PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Sensitivity of fasting glucose for gestational diabetes mellitus screening in Mexican adolescents based on International Association of Diabetes and Pregnancy Study Groups criteria: a diagnostic accuracy study based on retrospective data analysis
AUTHORS	Reyes-Muñoz, Enrique; Sandoval-Osuna, Norma; Reyes-Mayoral, Christian; Ortega-González, Carlos; Martínez-Cruz, Nayeli; Ramírez-Torres, María; Arce-Sánzhez, Lidia; Lira-Plascencia, Josefina; Estrada-Gutiérrez, Guadalupe; Montoya-Estrada, Aracel

VERSION 1 – REVIEW

REVIEWER	Katrien Benhalima UZ Leuven, Belgium
REVIEW RETURNED	23-Jun-2017

GENERAL COMMENTS	This is an interesting retrospective study evaluating the sensitivity and specificity of a fasting glucose for GDM screening when using the IADPSG criteria for GDM in an adolescent Mexican population. The paper is well written. However, due to the small sample size, no conclusions can be made concerning pregnancy outcomes nor on risk factors for GDM in their population. 1. The authors should clarify in the method section why treatment for GDM was only considered when at least two values were abnormal. On which guidelines is this based? How might this have impacted on pregnancy outcomes? 2. The authors should also clarify whether women (with risk factors or universally) were screened for unknown overt diabetes in early pregnancy as is now also recommended by many societies? If not, they should explain why this was not done. 3. Authors should provide data on the % of women with overweight and obesity in the GDM and non-GDM groups. Are other data on general characterisctics available (smoking, family history of diabetes...)? 4. Authors should provide some background information by describing how adolescent pregnant women compare to the general pregnant population in Mexico (lower socio-ecomoic status, more often obese...or not) Minor comments: line 8-9: the 'International...' criteria instead of International ...criteria line 24: 'delivered' instead of 'resolution of pregnancy' line 38: 'on' the receiver operating... instead

REVIEWER	Karoline Nielsen

	Dept. of Public Health, University of Copenhagen, and Steno Diabetes Center Copenhagen, Denmark
REVIEW RETURNED	25-Jun-2017

GENERAL COMMENTS	Overall comments: This paper's stated objective is to evaluate the usefulness of fasting glucose for GDM screening in Mexican adolescents using the IADPSG criteria. The study also has a secondary outcome, namely to compare perinatal outcomes between those with GDM and those without. Given the continuous debate on appropriate and also feasible GDM screening and diagnostic criteria especially in low and middle income settings, this paper is a welcoming contribution to the existing literature. However, the manuscript would require some revision and clarification. 1. First of all, the rationale for the study should be strengthened. Perhaps because the authors seem to have more than one aim with their investigations, it becomes unclear what overall problem they are actually trying to address. Hence, do they 1) seek to describe the occurrence of GDM among adolescents, 2) seek to identify a more simple and feasible screening approach and diagnostic criteria, or 3) examine whether there are any excess risk of adverse perinatal outcomes in women diagnosed according to IADPSG criteria.? I think focusing on one of these would make the paper stand out much stronger. Depending on which of these three aims is of primary interest, the background and discussion sections should include more references to the literature within that specific area (e.g. GDM in adolescents, feasibility of GDM criteria or outcomes in GDM diagnosed according to IADPSG). 2. In the introduction, it would be relevant to know what the GDM prevalence is in the adult pregnant population in Mexico. 3. The authors could elaborate on their statement that 'Screening for GDM among adolescent women is a controversial topic'. Why this is the case is not really clear. See also comment 1. 4. What is the GDM diagnostic criteria currently used in Mexico? Is that the IADPSG or the National Institute of Health and Care Excellence? This should be made clear. What glucose levels would result in treatment for GDM? This is important to understand the secondary objective of the study. 5. On page 6, the authors note a number of conditions which would exclude women from their study. But should women with other pathologies be excluded in study on GDM prevalence? At least the authors need to present their arguments for doing so. The condition that without a doubt would make sense to exclude is pre-existing type 1 or type 2 diabetes, but this is not mentioned – why? 6. The continuous variables are expressed as means. Medians might be more appropriate for non-normally distributed variables. 7. Table 1: units e.g. year, kg etc should be added. 8. If the aim is to investigate GDM occurrence in adolescents, it could be useful to have other characteristics included if available. Especially family history of diabetes and socioeconomic position. 9. On page 10, the authors state that cut-offs at 85 and 90 mg/dl have the same specificity. I think this statement is debateable based on table 2. 10. In the part of the study which focuses on assessing the use of other fasting glucose cut-offs – is the purpose to identify a fasting cut-off used for screening or diagnosis? The authors write screening, but I get the sense that they actually mean diagnosis. This should be

