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Jin-Lei Wang, Director, Editorial Office  
Baishideng Publishing Group Co., Limited

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 4035-revised.doc).

Title: LIVER DISEASES IN PREGNANCY: DISEASES UNIQUE TO PREGNANCY

Author: Khulood T. Ahmed, MD; Ashraf A. Almashhrawi, MD, MSc; Rubayat N. Rahman, MD, MPH; Ghassan M. Hammoud, MD, MPH; and Jamal A. Ibdah, MD, PhD\*

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 4035

The manuscript has been updated.

(1) Format has been updated as per revision policies for mini-reviews.

(2) Revision has been made according to the suggestions of the reviewers as follows:

**Reviewer 00009225:**

We appreciate the reviewer's interest in our manuscript.

1. *OHSS: Ovarian hyperstimulation syndrome:*

Authors' response: The review is mainly directed toward clinical entities that happen during pregnancy. Although OHSS fits in the general scheme of liver diseases in women, we consider this syndrome as an iatrogenic disorder that happens in women who are not pregnant and not unique to pregnancy. Therefore we have not included in this review of liver diseases unique to pregnancy.

2. Need to elaborate more on the role of elevated uric acid in the diagnosis of aflp:

Authors' response: In response to the reviewer's comment, we have added a paragraph in the revised manuscript to discuss the role of elevated uric acid in the diagnosis of AFLP.

3. Need to indicate in the section of icp that bile acid levels above 40 indicate delivery at week 37:

Authors' response: In response to the reviewer's comment, we have added a paragraph in the ICP section of the revised manuscript to address the reviewer's concern regarding bile acid levels.

**Reviewer 00005855:**

1. This is a concise and comprehensive review over the liver diseases unique to pregnancy. The reviewer considers this review provides useful information to the readers of The Journal. There are a few points to be addressed.

Authors' response: We appreciate the reviewer's interest in our manuscript.

2. The authors mentioned the impaired maternal of fetal mitochondrial fatty acid oxidation as an underlying mechanism of hyperemesis gravidarum, HELLP syndrome, and acute fatty liver of pregnancy. This is somewhat confusing, and this need additional detailed explanation or different roles among these diseases may be presented:

Authors' response: We agree with the reviewer comment. We have made changes in the revised manuscript to clarify the role of mitochondrial fatty acid oxidation impairment on maternal liver disease. A text was added to describe the hypotheses for development of hyperemesis gravidarum including potential role of mitochondrial fatty acid oxidation disorders with appropriate reference to the literature. We have also added details to the revised manuscript to expand on the role of impaired fatty acid oxidation in development of acute fatty liver of pregnancy and the underlying hypothesis. Reference to the studies that established the link between fetal fatty acid oxidation defects and acute fatty liver disease of pregnancy were included in the revised manuscript. Figure 1 was deleted as it was somewhat confusing.

3. In the Clinical presentation section of HELLP syndrome, the authors described that preeclampsia, HELLP syndrome, and acute fatty liver of pregnancy share similar presentations. This description should better come to the same section for acute fatty liver of pregnancy, since the latter comes to the end among these three diseases:

Authors' response: The paragraphs were rearranged in the revised manuscript as the reviewer suggested. AFLP section was moved before Preeclampsia and HELLP syndrome in response to the reviewer's suggestion.

4. Also the Table 2 should come to the end (after the original Table 3):

Authors' response: The Tables were rearranged to keep parallel with the text flow as the reviewer suggested.

**Reviewer 00003629:**

We appreciate the reviewer's interest in our manuscript.

1. The approach to liver-related problems unique for pregnancy is very superficial. Authors should expand more on the pathogenesis and management of the mentioned conditions and approach the whole subject in a more critical mind:

Authors' response: In response to the reviewer's concern, we have added more to the pathogenesis discussion as mentioned above. We have written this review as an overview of liver diseases that are unique to pregnancy to help clinicians reach a diagnosis and have a general outline for management of the clinical conditions presented, yet provide a concise description of pathogenesis. Nevertheless, we agree with the reviewer that expansion of the pathogenesis sections would strengthen the manuscript and we have done so in the revised manuscript. The management outlines presented should provide valuable insights in how to approach each entity without delving in details that can be attained from other sources (including the references in this review) once the clinician forms a clear roadmap for the diagnosis and management.

2. Abstract: It is very vague. Authors should mention the medical conditions they review in the article, grade their frequency and severity and make the Abstract more informative:

Authors' response: We have made changes in the abstract as the reviewer suggested.

3. Hyperemesis gravidarum, Management: What is the effect of HG on fetal mortality?

Authors' response: We have added a paragraph to address the effect of HG on fetal mortality.

4. Intrahepatic cholestasis of pregnancy [IHC], 2nd sentence from bottom: Consider revision. As it stands now it gives the impression that IHC is a predisposing factor for hepatitis C, cirrhosis and gallstones:

Authors' response: We have made changes in the sentence to clarify in response to the reviewer's comment.

5. IHC; Pathogenesis: Please give more information on this subject:

Authors' response: We have added a paragraph to give more information as the reviewer suggested.

6. IHC; Clinical presentation, 5th line from bottom): What is the level of "significant hyperbilirubinemia"?

Authors' response: We have added a sentence to address the reviewers question, with appropriate references.

7. HELLP; Management: Please make clear whether "bed rest" means staying at home, admitted in a hospital ward or ICU:

Authors' response: We have added a paragraph to clarify with appropriate references, as the reviewer suggested.

8. Hyperemesis gravidarum, 3rd line from top: Move ref #1 to the end of sentence:

Authors' response: Reference was moved as suggested.

9. Hyperemesis gravidarum, last line of page: "Erythrocytosis" instead of "polycythemia"?

Authors' response: Change of words was made as suggested.

10. Eclampsia; Pathogenesis: Armed Forces Institute of Pathology:

Authors' response: Suggested changes were made.

(3) References and typesetting were corrected

We believe that the comments made by the reviewers have greatly improved this mini-review. We have made all necessary changes as suggested.

Thank you again for publishing our mini-review in the *World Journal of Gastroenterology*.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Jamal A. Ibdah". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

Jamal A. Ibdah, MD, PhD