Author’s response to reviews

Title: Prevalence of Gestational Diabetes Mellitus and Associated Factors among Women Attending Antenatal Care at Gondar Town Public Health Facilities, Northwest Ethiopia

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Author’s response to reviews:

Point by point response to reviewers

Dear reviewers,

We duly acknowledge your efforts to give us very interesting and constructive comments on our manuscript. We have meticulously read all your comments and we have addressed almost all comments that you gave for us. The major revisions we made and the reflections we gave for your questions and comments are stated as follows;

Jean Baptsite Niyibizi (Reviewer 1) comments

Abstract

Comment 1: It is Ok

Methodology

Comment 1: page 7, 54-58: delete, it is a repetition and not necessary, no new addition

Response: We agreed on your comment without any reservation and, therefore, this paragraph has been deleted.
Comment 2: Authors need to show briefly how they assessed and confirmed depression?

Response: The comment has been accepted and the paragraph rephrased to briefly state how to assess and identified the presences of antenatal depression. In order to make this sentence clearer, it is revised as follows “The tool contains ten specific questions with four likert scale response options (most of the time, sometimes, not often, never), scored from 0 to 3 (a higher score indicated more depressive symptoms), which is simple to use, can be scored by simple addition. An EPDS score of 13 and more used to categorize the presence of antenatal depression.” (see page 7, line 19-23)

Results

Comment 1: It is good to include tables in results and anchor them briefly. But if the journal policy states so, there is no problem.

Response: We have already attached list of tables at the end of manuscript and each table is cited in the entire document as Journal style recommended. The table has to be inserted immediately after text during galley proof preparation by journal editors. (see the attached Table 1-4).

Comment 2: There is too much information on factors associated with GDM under results section, some of it, is like discussion. Please summarize it.

Response: We agreed on your comment without any reservation. Therefore, we have summarized the paragraphs about “factors associated with GDM’’ in the result section. (see page 10, line 17-27)

Discussion:

Comment 1: Generally avoid words such as our,…..or any other such pronoun. Please re-phrase them accordingly.

Response: The comment has been accepted and we have edited and rephrased them accordingly.
Comment 2: In discussion part, authors should also consider the sample size where the results were not agreeing with other studies

Response: The comment has been accepted and we have considered the sample size where the results were not agreeing with other studies. We have discussed this study result with other studies have sufficient sample size or unbiased sample for comparison and point out good evidence of differences.

Comment 3: On page 14, from line 21-34, delete because it is explained in methodology

Response: We thought reviewer question was on Page 13, line 21-34 rather than page 14, from line 21-34 (which was list of abbreviations). Even though this paragraph seems similar with methodology part, our interest on this paragraph was to discuss the strength and limitation of the study, therefore we have modified and rephrased the paragraph rather than deleted as a whole. (see page 13, line 7-17)

Conclusion:

Comment 1: On page 13, it is good in conclusion to put the overall prevalence and the most risk factors compared to others or order them respectively based on their significance.

Response: The comment has been accepted and corrected. We have concluded it them accordingly (see page 13, line 19-29).

References:

Comment 1: All online references, including reports should include the date of access (example ref. 1 on page 16)

Response: We have accepted and corrected. To be honest some of the online references has accessed during proposal development and some of references during manuscript preparation. Therefore we have put the date of access for online references accordingly. (See page 16, ref. 1, 12, page 17 ref. 22, 31, and page 18 ref. 43)
Ulla Kampmann (Reviewer 2) Comments

Comment 1: Page 3 line 52: There is not only one placental hormone that affects glucose metabolism in pregnancy. Please elaborate on this.

Response: The comment has been accepted. We have explained and revised the paragraph by added sentences as follows “Gestational diabetes mellitus commonly identified during the second or third trimester of pregnancy as a result of the placental hormone plays an important role in the adverse effect on glucose metabolism. As pregnancy progresses, various hormones such as estrogen, progesterone, leptin, cortisol, placental lactogen, and placental growth hormone promote a state of insulin resistance. Primarily, human placental lactogen produced by placenta raises maternal blood glucose level and makes a woman's body less sensitive to insulin leading to a higher-than-normal blood glucose level and perhaps GDM.” (see page 3, line 24-28 and page 4 line 1, 2).

Comment 2: Page 9 line 37: The authors write: No significant difference was observed between women with normal glucose profile and GDM as a result of drinking alcohol (P= 0.476) and coffee (P = 0.311). I do not understand this sentence. Is it that the use of coffee and alcohol did not differ in the GDM and the normal group? Please rephrase this.