	clarified. 11. In the part on perinatal outcomes, it should be made clearer 1) what diagnostic criteria were used to provide treatment. If that was the IADPSG, could it not be interpreted as simply the effect of treatment? In the discussion, it says that only 96% of those with GDM had treatment. This is information that should have been provided in the methods section. Moreover, if that is then to say that there are actually three groups: no GDM, GDM treated and GDM not treated. Would it not make more sense to compare these three groups? And power calculations should be based on detecting differences in perinatal outcomes. 12. P-values should be listed in table 4. 13. On page 14, it says that fasting glucose was altered in 84.4% of GDM cases. Earlier on it said that the proportion was 90.3%. Or are these not the same?

REVIEWER	Mukesh M. Agarwal California University of Science and Medicine, California, USA
REVIEW RETURNED	27-Jun-2017

GENERAL COMMENTS	Reyes-Munoz et al. wonder if fasting plasma glucose (FPG) is a reliable screening test for gestational diabetes mellitus (IADPSG criteria) in pregnant Mexican adolescents. In general, there are few available studies addressing GDM in the very young due to the low prevalence of diabetes type 2 (DM2) in the past; however, with the DM2 prevalence increasing in adolescents worldwide, this is a welcome study. Major comments: 1. Based on the data presented, the FPG seems to be a perfect test—something that most studies do not agree (please see major comment 2). A FPG threshold of 5.0 mmol/l, produced unreasonably good results: LR+ of 37.2 and LR- of 0.09, which are corroborated by the area under the ROC curve of 0.95 (1.0 is maximum), and uncanny sensitivity and specificity. Whenever we are presented with contrarian findings, it always worthwhile to look for errors in data collection. One could speculate (based on high numbers of GDM with elevated fasting plasma glucose compared to 1-h &2-h) that the DM1 and DM2 patients were not excluded from the study; if so, this is a major failing—and there is no specific mention that these women were excluded. The current definition of GDM precludes these patients with DM. If at all, how were women with DM ruled out and excluded? OGTT/HBA1c/ FPG in first trimester? 2. Most papers on FPG as a screening test for GDM confirm that it is a poor screening test for GDM because of the high FPR (see the iconic paper by Sacks DA. Obstet Gynecol. 2003; 101:1197-203; Donovan L. Ann Int Med 2013; 159:115-12) Thus, too many women without GDM have to undergo the OGTT obviating the FPG as a screening test for GDM. 3. If FPG (of the OGTT) picked up 28/31 (90.3%) adolescents with GDM, one may not even need the confirmatory OGTT in this population. To my mind, this FPG pick-up rate is abnormally high and unrealistic. In the HAPO data, the maximum identification was from Barbados (74%) and Bellflower, CA (73%) which has a large Hispanic population (Sacks Diab Care 2012 35:526-528). The authors must be able to provide some evidence and reasons for this discrepancy. As there were too many patients with high FPG, the sensitivity decreased by half (90% - 45%) with just 4 mg/dl difference from 90-94 mg/dl (Table 2). 4. Discussion, pages 14-15. More discussion is needed about GDM

	in adolescents worldwide. The current changing demographics of type 2, DM need to be elaborated. You can educate us on what different major guidelines (ADA, ACOG,CDA,CJOG,WHO,NICE, etc.,) tell us about screening of GDM in young teenagers. The studies used for comparison discussion mean precious little as the populations are different, as well as the age groups. Paragraphs 2-4 can be condensed into one. Minor comments: 1. Abstract: page 2, line24. Please delete, 'We excluded…. Pathology,' as not needed in abstract. Or rephrase. 2. Abstract: page 2, line44. The prevalence of GDM 6.3% must include the n (31). 3. Units: Whenever, mmol are used please make sure that a zero follows. So, 5 mmol/l must read as 5.0 mmol/l (Page 2, line 46 and page 3, line 3.). Also, millimoles needs one decimal place. So, I would round of 5.23 to 5.2 mmol/l. 4. Introduction, Page 4, line 30. IADPSG increases prevalence 3 times compared to ADA criteria. Prevalence is criteria dependent, so please mention GDM criteria used with the prevalence. 5. Introduction, Page 5, line 36. IADPSG recommendation for 75-g OGTT on all women is too demanding is a fact and not a conclusion. Please rephrase. 6. Introduction, Page 5, line 43 Reference 15 is from 2013 and not 'recent' in 2017. Please delete recent 7. Introduction, Page 5, line 51. How was the hypothesis that FPG of 85 mg/dl would have a sensitivity of 90% made? 8. Methods, Page 6, line 22. Please use the exact dates. 9. Methods, Page 6, line 33. Though oGTTs should be done 24—28 weeks, this seldom happens for all patients. Thus, many patients may come late for the first time, say at 32 weeks, others may be done during first trimester for 'clinical' reasons. If possible please mention how many OGTTS were done in each trimester. 10. Methods, Page 6, line 52. Were these numbers provided by the vendor or actual in the lab used in the study. The CVs must be quoted with the levels of glucose as CVs improve with rising glucose. Since the study depends on measuring the glucose accurately, the authors need to make sure glucose meets acceptable laboratory criteria (<2.9% analytic precision; bias of <2.2%; and a total error of <6.9% (NACB guidelines). Was the laboratory accredited by some external agency, local or international? 11. Results, Page 8, line 54. Of the patients were excluded in total (n=127), as major comment 1, what happened to women with DM 1&2? 12. Page 11, Table 2. Please shorten the table. All FPG values are not needed; about six values should suffice. Also, please use whole numbers for FPG in mg/dl and single decimal places for mmol/l. 13. The references are inconsistent. 14. How were all women with GDM treated? Oral drugs, diet and insulin (with number in each category). In summary, please tell us more about data collection, how diabetes antedating pregnancy was ruled out, and elaborate GDM in adolescence worldwide and in populations at risk. If you address all these issues, this manuscript would attain the excellence it deserves.

