Author’s response to reviews

Title: Epidemiology of Acute Kidney Injury in Hospitalized Pregnant Women in China

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Dear Editors:

We’d like to thank you and the reviewers for the valuable comments and suggestions on the manuscript. We have revised the manuscript accordingly and think the current version is substantially improved. At the end of the letter is our response to the editors’ and reviewers’ concerns.

Best regards,
Response to the Reviewers (The reviewers’ remarks are in bold italic)

Reviewer #1: Shibu Jacob (Comments to the Author):

1. It is a well written manuscript and brings out the incidence of AKI in pregnancy. How was informed consent obtained from all patients? It appears as a retrograde study by collecting data from electronic hospital records after ethical clearance. Kindly consider rewording the consent part of your paper incase written consent for this study has not been obtained.

Response: Thank you for the Reviewer’s compliment. This study is a retrospective study by collecting data from electronic hospital record as the reviewer’s mentioned. Therefore, it is impossible to obtain informed consent from all the patients involved in this study. In order to conduct this research, we have obtained the ethical approval from the Nanfang Hospital. And the Medical Ethics Committee of Nanfang Hospital approved this study protocol and waived patient consent. We are very sorry not to make this clear in the manuscript, and we have revised this part accordingly.

Reviewer #2 (Comments to the Author):

1. I wonder how the community-acquired AKI worked for those patients with "having multiple creatinine tests on or before the first day of hospitalization"; according to the criteria, patients would require a prior measurement or 48 hours to meet the AKI definition, how can it be established already on the first day without a previous measurement? Please clarify.
Response: Actually, for those patients, previous measurement of serum creatinine is essential. And those patients usually have serum creatinine tests in the clinic. Therefore, we have revised the sentences from "having multiple creatinine tests on or before the first day of hospitalization" to "having multiple creatinine tests in the clinic, comparing to the previous measurement, the increase in creatinine on the first day of hospitalization met the KDIGO definition" in order to make it clear enough to understand.

2. Could the authors elaborate on the 'acute fatty liver' as a major condition associated with AKI? How was this diagnosis established? Is this really an important risk factor, since only a small number of women in the cohort had AFL?

Response: Acute fatty liver of pregnancy is usually diagnosed clinically based on the characteristic symptoms (nausea, vomit, anorexia) and significant hepatic dysfunction. While, in our study, we identified AFLP through diagnostic code from all the participant hospitals. AFLP is rare in pregnant patients, and only 59 women have AFLP in our study. In order to eliminate the influence of low incidence on the odd ratio, we calculated the PAF, which has been explained in the manuscript and previous article, to identify the risk factors of pregnancy-related AKI. Therefore, we have the confidence to say that AFL is a significant risk factor for AKI in pregnant women in our study, which is also consistent with previous research[ref]. However, diagnosis from diagnostic code will underestimated the incidence of AFLP in the population, especially there is a large clinical overlap between AFLP and severe preeclampsia. We have added this limitation in the discussion part as well.

3. The fact that age was not a significant risk factor for pregnancy-related AKI is surprising. Could the authors re-analyze their data with age as a continuous variable (it seems as if they currently used a dichotomous variable <35 and <=35 yrs).

Response: Thank you for the review’s suggestion. We have re-analyzed our data with age as a continuous variable. It is still not a significant risk factor after excluding other confounding factors using Logistic regression model. To our knowledge, age was considered a significant risk factor for preeclampsia and other pregnancy-related complications, which were proven to be an important contributing factor for pregnancy-related AKI in our study. Therefore, we think that in
our current analysis, age is not a risk factor for pregnancy-related AKI after adjusting for other associated conditions.

4. Why were transplanted patients excluded, as they can experience AKI as well?

Response: It is true that transplanted patients can experience AKI as well. However, we did not include these patients because of the following two reasons. Firstly, few of pregnant women have kidney transplantation and previous large cohort studies did not include this population as well[ref]. Secondly, women with kidney transplantation history will not have the same pathophysiological change during pregnancy, either due to the use of immunosuppressant agents or only one working kidney. Therefore, we excluded transplanted patients in our study in order to make the conclusion clearer.

5. The population of this study was restricted to hospitalized patients. As such, I would suggest to make this even more clear e.g. in the Abstract: "This study is aim to determine the effect of pregnancy on the risk of AKI among women of childbearing age…” change to "This study aims to determine the effect of pregnancy on the risk of AKI among hospitalized women of childbearing age…” Similarly in the Conclusion: "The incidence of pregnancy-related AKI is 7.3% in China" change to "The incidence of pregnancy-related AKI is 7.3% among hospitalized women in China".

Response: Thank you for the Reviewer’s comments. We have revised the manuscript accordingly to make conclusion for our study more accurate.

6. In the introduction, AKI incidence during pregnancy of up to 56.9% seems a bit overstated, please consider removing the reference suggesting this as it seems highly unlikely.
Response: We agree that it is quite higher than that reported in other retrospective and prospective cohorts. We have re-written this part accordingly.

7. The grammar could be slightly improved, I noticed some typos.

Response: We are very sorry for our grammatical mistakes. We also have our manuscript reviewed by our co-workers who are fluent in English to improve the grammar.

8. Please provide costs in US$ as well.

Response: We have provided costs in US$ in the manuscript according to the current rate of exchange.

Yours sincerely,

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