Reviewer’s report

Title: The Role of Vitamin D in Pre-Eclampsia: A Systematic Review

Version: 0 Date: 20 Jan 2016

Reviewer: Laurie Twells

Reviewer’s report:

Thank you for asking me to review this article that reviews the role of Vitamin D in pre-eclampsia. The objective of the paper is to review the evidence that vitamin D status plays a role in the etiology and prevention of pre-eclampsia and to identify gaps in the research and therefore inform future studies and potential large scale randomized trials. I recommend this article for publication. However I would like to see more detail provided in the Methods section so that it is clear how the authors selected the studies that have been included in the current review.

The authors and the title suggest that the paper is a structured literature review and not a systematic review of the literature. If it is a systematic review than I suggest the authors use the PRISMA flowchart and checklist as well as include much more detail in the Methods Section. If the current paper is a broad level review which I think it is, then these may not be mandatory but more detail is still required in the Methods section.

General comments.

The paper is well written. The introduction presents the epidemiology of PE including its definition, prevalence, and its associated morbidity and complications as well as suggesting several hypotheses that might explain a potential link between Vitamin D and the development of PE.

The Methods section is rather short. I would like to see more detail in the Methods Section. For example details on: the search strategy used, the eligibility criteria for inclusion in the review, how the articles were screened (was there only one reviewer?). If two reviewers how were articles screened and how was consensus on inclusion reached? As well please include the numbers of articles included and excluded in Figure 1 so they are consistent with the paragraph in the Methods section. For example please clarify within the Figure the number of studies included in the current review. As it stands if 108 studies were excluded, then remaining studies would be 21 not 28 as is presented in the figure. Also how many studies were included under each final heading.

Based on the structured literature review and inclusion of studies that meet the eligibility criteria (although it is not clear exactly how many studies this is), the Results section identifies and describes the evidence for: the biological plausibility of the relationship between Vit D and PE, Vit D as an anti inflammatory agent, Vit D as a BP regulator, Vit D and its' receptor in Ca homeostasis, Vit D and its association with birth outcomes and Vit D and its positive and
negative relationship with PE. The studies are described well with many of limitations of the studies highlighted.

Based on the evidence presented, the authors suggest the relationship between vitamin D and the development of PE is inconsistent and that many studies should be interpreted with caution. This conclusion follows on from the evidence presented in the Results section. However as if often the case with observational studies, the results may be a function of poor study design and/or methods used to ascertain exposure status. In observational studies ensuring groups are similar enough to make fair comparisons is challenging making the adjusting of confounding variables important (but not always done adequately in studies). Finally measuring Vitamin D levels (the exposure) is difficult and the recommendations for dosing is not always consistent. All the above make studying the relationship between Vitamin D and PE challenging which is discussed in the paper.

Following on from the Results, the authors conclude that the evidence that Vit D plays a role in the development of PE is inconsistent and has not been demonstrated. They suggest dose response studies linking supplementation with biological mechanisms should be undertaken before large scale RCTs. I would agree with these conclusions.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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