VERSION 1 – AUTHOR RESPONSE

Editorial Requests:
C: Please justify why the diagnostic validity of the test was not confirmed in a second independent population. Please acknowledge this as a limitation of the study.
R: The diagnostic validity of the test was not confirmed, so a future study to validate it is needed. We added this point as a limitation of the study.
C: Please revise the title to indicate that this is a diagnostic accuracy study based on retrospective data analysis.
R: We added in the title of manuscript, that this is a diagnostic accuracy study based on retrospective data analysis.

Reviewer: 1
C: The authors should clarify in the method section why treatment for GDM was only considered when at least two values were abnormal. On which guidelines is this based? How might this have impacted on pregnancy outcomes?
R: We added this paragraph; "During the study period, at our Institution GDM was diagnosed based on the observation of two or more abnormal values during a 75-g/2-h OGTT; fasting ≥95 mg/dL (5.3 mmol/L), 1-h ≥180 mg/dL (10 mmol/L) and 2-h ≥155 mg/dL (8.6 mmol/L) according with the Fifth International Workshop-Conference on Gestational Diabetes Mellitus recommendations. [16]" We are reporting pregnancy outcomes in this study to explore the impact of no intervention for GDM in this small group of adolescents.
C: The authors should also clarify whether women (with risk factors or universally) were screened for unknown overt diabetes in early pregnancy as is now also recommended by many societies? If not, they should explain why this was not done.
R: In our institution, we perform a universal screening, we included only women with OGTT between 24 and 28 weeks of gestation that is the recommendation in most international guidelines in women without high risk factors to development GDM. Women included in the study were not screened for unknown overt diabetes in early pregnancy because most adolescent women in our Institution request prenatal care in the middle of second trimester. We added this point in the discussion section.
C: Authors should provide data on the % of women with overweight and obesity in the GDM and non-GDM groups. Are other data on general characteristics available (smoking, family history of diabetes...)?
R: We now provide this data in table 1.
C: Authors should provide some background information by describing how adolescent pregnant women compare to the general pregnant population in Mexico (lower socio-economic status, more often obese...or not)
R: We added this information describing adolescent pregnant women compared to the general pregnant population in Mexico.
C: Minor comments:
line 8-9: the 'International...' criteria instead of International ...criteria
line 24: 'delivered' instead of 'resolution of pregnancy'
line 38: 'on' the receiver operating... instead of 'in' the receiver...
line 56: 'INPer' should be corrected
R: All minor comments were assessed in the revised manuscript.

Reviewer: 2
C: First of all, the rationale for the study should be strengthened. Perhaps because the authors seem to have more than one aim with their investigations, it becomes unclear what overall problem they are actually trying to address. Hence, do they 1) seek to describe the occurrence of GDM among adolescents, 2) seek to identify a more simple and feasible screening approach and diagnostic criteria, or 3) examine whether there are any excess risk of adverse perinatal outcomes in women diagnosed according to IADPSG criteria.? I think focusing on one of these would make the paper

