions are incorporated and the subsequent re-review is positive.*

**Response:** We are grateful to the editor for the positive comments and for recognizing the significance of our work.

1. *When you send back, please provide the format of doc, not the format of PDF.*

**Response:** We have submitted word doc. files.

2. *Please provide language certificate letter by professional English language editing companies*

**Response:** We have attached it.

3. *In order to attract readers to read your full-text article, we request that the first author make an audio file describing your final core tip. This audio file will be published online, along with your article.*

**Response:** We have attached it.

4. *Please put the reference numbers in square brackets in superscript at the end of citation content or after the cited author's name.*

**Response:** We have corrected them.

5. *Please add references.*

**Response:** We have added it.

6. *Make Table 1A and Table 1B into Tables 1 and 2, or combine into one table. o graphics, boxes, or embedded tables. Please provide Word (preferred), Excel format.*

Response: We have modified and added word doc. file.

### **Reviewer #1**

1. *Title, running title and thereafter in the manuscript. Consider “..... liver diseases during pregnancy”*

Response: We have modified the title and running title.

2. *Introduction. It could be useful to add one or two paragraphs with brief description of normal and physiological liver and gall bladder changes during normal pregnancy, including laboratory values.*

Response: We agree with the reviewer. We have added the paragraph in Introduction. (p4, line 2-6).

3. *Main text. Consider presentation of the pregnancy-related liver diseases in time-related order in which these abnormalities can be seen during pregnancy. Namely, during the first, second and finally during the third trimester.*

Response: We agree with the reviewer. We have significantly modified the order of presentation according to the period in which the diseases can be seen. With this modification, the order of the references has also been modified.

4. *Page 9. ICP section, last paragraph. Clarify that ICP resolves after delivery and "often" recurs in subsequent pregnancies.*

Response: We have modified the description.

5. *The review is concentrated on liver disease peculiar to pregnancy. Consider inclusion of a chapter “Pregnancy in pre-existing liver disease” (chronic viral hepatitis, autoimmune and cholestatic liver diseases, metabolic liver diseases, liver tumors in pregnancy and liver transplantation and pregnancy).*

Response: We have added the descriptions in the paragraph of “PRE-EXISTING or CO-INCIDENT LIVER DISEASE DURING PREGNANCY”.

6. *Clarify that lamivudine, adefovir, entecavir and interferon are drugs of pregnancy category C and should be used only if the benefit for mother and fetus clearly outweighs the risk, while telbivudine and tenofovir are pregnancy category B, thus should be preferred if anti-HBV treatment is indicated before delivery. Also, d-penicillamine is pregnancy category D and several abnormalities have been reported in children, whose mothers were taking this drug during pregnancy (Yalaz M et al. Minerva Pediatr. 2003 Dec;55(6):625-8, Hanukoglu A et al. J Pediatr. 2008 Dec;153(6):864-6) .*

Response: We have added the description in the paragraph.

### **Reviewer #2**

*More emphasis and some more information should be provided for the management of pre-existing liver disease.*

Response: We have added the descriptions to provide the information regarding the management of

pre-existing liver disease.

### **Reviewer #3**

*Authors reviewed recent advances in understanding and treating liver disease in pregnancy. Manuscript is well-written. This information will contribute to physicians for diagnosis of disease and optimum management of patients.*

**Response:** We are grateful to this reviewer for the positive comments and for recognizing the significance of our work.

- 1. Authors described the pre-existing or co-incident liver disease during pregnancy. As author mentioned that pregnancy itself causes significant changes in physiological conditions, effects and treatments on pre-existing liver disease during pregnancy is also important. Please describe this section more precisely. It is helpful for readers.*

**Response:** We agree with the reviewer. We have added the description in the paragraph.

- 2. Is it necessary for acknowledgments to Enago? It is English language editing company.*

**Response:** We have removed the sentence.

As well as the points shown above, references and typesetting were corrected.