Peer Review File

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This is a commentary about the new ACOG recommendations regarding viral hepatitis in pregnancy from a pediatric perspective. The topic is of great importance, though the commentary would benefit from improved organization, clarity and additional details. Would recommend noting in the into and/or conclusion that ACOG provides guidance for the US context, but these recommendations could be adopted worldwide for significant impact. However, resource constrained setting might not have the resources to implement the guidance.

Reply: As suggested by the Reviewer, we have now clearly stated in the Conclusion section that although ACOG guidelines are based on the United States context, these recommendations should be adopted worldwide, with possible barriers in limited resource-settings.
Changes in the text: page 10, lines 256-9

1.Table 1: Recommend adding HBV DNA level where treatment during pregnancy would be considered as clinicians may refer to this table to guide practice.
Reply: We have now specified the HBV DNA level in the Table, which has now complete data to guide clinical practice.
Changes in the text: table 1, page 1, line 3

2.Line 41: This section is regarding both management before pregnancy as well as screening during pregnancy. The sub heading should be updated. I would recommend paragraphs HBV vs. HCV (like there is now, but with improved clarity) where both pre-pregnancy management is discussed and screening or combining HBV and HCV – discussing pre-pregnancy management then screening during pregnancy.
Reply: As suggested by the Reviewer, we have re-arranged as follows the paragraph "Management before pregnancy": a short introduction on management before pregnancy and screening during pregnancy, subheadings on HBV and HCV. We believe that it now clearer to the reader.
Changes in the text: pages 2-3-4, lines 41-78

3.Lines 46-47: "as not effective intervention to reduce the risk of transmission…". This phrase is not clear. Also, the sentence is long and would benefit from being 2 sentences. Also, the reason the pre-pregnancy treatment is challenging is that there is not a clear clinical pathway for HBV/HCV screening and treatment in routine care, like there is in pregnancy. Healthy women of reproductive age do not often present for viral hepatitis screening.

Reply: We split the sentence in 2 and rearranged the phrase to improve clarity. We underlined in the introduction section of the paragraph "Management before pregnancy" that management in pre-pregnancy is challenging and complex.

Changes in the text: pages 2, lines 42-6

4.Lines 50-53: Clarify that ACOG recommends universal HCV/HBV screening during pregnancy. Also note that universal screening in pregnancy allows for accurate identification of HCV/HBV exposure and thus perinatal transmission risk. However, new HBV or HCV acquisition late in pregnancy would result in a negative screening test earlier in pregnancy and perinatal transmission. Thus, those with identifiable risk factors in pregnancy should be re-screened at delivery. Those children that are removed from the home and birth exposures are unknown, should be screened for HBV and HCV.

Reply: As suggested by the Reviewer, we have now underlined in this paragraph that ACOG recommends universal HCV/HBV screening during pregnancy and the possible limitations of screening during pregnancy for exposed newborns. We believe the paragraph is now more complete and clearer.

Changes in the text: page 3, lines 52-7

5.Lines 70-71: What year was this study regarding the low HBV birth dose.

Reply: We have now updated the data on vaccine coverage according to WHO 2022 data and changed the reference.

Changes in the text: page 4, lines 92-5

6.Lines 82-87: There are several other risk factors for perinatal transmission. Recent work by M Persad published in Obstetrics and Gynecology 2023 showing antenatal vaginal bleeding as a risk factor.

Reply: We have now expanded the paragraph and better specified risk factors for perinatal transmission according to ACOG guidelines.

Changes in the text: page 5, lines 127-33

7.Line 101: Chappell 2020 actually had 9 participants (8 participants had evaluable PK). In addition, there was a recent study of SOF/VEL PK in 10 participants that was presented at CROI 2023 https://www.croiconference.org/abstract/sofosbuvir-velpatasvir-pharmacokinetics-in-pregnant-women-with-hepatitis-c-virus/

Reply: We thank the Reviewer for these observations. We have now specified the correct number of participants for the 2020 study by Chappell *et al.* and added the 2023 abstract by Chappell *et al.* in the text and in the references.

Changes in the text: page 6, lines 146-51

8.Lines 116-117: The registry is of critical importance because it has potential to capture safety of first trimester exposures that would not be available in prospective clinical trials.

Reply: We have now added in the text the Reviewer's important observation, underlining a further significant aspect of the registry.

Changes in the text: page 7, lines 168-70

9.Lines 120-121: Utilization of DAAs in the late second and early 3rd trimester would essentially eliminate teratogenic effect as organogenesis is complete by 16 weeks' gestation.

Reply: We added this comment, with further strengthens the elements towards DAA use in pregnancy

Changes in the text: page 7, lines 174-5

10.Lines 152-153: Consider mentioning tolerability of INF-based regimens.

Reply: We have now added a sentence concerning the current low use of INF-based regimens in pediatric patients.

Changes in the text: page 8, lines 209-11

11.Lines 185-189: There is also a recommendation for HBV vaccination in pregnancy for those that are HBV nonimmune. Notably, ACOG recommends triple screen for HBV at least once. Though admittedly many centers have not adopted this recommendation.

Reply: We have now added the recommendation for HBV vaccination in pregnancy and better specified the indication for triple screening in the "Management before pregnancy" paragraph.

Changes in the text: page 10, lines 243-2. Page 3, lines 62-7