stand out much stronger. Depending on which of these three aims is of primary interest, the background and discussion sections should include more references to the literature within that specific area (e.g. GDM in adolescents, feasibility of GDM criteria or outcomes in GDM diagnosed according to IADPSG).
R: The primary goal of the study was to evaluate the usefulness of fasting glucose for gestational diabetes mellitus (GDM) screening in Mexican adolescents using the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria. We clarified this point and added references in the introduction and discussion sections. We assessed as secondary aims to report the prevalence of GDM and explore perinatal outcomes in adolescents with and without GDM.
C: In the introduction, it would be relevant to know what the GDM prevalence is in the adult pregnant population in Mexico.
R: We added the prevalence of GDM in adult Mexican women.
C: The authors could elaborate on their statement that 'Screening for GDM among adolescent women is a controversial topic'. Why this is the case is not really clear. See also comment 1.
R: We further elaborated about these points in the introduction section.
C: What is the GDM diagnostic criteria currently used in Mexico? Is that the IADPSG or the National Institute of Health and Care Excellence? This should be made clear. What glucose levels would result in treatment for GDM? This is important to understand the secondary objective of the study.
R: Currently in Mexico each institution can use any international criteria for GDM diagnosis. In our Institution, we use the Fifth International Workshop-Conference on Gestational Diabetes Mellitus recommendations and this is now mention in the corrected manuscript, describing the criteria.
C: On page 6, the authors note a number of conditions which would exclude women from their study. But should women with other pathologies be excluded in study on GDM prevalence? At least the authors need to present their arguments for doing so. The condition that without a doubt would make sense to exclude is pre-existing type 1 or type 2 diabetes, but this is not mentioned – why?
R: We now mention that women with any type of pregestacional diabetes were excluded. We excluded women with other pathologies, to achieve external validity and moreover, these pathologies could affect the perinatal outcome confounding the result interpretations.
C: The continuous variables are expressed as means. Medians might be more appropriate for non-normally distributed variables.
R: All continuous variables in table 1 had now normal distribution, we changed the number of pregnancies to ordinal variable and are now show as frequency and percentage.
C: Table 1: units e.g. year, kg etc should be added.
R: We added units in table 1.
C: If the aim is to investigate GDM occurrence in adolescents, it could be useful to have other characteristics included if available. Especially family history of diabetes and socioeconomic position.
R: We provide data on general characteristics: overweight, obesity and family history of diabetes in table 1, even though prevalence of GDM is a secondary aim, we think that is pertinent because the limited information about it.
C: On page 10, the authors state that cut-offs at 85 and 90 mg/dl have the same specificity. I think this statement is debatable based on table 2.
R: We agree with the reviewer and this statement has been eliminated.
C: In the part of the study which focuses on assessing the use of other fasting glucose cut-offs – is the purpose to identify a fasting cut-off used for screening or diagnosis? The authors write screening, but I get the sense that they actually mean diagnosis. This should be clarified.
R: Currently in our institution and the most international guidelines suggest performing universal screening using one step strategy with OGTT in all pregnant women. The goal of our study is to identify a cut-off for fasting glucose for screening and then perform an OGTT for diagnosis of GDM; it could identify the most cases of GDM, performing a less number of OGTT in adolescent women. We clarify this point in the introduction section.
C: In the part on perinatal outcomes, it should be made clearer 1) what diagnostic criteria were used to provide treatment. If that was the IADPSG, could it not be interpreted as simply the effect of

treatment? In the discussion, it says that only 96% of those with GDM had treatment. This is information that should have been provided in the methods section. Moreover, if that is then to say that there are actually three groups: no GDM, GDM treated and GDM not treated. Would it not make more sense to compare these three groups? And power calculations should be based on detecting differences in perinatal outcomes.
R: We clarify current criteria used at our institution to provide specific treatment for GDM in the methods section. We analyzed two groups for perinatal outcomes because only one adolescent was diagnosed with GDM according with our institutional criteria. We think that it is important to explore perinatal outcomes because 30 of 31 (96.7%) women did not receive GDM-specific treatment and the perinatal outcomes were similar in adolescents with and without GDM. Although the power calculation is not adequate for detecting differences in perinatal outcomes, it provides a new question about the effect of GDM diagnosis using the IADPSG criteria among adolescent women; this was highlighted as limitation of the study.
C: P-values should be listed in table 4.
R: We added p-value in table 4.
C: On page 14, it says that fasting glucose was altered in 84.4% of GDM cases. Earlier on it said that the proportion was 90.3%. Or are these not the same?
R: The correct proportion is 90.3 (28/31), it was corrected in the revised manuscript.