Response: Sorry for the confusing statement on Page 9 line 37. Yes, we mean, regarding the exposure of alcohol and coffee did not differ in the GDM and normal group of pregnant women. In order to make this sentence clearer, it is revised as follows “Concerning exposure to drinking alcohol and coffee, no statistically significant difference was observed among women with normal glucose profile and GDM at P = 0.476 and P = 0.311 respectively.” (see page 9, line 23-25).

Comment 3: Some of the sentences are in tense and some in past tense especially in the background section. Please you the same tense.

Response: We have accepted and edited the sentences accordingly.

Xudong Liu (Reviewer 3) Comments

Comment 1: Please provide the formula you used to calculate the sample size or give a citation.
Response: The comment has been accepted and we have put the sample size calculation formula (single population proportion formula with the following statistical assumptions) and cited the appropriate reference used for assumption of P (prevalence) of GDM previously to calculate the minimum required sample size for a significant result. (see the detail on page 5, line 3-14).

Comment 2: Is there any difference between pregnant women who joined in the study and those who did not join in the study? What about the nonresponse bias?

Response: We found out that your question is very interesting.

There is no any difference between the two groups (joined vs not joined) in the study the majority of socio demographic variables except on educational status and income level. To make clear we have added sentences as follows “The characteristics of pregnant women who of included and excluded in the final analysis were similar in terms of key socio demographic variables such as residence (P = 0.835), maternal age (P = 0.0691), parity (P = 0.544), gravidity (P = 0.109), marital status (P = 0.734), MUAC (P = 0.08), employment status (P = 0.056). However women with complete data were on average attended secondary educational level and above and had higher income level than those who were excluded in the analysis.” (see page 9, line 5-10).

Regarding the non-response bias at the initial visit all invited participants were accepted to participate in the study and consented to come fasting for regular OGGT. During initial visit the data collectors were retrieved some information from there chart and appointed to regular test. Study participants have well responded on the variables included in the analysis (eg. Dietary diversity, physical activity, depression…). However, only few participants responded on their HIV status during interview as a resulted we cannot analyzed and assessed the association of HIV and GDM. Generally, based on the high ANC attendance rate and high response rates of our study population can be seen as representative of the majority of the pregnant women in the studied areas.

Comment 3: Page 5, Lines 31-36. The author stated that some people were advised to take repeated test of OGGT, so what is the proportion of these subjects; and how did the author deal with results from two tests?

Response: Again, We found out that your question is very interesting.

To elaborate is the proportion of these subjects re tested and which result used to ascertain for GDM diagnosis, and make the sentences clear we have revised the sentences as follows “…Besides, 352(34.3%) women had at least one type of risk factors for GDM (pre pregnancy BMI ≥ 30 Kg/m2, MUAC ≥ 28 cm, age ≥ 35 years, previous macrosomia, glycosuria, history of
GDM, family history of diabetes, previous poor pregnancy outcome or developed pregnancy-related complications) were advised to repeat the test at 32-36 weeks even if their OGTT results were negative at regular tests and GDM diagnosis ascertained by the second test.’’ (see page 5, line 25-30 and page 6, line 1-4).

Comment 4: How did the recall bias or report bias was controlled?

Response:

As we all know, one of the hard part of data collection in the research is recall bias or report bias. Participants in a study are systematically more or less likely to recall and relate information on exposure depending on their outcome status, or to recall information regarding their outcome dependent on their exposure. However, it is manageable to those with a particular outcome or exposure to remember events more clearly or amplify their recollections by using well trained data collectors or interviews. As we have clearly in the method part we have used tools which is minimize recall bias.

For example:

1. Gestational age: Gestational age was calculated according to the first day of their last normal menstrual cycle (LNMP) (for women with regular cycles) combined with first-trimester ultrasonography (if available). But, estimating gestational age by recall may be prone to some error because some women may have irregular menstrual cycle. We have also checked the gestational age from ANC card. Since most of pregnant women comes from urban community (Gondar town) they are aware about the purpose of early first-trimester ultrasonography which is considered more accurate and for most participant the early ultrasound data is available and mainly we have used it ultrasonography for those with irregular cycles or those who could not remember their LMP.

2. Dietary diversity score: Dietary intake assessment was based on data collected using the 24-hour recall method. Recall bias is common in dietary recall methods and sometimes foods consumed outside home are forgotten. This bias was minimized by using trained interviewers prompting for such occasions. Although a single 24-hour recall was thought to be sufficient, bias due to day-to-day variation of consumption cannot be ruled out completely. Up to seven days recall period was recommended and thought to be sufficient to minimize memory error.

3. Physical activity: Physical activity was assessed retrospectively by using the short form of the International Physical Activity Questionnaire (IPAQ). The IPAQ short form assesses specific types of activity such as walking, moderate intensity activities and vigorous intensity activities. Women were asked to recall their activities from the day of the interview up to seven
days backward. The IPAQ short form seven days recall period was recommended and thought to be sufficient to minimize memory error.

