January 12, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6283-edited.doc).

Title: From Conception to Delivery: managing the pregnant IBD patient

Authors: Vivian W Huang and Flavio M Habal

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6283

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) This is a well-organized and well-written review summarizing the current information about the management of the pregnant IBD patient. One minor concern is that the authors should expand the section of IBD patients after delivery, especially during the breastfeeding phase.

Authors Response (addition of E) BREASTFEEDING section):

- As suggested, it is important to understand the interaction between IBD and breastfeeding, and therefore an additional section on the effects of breastfeeding on disease activity, effects of breastfeeding on risk of offspring developing IBD, and medication use during breastfeeding has been added to the review.

(2) IBD is a chronic illness in which the intestine, bowel, or another part of the digestive tract become inflamed and ulcerated. The disease can occur at any age, but it is most common between the ages of 15 and 30. People with IBD experience periods of severe symptoms. These are followed by periods with no symptoms that can last for weeks or years. Unfortunately, there is no way to know when a remission will occur or when symptoms will return. It is well known that people with IBD disease may have a more difficult time getting pregnant. Most patients are concerned about how IBD and the medication might affect the pregnancy. They are also worrying about whether having a baby could affect their IBD. The good news is that the great majority of women with Ulcerative Colitis (UC) or Crohn's Disease (the two most common forms of IBD) can expect a normal pregnancy and a healthy baby. This fact is already discussed in several reviews and articles. It is also well known that most of the drugs prescribed for IBD do not affect fertility, but there are a few exceptions. However, it is important to discuss pregnancy with the patient again and again because questions and informations from internet often irritate patients and the same questions are often asked the doctors. It is also well known, that some doctors feel still insecure about pregnancy and continuing therapy in IBD patients. From this aspect this is a nice review, although without new and noticeable informations, but this review gives a good overview about the topic. It is worth to be published in the journal.

Authors Response: Thank you for the comments.

- Although there is much literature, and many reviews on the topic of pregnancy in IBD,

most patients with IBD and physicians managing women with IBD still are not comfortable about their knowledge and understanding of the interaction between IBD, IBD medications, and surgery on fertility, pregnancy outcomes, and breastfeeding, and vice versa. Some reviews provide a literature review without practical points for applications. This updated review tries to provide the clinician with "action points" that they can take away after reading about the literature regarding reproduction in IBD, and we hope after reading this review, clinicians will feel more comfortable discussing the topic with their patients, to provide them with the knowledge they need to make informed decisions.

(3) Not a bad review but several similar (and better) were published during the last year. Congenital malformation risk should be discussed in more detail. An additional point is the need to delay vaccinations in an infant with an in utero anti-TNF exposure- usually the recommendation is 6 moths and not 12. Also it is less clear whether ADA should be stopped at the beginning of 3d trimester- the risk of a flare is higher then with IFX

Authors Response: Thank you for the comments, changes have been made as follows:

- The literature suggests that the congenital malformation risk previously reported in earlier studies may be due to confounders of maternal age, smoking, etc, and this has been added to the manuscript under "Conception and beyond: what is the effect of IBD activity on the pregnancy?"
- The study by Mahadevan (2013) reports that infliximab and adalimumab levels were detected in infants exposed in utero as long as 6 months, with the longer detection period being the infant who had been exposed to infliximab closest to time of delivery. However, since individual maternal and neonatal clearance of the drug may vary, it is unclear if 6 months is adequate for all cases, and individual circumstances may warrant trying to obtain infant anti-TNF levels before administering live vaccines to the infant exposed to infliximab or adalimumab in utero. The manuscript was revised to recommend avoiding live vaccinations for "at least 6 months".
- Regarding stopping ADA at the beginning of the third trimester, because it is given weekly or bi weekly, there is a possible risk of flaring that may be higher than with IFX. This has been expanded on under the Biologics medication section.

(4) This manuscript was well written and worthy of publication.
Authors Response: Thank you for the comments.

3) References and typesetting were corrected

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

Sincerely yours,

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