Reviewer: 3
Major comments:
C: Based on the data presented, the FPG seems to be a perfect test—something that most studies do not agree (please see major comment 2). A FPG threshold of 5.0 mmol/l, produced unreasonably good results: LR+ of 37.2 and LR- of 0.09, which are corroborated by the area under the ROC curve of 0.95 (1.0 is maximum), and uncanny sensitivity and specificity. Whenever we are presented with contrarian findings, it always worthwhile to look for errors in data collection. One could speculate (based on high numbers of GDM with elevated fasting plasma glucose compared to 1-h &2-h) that the DM1 and DM2 patients were not excluded from the study; if so, this is a major failing—and there is no specific mention that these women were excluded. The current definition of GDM precludes these patients with DM. If at all, how were women with DM ruled out and excluded? OGTT/HBA1c/ FPG in first trimester?
R: According with inclusion criteria, women were selected only if they had an OGTT between 24 to 28 weeks of gestation. Most adolescent with type 1 or 2 diabetes are referred to our hospital before 24 weeks of gestation and we did not perform an OGTT in these patients. This point was clarified in the methods section of the corrected manuscript. In the present study we did not identify any women with type 1 or 2 diabetes during the OGTT between 24 and 28 weeks of gestation. We did not include women with OGTT before 24 weeks of gestation because most guidelines recommend perform OGTT in the first prenatal visit in women with high risk of GDM, which is not frequent in adolescent women.
C: Most papers on FPG as a screening test for GDM confirm that it is a poor screening test for GDM because of the high FPR (see the iconic paper by Sacks DA. Obstet Gynecol. 2003; 101:1197-203; Donovan L. Ann Int Med 2013; 159:115-12) Thus, too many women without GDM have to undergo the OGTT obviating the FPG as a screening test for GDM.
R: We agree with the reviewer comment, however the paper by Sacks et al., is a study performed in 1998-1999, with different GDM diagnostic criteria (two step approach OGCT and OGTT 100g-3h) and predominantly in adult women with mean maternal age of 28 years and our study involves adolescents with IADPSG diagnostic criteria. In their systematic review, Donovan L., et al, concluded that oral glucose Challenge test (OGCT) and measurement of fasting plasma glucose level (at a threshold of 4.7 mmol/L [85 mg/dL]) at 24 weeks' gestation are good at identifying women who do not have GDM. The OGCT, a glucose load test, is better than the fasting plasma glucose test (4.7 mmol/L [85 mg/dL]) at identifying women who have an abnormal response to larger glucose load tests. However, there are no studies comparing OGCT or FPG using IADPSG diagnostic criteria in adolescent women.

C: If FPG (of the OGTT) picked up 28/31 (90.3%) adolescents with GDM, one may not even need the confirmatory OGTT in this population. To my mind, this FPG pick-up rate is abnormally high and unrealistic. In the HAPO data, the maximum identification was from Barbados (74%) and Bellflower, CA (73%) which has a large Hispanic population (Sacks Diab Care 2012 35:526-528). The authors must be able to provide some evidence and reasons for this discrepancy. As there were too many patients with high FPG, the sensitivity decreased by half (90% - 45%) with just 4 mg/dl difference from 90-94 mg/dl (Table 2).

R: This discrepancy could be explained by maternal age and ethnic group; in our study, the mean of maternal age was 15.9 ± 1.6 vs 29.2 ± 5.8 in HAPO study. Gopalakrishnan et al., reported among North Indian women diagnosed with GDM according to IADPSG criteria, that 91.4% had abnormal fasting plasma glucose (FPG), which are similar to our findings. Likewise, Trujillo et al., reported in Brazilian women using IADPSG criteria that a fasting plasma glucose cut-off value of 85 mg/dL indicated that only 18.7% of all women needed to undergo an OGTT with a detection rate of 92.5% of all GDM cases, while the 90 mg/dL cutoff had a detection rate of 88.3% cases of GDM and an OGTT would indicate in only 4.2% of all women, it is similar to our study. These reasons for discrepancy were added in the discussion of the corrected manuscript. Additionally, we mention as limitation of the study that the diagnostic validity of the test was not confirmed in a second independent population and it should be confirmed in a prospective study.

The sensitivity decreased by half because between 90 and 94 mg/dL is included the diagnostic cut off for GDM that is ≥92 mg/dL according with IADPSG. If we would use 94 mg/dL as a cut-off point for screening, women with GDM diagnosed with glucose levels of 92 and 93 mg/dL are lost, which decreases sensitivity.

C: Discussion, pages 14-15. More discussion is needed about GDM in adolescents worldwide. The current changing demographics of type 2, DM need to be elaborated. You can educate us on what different major guidelines (ADA, ACOG,CDA,CJOG,WHO,NICE, etc.,) tell us about screening of GDM in young teenagers. The studies used for comparison discussion mean precious little as the populations are different, as well as the age groups. Paragraphs 2-4 can be condensed into one.

R: We added more discussion about GDM in adolescents worldwide, and discus international guidelines recommendations about it. We have condensed paragraph 2-4 and we now discuss differences in populations and maternal age with other studies that propose fasting glucose as screening tool for GDM.

C: Abstract: page 2, line24. Please delete, 'We excluded…. Pathology,' as not needed in abstract. Or rephrase.

