

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 34813

Title: Impact of Inflammatory Bowel Disease Activity and Thiopurine Therapy on Birth Weight: A Meta-analysis

Reviewer's code: 00742373

Reviewer's country: United States

Science editor: Yuan Qi

Date sent for review: 2017-06-01

Date reviewed: 2017-06-07

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The meta-analysis manuscript titled "Impact of Inflammatory Bowel Disease Activity and Thiopurine Therapy on Birth Weight: A Meta-analysis" includes nine reported raw data for meta analysis and reviewed relevant articles on the effect of disease activity and thiopurine use on the risk of low birth weight (LBW) or small for gestational age (SGA) among pregnant women with IBD. The authors found an increased risk ratio of both SGA and LBW in women with active IBD, they also found a high risk of LBW in women when using thiopurines during pregnancy but considered this may be related to the disease activity since no significant effect on LBW when adjusted for disease activity. The paper concluded that women with active IBD during pregnancy have a higher risk of LBW and SGA and should be treated. The individual impact of the IBD activity and thiopurine treatment during pregnancy to the LBW and SGA has not been systematically evaluated. For IBD activity and thiopurine use for IBD during pregnancy still remains conflict from different data. Since the significant relationship between IBD and LBW, it is

important to performed a systematic review and meta-analysis to identify the pooled effect of disease activity or thiopurine use on LBW and SGA in women with IBD. This manuscript provided the important information for this topic. The study is very well designed. The inclusion criteria of the observational studies are clear. The articles related to IBD and pregnancy are widely searched and reviewed. Study selection and data collection are reasonable and representable. The analysis methods are dependable. Concern and suggestions: * In addition to the treatment with thiopurines, is there any other treatment used to the patients? * Pregnant women with active IBD have higher neonatal LBW and SGI. These women were also treated with thiopurine. How to distinguish the outcome of higher LBW and SGI caused by active IBD or by thiopurine? * In treatment & LBW or treatment & SGA, the cases in the non-thiopurine exposure not only included the IBD active cases, but also included IBD non-active cases. As this way, it is hard to compare the effect on LBW/SGA were only by thiopurine or activity of IBD. If the authors can compare the LBW/SGA between active IBD and active IBD with thiopurine treatment, the result will be more powerful to demonstrate if thiopurine has side effects on fetal growth. * Figure 1: the figure is not clear. * In the section of Results, the last paragraph, please describe more detail for the sentence: when we only included the study that adjusted for disease activity were included, there was no significant effect of thiopurines on LBW. * The duration of IBD activity and exposure to thiopurine is not defined in the study. The reviewer consider this is a important factor related to the effects to outcomes of pregnancy.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 34813

Title: Impact of Inflammatory Bowel Disease Activity and Thiopurine Therapy on Birth Weight: A Meta-analysis

Reviewer's code: 00742054

Reviewer's country: Australia

Science editor: Yuan Qi

Date sent for review: 2017-06-01

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

Thank you for this interesting and important research! Below are my comments: - Methods, Study selection: the item 5 explains the criteria of studies that were included in this meta-analysis. I see from the text that the authors mention the "inclusion criteria was not otherwise restricted by study size, language or publication type". Does this mean that you evaluated studies in other languages as well? If yes, how did you do this as there might have been several different languages other than English. Please clarify or revise. -Results: para 3: the authors mention that "There was not a homogeneous definition of 'active disease' in the included studies". I believe it would be interesting and also important to the readers to know which definitions were used in different studies. The authors may put the definitions and related studies in a table. - Table 1 needs amendment and following information needs to be in the table: Study ID, Sample size, Study design/recruitment/study period, number of patients with/without active disease, outcomes. - Also, please put reference next to each study in the Table 1 and



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Supplementary table S2. - Supplementary Table S1 can be removed from the article as it does not add to the knowledge of the readers about the studied issues.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

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Title: Impact of Inflammatory Bowel Disease Activity and Thiopurine Therapy on Birth Weight: A Meta-analysis

Reviewer's code: 02453249

Reviewer's country: Italy

Science editor: Yuan Qi

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
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		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The authors performed a meta-analysis to investigate the effect of disease activity or thiopurine use on low birth weight (LBW) and small for gestational age (SGA) in women with Inflammatory Bowel Disease (IBD). This scientific question proposed is interesting because there are conflicting data on this topic. The structure of the manuscript is complete. The meta-analysis was conducted with guidance provided by Cochrane Handbook for Systematic Reviews and is reported according to PRISMA guidelines. Study quality and risk of bias were assessed according to the Newcastle-Ottawa Scale (NOS) guidelines. However, subjects data were not adequately described in the manuscript, the authors should provide a table with demographical and clinical characteristics of pregnant women with IBD. The source of the data is reliable, however the authors should explain more specifically the reasons of exclusion of 22 studies, and the forest plot showed in figure 4 (RR of SGA based on Thiopurine exposure) should be implemented by other relevant studies. The analysis based on only two articles is not

statistically powerful. In addition, the results of sensitivity analysis are not clear. The present meta-analysis, that included 9 studies, suggests that women with active disease during pregnancy have an increased risk of SGA and LBW in their neonates. Women on thiopurines during pregnancy had a higher risk of LBW compared with non-treated women, but when adjusted for disease activity there was no significant effect on LBW. No differences were observed regarding SGA. These results answered the proposed question and achieved the aim of the study. The conclusions of the manuscript show that the presence of active IBD during pregnancy is a risk factor for both SGA and LBW in women with IBD. Independent of disease activity, thiopurine use does not increase the risk of either SGA or LBW. We found two pertinent references using the keywords reported in the abstract that can be potentially useful for the manuscript. ("Association between maternal inflammatory bowel disease and adverse perinatal outcomes" Getahun D. 2014; "Pregnancy outcomes in women with inflammatory bowel disease--a population-based cohort study" Kornfeld D. 1997) The results of this manuscript should be considered in treatment decisions during pregnancy because they suggest that women with active disease have an increased risk of LBW and SGA.