

Review of: "Adverse Effect of Diclofenac Exposure during Pregnancy on Mother and Fetus; A Systematic Review"

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Potential competing interests: The author(s) declared that no potential competing interests exist.

Reviewer # 1 Comments

The authors, Handiso *et al* presented a review article on "*Adverse effect of diclofenac exposure during pregnancy on mother and fetus; A systematic review*" for publication in the journal 'Qeios'. Although selection of the theme is a matter of concern for pregnant women if Diclofenac or its derivatives are taken during 1st, 2nd and/or 3rd trimester(s) of pregnancy and its potential reproductive toxicity, teratogenicity and other pregnancy outcomes, but this reviewer has some concerns which are as following:

1. As mentioned in the title, the present review is based on evaluating adverse effects of diclofenac exposure on **mother** and fetus, but reports on this issue (especially on mother) have not been mentioned in the text. Therefore, authors are advised to revise the title accordingly.
2. Since clinical reports on the present issue are limited in number and space (global perspective), and contradictory with animal studies, a consistent opinion or conclusion may not be established. Occasionally animal studies are self contradictory (within animal models). Even a specific narrative on this relevant issue may not be developed in the light of availability of literature.
3. In this review, comparative data on exposure period (1st/2nd/3rd trimester or entire pregnancy), therapeutic doses, plasma concentration (C-max), genetic variability (races/population), age factor etc. were not placed on record. Therefore, a holistic approach is required.
4. The data of present study is limited with reproductive toxicity, teratogenicity/birth defects (external/internal including skeletal) and some organs study (histopathological), whereas majority of other observations like fetal, neonatal and postnatal growth and development trajectories, neurodevelopmental changes in children, neurobehavioral consequences in adolescents and other imperative features have not been taken into account. In my opinion, a systematic review needs comprehensive perspective or narration. The authors may upgrade the present review accordingly in the interest of academicians and pregnant women. The authors are advised to consult a review article of Bourke et al (2014) published in *Pharmacol. Rev.* 66, 435-365, 2014 entitled "Prenatal Antidepressant Exposure: Clinical and Preclinical Findings" for a wide-ranging review.
5. The authors presented a well defined scientific approach for search study, inclusion criteria, data collection and their synthesis, data extraction and methodological quality; and off course statistical analysis (not required in this study).
6. The deficiency of this review is very limited studies available for review, inconsistent/contradictory data on clinical and non-clinical literature and limited number of parameters/domains selected.

Overall, the present review article is not suitable for publication in the present form.