R: We agree and eliminated the phrase in the corrected manuscript.

C: Abstract: page 2, line44. The prevalence of GDM 6.3% must include the n (31).

R: We include n value (31/493) in the corrected manuscript.

C: Units: Whenever, mmol are used please make sure that a zero follows. So, 5 mmol/l must read as 5.0 mmol/l (Page 2, line 46 and page 3, line 3.). Also, millimoles needs one decimal place. So, I would round of 5.23 to 5.2 mmol/l.

R: The units and values were corrected in the revised manuscript.

C: Introduction, Page 4, line 30. IADPSG increases prevalence 3 times compared to ADA criteria. Prevalence is criteria dependent, so please mention GDM criteria used with the prevalence.

R: We added GDM criteria with the prevalence.

C: Introduction, Page 5, line 36. IADPSG recommendation for 75-g OGTT on all women is too demanding is a fact and not a conclusion. Please rephrase.

R: It was corrected in the revised manuscript.

C: Introduction, Page 5, line 43 Reference 15 is from 2013 and not 'recent' in 2017. Please delete recent

R: The word recent was deleted.

C: Introduction, Page 5, line 51. How was the hypothesis that FPG of 85 mg/dl would have a sensitivity of 90% made?

R: We elaborate the hypothesis based on the finding of the systematic review by Donovan L et al. that in adult women FPG of 85mg/dL had a sensitivity of 85%.
C: Methods, Page 6, line 22. Please use the exact dates.
R: It was corrected in the revised manuscript.
C: Methods, Page 6, line 33. Though OGTTs should be done 24—28 weeks, this seldom happens for all patients. Thus, many patients may come late for the first time, say at 32 weeks, others may be done during first trimester for 'clinical' reasons. If possible please mention how many OGTTS were done in each trimester.
R: In our institution we perform a universal screening including only women with OGTT between 24 and 28 weeks of gestation that is the recommendation in most international guidelines in women without high risk factors to development GDM. The initial inclusion criterion was OGTT between 24 and 28 weeks of gestation, so adolescent women with OGTT in other weeks were not include. Women included in the study were not screened for unknown overt diabetes in early pregnancy because most adolescent women in our
Institution request prenatal care in the middle of the second trimester. We added this point in discussion section.
C: Methods, Page 6, line 52. Were these numbers provided by the vendor or actual in the lab used in the study. The CVs must be quoted with the levels of glucose as CVs improve with rising glucose. Since the study depends on measuring the glucose accurately, the authors need to make sure glucose meets acceptable laboratory criteria (<2.9% analytic precision; bias of <2.2%; and a total error of <6.9% (NACB guidelines). Was the laboratory accredited by some external agency, local or international?
R: It was clarified in the corrected manuscript in the first paragraph of procedure.
C: Results, Page 8, line 54. Of the patients were excluded in total (n=127), as major comment 1, what happened to women with DM 1&2?
R: Women with diabetes type 1 or 2 were excluded and this is now clear in the revised manuscript.
C: Page 11, Table 2. Please shorten the table. All FPG values are not needed; about six values should suffice. Also, please use whole numbers for FPG in mg/dl and single decimal places for mmol/l.
R: We considered that table 2 is essential for the study, because shows all values of fasting glucose of ROC curve analyses. We selected three whole values for FPG that are show in table 3. Single decimal place for mmol/L was corrected in the revised manuscript.
C: The references are inconsistent.
R: The references were reviewed and corrected in the revised manuscript.
C: How were all women with GDM treated? Oral drugs, diet and insulin (with number in each category)
R: Only one GDM women was treated with diet. The rest of GDM adolescent women did not receive specific treatment for GDM.

VERSION 2 – REVIEW

REVIEWER	Karoline Nielsen Department of Public Health, University of Copenhagen, Denmark
REVIEW RETURNED	03-Aug-2017

GENERAL COMMENTS	Abstract: In the sentence about secondary measures, delete 'explore'. Introduction: Spell out ADA first time used.

