

Manuscript Number 26320

**Title Gestational diabetes mellitus: screening with fasting plasma glucose**

Response to Reviewers

Reviewer 1 # 02951290

This manuscript represents a comprehensive and ultimately competent review of the most important issue regarding possibility to screen for gestational diabetes with fasting plasma glucose (FPG). However, few important issues regarding FPG might be mentioned in order to achieve "the understanding of all the caveats, crucial to be able to use FPG for investigating glucose tolerance in pregnancy", as stressed in the Abstract (these should be regarded as minor remarks): - preanalytical variability of plasma glucose, which can seriously compromise screening/diagnostic performance if rigorous and often impractical sample processing procedures are strictly followed. - critical appraisal of glucometer use for the GDM screening purpose, particularly regarding analytical (in)accuracy and reproducibility (lot-to-lot variability of test-strips). - biological variability of FPG, another underestimated problem in GDM diagnosis/screening based on a single cut-off approach. Technical remarks - there are few typesetting errors and duplicate words within the same sentence. - HbA1c is incorrectly abbreviated as HBA1c throughout the text.

*The author being a chemical pathologist fully appreciates your valuable comments. The laboratory quality is often underestimated. We have published a paper in 2015 which highlighted these comments (Agarwal MM, et al. Gestational diabetes mellitus prevalence: Effect of the laboratory analytical variation. Diabetes Res Clin Pract 2015; 109:493-499). We have added a very brief new section to the manuscript—just to avoid adding bulk. We hope you like our final version.*

*We have corrected the errors mentioned in the technical remarks.*

*We do appreciate the time that you spent to look at our manuscript. We thank you for your generous comments.*

Reviewer 2 # 02446088

Comments

1. P3 Para 1 Clearly define type 1 and type 2 diabetes to differentiate them from GDM.

*We have added the ADA definition of Type 1 & 2 diabetes. This does help to differentiate from GDM. Thank you.*

2. P4 Para 1 There should be a drive for consensus on GDM screening and diagnosis. State which guidelines are best suited globally given accuracy, cost and practical considerations.

*The most accepted guideline is the IADPSG. The preeminent organization FIGO has recommendations how to adapt it in all countries (The author was on the organizing committee). We have provided a reference of FIGO—which is followed worldwide by all obstetric organizations.*

3. P4 Para 2 Briefly define fasting glucose, fructosamine and HbA1c in the context of screening.

*We have published 2 papers on fructosamine and HbA1c as screening tests. For keeping it short, we have just summarized the current thoughts of screening with them. Thank you for this comment.*

4. P5 Para 2 Briefly discuss new developments or future directions e.g. are biomarkers specific to GDM being identified and validated?

*We have added some information about the new biomarkers in GDM. None of them have reached enough sensitivity/specificity to replace the OGTT.*

5. P6 Para 3 The risk factor profiles prior to screening, followed by glycemia testing should be commented on.

*We have elaborated on the risk factors for GDM. The NICE 2015 guidelines uses them. It was an oversight. Thank you.*

6. P6 Para 4 Comment on the feasibility of OGTTs prior to pregnancy, for the first, second and/or third trimester in high risk women. Despite the practicality and additional costs, early diagnosis may lead to better outcomes for the mother and child.

*We have added the St. Carlos Study with states this fact.*

7. For glucose load, dosages could be more accurate e.g. based on body weight and metabolic rate. Briefly comment.

*We have already stated that one of the problems of the OGTT is that it is not standardized for body weight.*

8. List some warranted improvements for OGTTs as a test given its limitations. For example, in high risk women, measuring insulin during OGTTs could determine insulin resistance in the women in the absence of GDM. These women may have GDM in future pregnancies.

*We have added a comment to this effect. We have also added a reference.*

9. A deliverable of this review should be more lucid guidelines or a framework on GDM screening and diagnosis in the context of the existing literature and practices.

10. Other comments P5 Para 1 prefect to perfect P6 Para 1 rephrase

*Thank you. We have corrected this error.*

P7 Para 1 Amend as this is conflicting and has some repetition.

*Amended.*

P9 Standardized procedures and customization to ethnicity can improve reproducibly.

*We have added this comment. Thank you.*

P11 mg/dl convert to mmol/l

*We have converted to mmol/l. This was an oversight. Thank you for picking up this oversight..*

P15 Para 2 What were the relative costs?

*We have referenced a paper that we published on the costs (#63). We have elaborated on costs in the section that follows.*

Table 1 Delete Currently vogue Table 2 FPG screening tests

*Deleted.*

Table 3 Revise title

*Revised.*

*Thank you for your outstanding comments. They have really helped to imrove our manuscript. We do appreciate all the time that you have spent on our manuscript.*

Reviewer 3 # **00233953**

Interesting topic However, the manuscript is far too long and should be reduced by ½

*We do appreciate that we should trim our manuscript. We also understand that too much length is counterproductive. Being a comprehensive review, we find it hard to cut it to half. We have tried to be as succinct as possible; however, the three other reviewers want us to add additional*

*information. We found it hard to reconcile the manuscript to your comment. But we tried our best. We hope that you are happy with our final version.*

*Again, we appreciate your effort with our manuscript.*

Reviewer 4: # 00506304

In this editorial article, Agarwal discusses the benefit of fasting plasma glucose (FPG) measurement for screening of gestational diabetes mellitus (GDM). Normally, the diagnosis of GDM requires 2 h, 75-g oral glucose tolerance test, but a reliable screening test is necessary for reduction of time and cost. FPG is one of the promising candidates for GDM screening, and FPG in early pregnancy may be predictive for GDM in late pregnancy. However, FPG is probably more appropriate to rule out GDM. In general, this article is comprehensive and covers most aspects of GDM screening. It may be helpful if a brief information regarding the pathogenesis of GDM as well as a diagram showing a practice guideline of GDM screening are added in the article.

*We have briefly added the pathogenesis of GDM. We have, as per your suggestion, added a figure (Figure 2) to diagrammatically represent our suggested algorithm. Your comments have been a big help. Thank you for your constructive comments. We appreciate your time.*