4. Antenatal depression: antenatal depression was measured by using the Edinburgh Postnatal Depression Scale (EPDS) screening tool developed and revised for use in an Ethiopian context. The EPDS is a brief screening tool that contains 10 specific questions with four Likert scale response options (most of the time, sometimes, not often, never), is simple to use, can be scored by simple addition, free to use, has been validated in urban settings of Ethiopia. The EPDS tool is intended to measure the feelings that the mother has experienced over the previous week and seven days recall period was recommended and thought to be sufficient to minimize memory error.

See the detail in the method section (data collection section) example on page 6

Comment 5: Page 8, Line 14, what is "data summary mechanisms"
Response: Sorry for the confusion, we said data summary to indicate the use some of the measure of data such as mean, SD, and the range as data summary mechanism in addition to others specified in the data analysis part of method section. In order to make this sentence clearer, it is revised as follows “Descriptive statistics, like frequency, percentage, and mean, SD, and the range were used for the presentation of variables. Tables and figure were also used for data presentation…..”(see page 8, line 17-19).

Response:

Comment 6: Page 9, Line 34, for " (P = < 0.001)", It is easy to generate ambiguity. Please put it another way
Response: The comment has been accepted and corrected. We have articulated the sentences in the way “Normal glucose level was more common among women having high physical activity level (33.4% vs 17.6%) and adequate dietary diversity (51.5 % vs 27.5 %) than women with GDM.” (see page 9, line 21-23).

Comment 7: the largest limitation of this study is cross-sectional design, which restricted causal inference. How did the author deal with the reverse causation? any other limitation in this study?
Our study was cross-sectional in nature and screening was done during ante natal clinic visits. Women were not followed until delivery, and women who might have un-diagnosed type 2 diabetes were classified as having GDM, although these were Few.
Response: We found out that your question is very interesting.

Though, temporal relationship and reverse causation are common causes for concern in many observational studies, especially in a cross-sectional study setting. However, it is unlikely that reverse causation between risk factors and GDM affected our results because, we excluded cases that reported having pre-existing diabetes mellitus or overt diabetes mellitus, pre-existing diabetes mellitus or overt DM, chronic diseases, medications that may affect glucose metabolism such as steroids, β-adrenergic agonists, anti-psychotic drugs which means that we are limited the shared risk factors before prior to their GDM and verified that the risk factors highly occurred during interview or before some cases eg. previous pregnancy complications (or no reverse causation). As we clearly stated in the method section (see page 5, line 20-24), the screening at first visit (20 - 23+6 weeks of gestational age) was carried out according to the recommendations of the international guideline mentioned in order to rule out pre-existing in order to rule out pre-existing diabetes. In addition, women were followed pregnant women until delivery (as part of other papers for outcome of GDM). However, as cross-sectional design, which restricted causal inference and have limitation in revealing the temporal sequence between the factors and the outcome variable. So we have added a sentence as limitation of study as follows. “Moreover, due to the nature of study design which restricted causal inference and could not reveal the temporal sequence between the factors and the outcome variable which could be limitation of the study.” (see page 13, line 15-17).

Comment 8: Please show the full word of the abbreviation under each table or figure

Response: The comment has been accepted and corrected.

Comment 9: Please show under the table confounders which were adjusted for variables

Response: The comment has been accepted and corrected.

As we stated in the method part (data analysis section) Binary logistic regression model was used to identify factors associated with GDM. Variables with P-value of ≤ 0.20 in the bivariate analysis were exported by enter method to the multivariate analysis to control the possible effect of confounders. We were excluded variables in the tables such as previous history of CS, residence, gravidity, drinking alcohol, coffee had p value of > 0.2 in bivariate LR. Therefore all variables in the table has P-value of ≤ 0.20, and they were adjusted to identify the potential confounders. We have put the confounders which were adjusted for variables at end or foot note Table 4.
Comment 10: Need language modification

Response: The comment has been accepted and corrected.

We have done language modification accordingly and edited by language editor as well.

Comment 11: Did the study have Ethical approval? If have, which committee approved it? Ethical Approval Code?

Response: Yes, we have clearly stated in the original manuscript in the declaration section (subsection of Ethics approval and consent to participate) as the journal recommended to put here.

The study was conducted after ethical approval was obtained from the Institutional Review Board (IRB) of the University of Ibadan/University College Hospital (Ref.No; UI/EC/17/0435) and the IRB of the University of Gondar (Ref.No; O/V/P/RCS/05/811/2018).” (see page 14, line 16-18).

Response:

Additionally, all other technical issues, sentence and grammar errors have been addressed.

Thank you for your valuable comments!

The Authors