	The sentence "… additionally most Mexican adolescent women are primigravid and have lower socio-economic status than adult women" – add 'pregnant' so that it says "additionally most pregnant Mexican adolescent..". Also, is higher socio-economic status associated with increased risk of GDM in Mexico? The association btw socio-economic status and GDM seems to depend on the country (and income level of that country). For the argument here to make sense, we should be informed how the association is in Mexico. The authors mention two different places that screening for GDM among adolescent women is a controversial topic. I think this should be placed together. Methods: The authors state that only adolescents with an OGTT between 24-28 weeks of gestation are included. We are informed that this number is 620. It would be useful to know how many 12-19 year old pregnant women did not have the OGTT at 24-28 weeks i.e. the proportion of women actually screened? At least some indication in the discussion about whether most pregnant adolescent women were screened or not. Results Would suggest you change the legend of table 1 to 'Characteristics of 493 ….' Discussion On page 18, the authors argue that even though there were no difference in the perinatal outcomes, using the IADPSG criteria could be beneficial because it identifies women at long-term risk for type 2 diabetes and early intervention could reduce the incidence of type 2 diabetes. While I do largely agree with this, I do believe it needs to be modified slightly and references potentially added. To my knowledge there are still no studies showing that women with GDM according to the IADPSG criteria (but not the former criteria) are at increased risk of t2dm. If the authors know of such studies, I'd recommend they refer to them. Likewise, most studies refer to the DPP papers by Ratner et al or Aroda et al when stating that the incidence of t2dm, can be reduced in women with prior GDM through interventions. The DPP, however, is based on IGT status (and with intervention around 12y after the index GDM pregnancy, so 'early intervention' can be debated. A recent systematic review by Pedersen et al 2017 could perhaps shed some more light on earlier interventions) and not IFG. In other words, I think the authors need to be a bit more careful in their wording here. Rather, I think the authors should put more emphasis on the fact that this is a young and very vulnerable group – thus, IF their conversion rate to t2dm is the same as what has been shown in various studies, they would likely develop t2dm at a very young age. Also, they would be likely to have subsequent pregnancies and recurrent GDM. On page 18, the authors write that they 'did not identify any women with type 1 or 2 diabetes during the OGTT between 24 and 28 weeks of gestation that could be attributable to sample size'. How did you assess this? Is this conclusion based on the glucose levels (i.e. diabetes in pregnancy as per WHO 2013 criteria) or based on sustained hyperglycaemia after delivery or how?

	Overall: There are a number of typos and spelling errors in the corrected version, which should be checked.

REVIEWER	Mukesh M. Agarwal California University of Science & Medicine USA
REVIEW RETURNED	03-Aug-2017

GENERAL COMMENTS	Reyes-Munoz et al. have submitted a revised version of their manuscript on screening Mexican adolescents for GDM by fasting glucose (FPG) using the 75-g OGTT (IADPSG criteria) as gold standard. I read this paper as if I was reading it for the first time; this approach helps to review to become more objective. I also looked at the answers provided by the authors to my initial queries. Many questions still linger. Major comments 1. My major concern about how the data was collected is still disconcerting. We need to be reassured that the patients were not collected at random and many of them were not missed out. In three years, there were 620 adolescents with OGTT at 24-28 weeks. Please let us know how large was your hospital and how many deliveries are conducted each year. If 11% of the deliveries are in adolescents, the hospital should have around 6500 deliveries during this period. Furthermore, in any hospital anywhere in the world (tertiary or otherwise), patients (self or physician referred) come during any trimester. So, there must be patients who were picked up in 24-28 weeks by the OGTT who had diabetes. The data on how many women had pregestational DM, (and with other exclusion criteria) and not used in the study must be provided in much more detail. If data was obtained from maternal and neonatal records, was the data was presumably from electronic records (which is more robust). We need more details about how these adolescent women identified? From age of patients? Please clarify all these points in the paper. 2. The entire literature on FPG confirms that at sensitivities of 80-90%, the specificities are around 60%- 70% (Gestational diabetes mellitus: Screening with fasting plasma glucose. World Journal of Diabetes. 2016; 7:279-289). Even Perucchini's (BMJ. 1999; 319:812–815) well known study at sensitivity of 81% showed specificity of 76%. At higher sensitivities, the specificity would be even lower. Understandably, the population is different as well as the criteria. However, even with IADPSG, a) The study from Brazil (ref 32) showed that at a sensitivity of 92.5%, the specificity was 78.4 and b) The study from UAE (ref 18) at a sensitivity of 88.9%, the specificity was just 60.1%. This is a population where DM is among the highest (second highest for many years) in the world. How is the FPG performing much better in a Mexican adolescent population? Though not many figures are available on adolescents (which makes this paper attractive), one can only speculate about FPG from the available literature from other populations. In general, we go by probabilities, not possibilities: anything is possible. Thus, once it is shown that the data collection is robust, the authors must be able to speculate further at the reasons for this super

