Author’s response to reviews

Title: The effects of daily meteorological perturbation on pregnancy outcome: Follow-up of a cohort of young women undergoing IVF treatment

Authors:

Mingpeng Zhao (zhaomp@link.cuhk.edu.hk)
Haoyang Zhang (zhanghaoyang0@hotmail.com)
Tarah Waters (tarahwaters@gmail.com)
Pui Wah Chung Jacqueline (jacquelinechung@cuhk.edu.hk)
Tin Chiu Li (tinchiu.li@cuhk.edu.hk)
Yiu Leung Chan (drdcyl16@cuhk.edu.hk)

Version: 2  Date: 24 Oct 2019

Author’s response to reviews:

Dear Editor,

Thank you for arranging a timely review of our manuscript. We are pleased to know that our work is of general interest for the readers of Environmental Health. We have carefully evaluated the reviewer’s comments and thoughtful suggestions responded to these suggestions point-by-point and revised the manuscript accordingly. All changes made to the text are in tracked changes and highlighted so that they may be easily identified. With regard to the reviewers’ comments and suggestions, we wish to reply as follows:

RESPONSE TO REVIEWER #1’s COMMENTS:

1. The authors were analysing meteorological data from the start of ovarian stimulation (CYCL) only. Those using the antagonist protocol should be eligible to join the study and there is no need to exclude them, and they can be incorporated in the main group instead of in a separate subgroup. For this reason, what the authors are discussing in lines 398-401 is not quite relevant.

Response: Thank you for your comment. Although we have focused on the long protocol, we also presented description and analysis of 1 ) data of antagonist protocol patients and 2 ) data of both long and antagonist protocol patients in revised supplementary data (Supplement 1) which showed that there was no significant meteorological variations effect. It suggested that protocol may be an effect
modifier of the meteorological effect on pregnancy outcome. For this reason, we are uncertain if the two types of the protocol should be combined. Nevertheless, there were only 257 cases in the antagonist protocol compared with 860 cases in the long protocol and descriptive analysis showed their characteristics are different. The negative finding in the antagonist group could be a genuine finding or it could well be due to a Type II error i.e. the relatively small sample size or covariates we have not measured or considered. Under the circumstances, we felt it was better all-round not to combine the two groups.

We have also added a sentence in the method section to explain why the analysis of the antagonist protocol was included in the supplementary table but not in the main text “During the period of study, the majority of the stimulation protocol used was the long protocol (860, 80%). Other stimulation protocols including the antagonist protocol were not included because there were too few cases for proper statistical analysis.”

We are also grateful for the suggestion regarding the discussion in lines 398-401, which we have now revised in our revised manuscript “In additional observation, we analysed the patient underwent antagonist protocol (Supplement 1, Section A), in which the meteorological variations did not show any significant effect. Moreover, when incorporated the antagonist protocol data into the long protocol data, the meteorological effect was masked (Supplement 1, Section B). This overall result may indicate that the meteorological effect was sensitive to stimulation protocol however the exact underlying reason was not well understood.”

2. Thanks the authors for looking into the issue of missing/wrong data mentioned in the previous version. I suggest the sentence within the brackets in line 126-127 (tracked copy) be deleted as it is a bit odd to highlight individual cases of wrong electronic data entry. It is fine enough as long as they indicated that they had exercised a mechanism to verify their data, which is more important. May I clarify if the authors had already included these cases (with "incorrect or missing data" originally) back and repeated the data analysis? Have all the figures been updated accordingly?
Response: Thank you for your suggestion. We have deleted the mentioned sentence accordingly. In the previous and this revision, we have included the “incorrect or missing data” cases back and repeated the data analysis. All the figures and tables have been updated accordingly.

3. I appreciate to see the analyses based on the first IVF cycle and in patients undergoing repeated cycles separately. I think it is a very good approach to address their research hypothesis.
Response: Thank you for your appreciation. Your comments do increase the quality of our manuscript.

4. Line 302 of the tracked copy: "7th to 9th months" can be deleted; I think the authors just mean July to September.
Response: Thank you for pointing out this. We have deleted accordingly.

5. Lines 314-315 of the tracked copy: "The proportion of this subgroup of patients was balanced in both clinical and laboratory data". Please explain more clearly what does this sentence mean.
Response: Thank you for your comment. We have explained more in the revised manuscript “The distributions of both clinical and laboratory data of the subgroup population among four seasons were balanced.” (line 314-315 of the tracked copy)

6. Lines 316-317 of the tracked copy: "the pregnancy probability increased during CYCL to ER to or OR and OR to ER" - meaning not clear.
Response: Thank you for your comment. We have revised the sentence to make it clearer “The analysis of meteorological variation (Figure 3) shows, that in this subgroup of patients, the pregnancy
probability was positively associated with the average temperature form CYCL to OR and OR to ER.”
(line 316-317 of the tracked copy)

7. Table 4: Please define what is the "subgroup" referring to here. The caption of the table should be self-explanatory without referring back to the main text.
Response: Thank you for pointing out this. We have revised the caption of the table “Table 4. Demographic information and laboratory outcomes of patients who underwent two cycles with only one clinical pregnancy outcome.”