	performance of the FPG. Minor comments 1. Page 7, procedure: The laboratory is certified by ISO 9001:2115—this is a management certification program and not specific to laboratories. Incidentally, ISO 15189 is for laboratories. Is the lab certified by a local Mexican laboratory authority? Or by an international agency like College of American Pathologists. This is critical as even a simple test like glucose can vary 10- 25% from the its correct target value (i.e., the bias). 2. The coefficient of variation (CV) must also have the corresponding glucose values. This is because the relationship between analyte is usually a reversed J shaped curve. As the glucose values increase, the CV will decrease and then rise again. 3. The authors persist that Table 2 is needed. It is copied 'at verbatim' from SPSS. SPSS reports values as 64.5 mg/dl and not 64.0 (and so on) mg/dl. When one converts small increments in mg/dl to mmol/l, one lands up with 2-3 similar numbers in mmol/l (due to rounding). The results are about the same and do not matter. It only clutters the table and confuses the lay reader. Thus, in my view, it would be better to add few more FPG values in Table 3 and delete Table 2 completely. It would be much more informative to add more values to table 3 with all the details of PPV, NPV, LR+, LR-.If you read similar studies, almost none give all possible values—and for a reason. I would omit it.

VERSION 2 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 2

Abstract:

C: In the sentence about secondary measures, delete 'explore'.

R: We delete "explore" in the corrected manuscript.

Introduction:

C: Spell out ADA first time used.

R: We spell out ADA in first paragraph that it was mentioned in the corrected manuscript.

C: The sentence "… additionally most Mexican adolescent women are primigravid and have lower socio-economic status than adult women" – add 'pregnant' so that it says "additionally most pregnant Mexican adolescent..".

R: Thanks, we add pregnant in the corrected manuscript.

C: Also, is higher socio-economic status associated with increased risk of GDM in Mexico? The association btw socio-economic status and GDM seems to depend on the country (and income level of that country). For the argument here to make sense, we should be informed how the association is in Mexico.

R: We corrected the paragraph "lower socioeconomic status in Mexico is associated with increased risk of GDM" in the corrected manuscript.

C: The authors mention two different places that screening for GDM among adolescent women is a controversial topic. I think this should be placed together.

R: We agree. It was corrected in the corrected manuscript.

Methods:

C: The authors state that only adolescents with an OGTT between 24-28 weeks of gestation are included. We are informed that this number is 620. It would be useful to know how many 12-19 year old pregnant women did not have the OGTT at 24-28 weeks i.e. the proportion of women actually screened? At least some indication in the discussion about whether most pregnant adolescent women were screened or not.

R: We perform an OGTT 75g-2h to all pregnant women that received prenatal care in our Institution. We added these paragraphs in the corrected manuscript.

"During the study period, there were 11,618 births at our institution of which 2,122 occurred in adolescent women. In total 1,315 pregnant adolescent women had received a 75-g/2-h OGTT. Of these women 364 had received an OGTT between 29 and 35 weeks of gestation and 331 had received an OGTT before 24 weeks of gestation and were not eligible for the study"

"Most adolescent women who do not receive OGTT only received attention for hospitalization or delivery from various causes including: preterm labor, premature rupture of membranes, preeclampsia and labor in active phase. During the study period 32 pregnant adolescent women with a previous diagnosis of some type of diabetes and had not received an OGTT, 19 adolescents with pre-gestational diabetes (8 with type 1 diabetes and 9 with type 2 diabetes), and 13 with GDM were referred to our institution"

C: Would suggest you change the legend of table 1 to 'Characteristics of 493 ….'

R: We change the legend of table 1 in the corrected manuscript.

Discussion

C: On page 18, the authors argue that even though there were no difference in the perinatal outcomes, using the IADPSG criteria could be beneficial because it identifies women at long-term risk for type 2 diabetes and early intervention could reduce the incidence of type 2 diabetes. While I do

largely agree with this, I do believe it needs to be modified slightly and references potentially added. To my knowledge there are still no studies showing that women with GDM according to the IADPSG criteria (but not the former criteria) are at increased risk of t2dm. If the authors know of such studies, I'd recommend they refer to them. Likewise, most studies refer to the DPP papers by Ratner et al or Aroda et al when stating that the incidence of t2dm, can be reduced in women with prior GDM through interventions. The DPP, however, is based on IGT status (and with intervention around 12y after the index GDM pregnancy, so 'early intervention' can be debated. A recent systematic review by Pedersen et al 2017 could perhaps shed some more light on earlier interventions) and not IFG. In other words, I think the authors need to be a bit more careful in their wording here. Rather, I think the authors should put more emphasis on the fact that this is a young and very vulnerable group – thus, IF their conversion rate to t2dm is the same as what has been shown in various studies, they would likely develop t2dm at a very young age. Also, they would be likely to have subsequent pregnancies and recurrent GDM.

R: We agree with the commentary, there are still no studies about the risk of Type 2 diabetes in women with GDM diagnostic by IADPSG, we eliminated this part of the paragraph, and put more emphasis on the risk of recurrent GDM and the risk of type 2 Diabetes at young age.

C: On page 18, the authors write that they 'did not identify any women with type 1 or 2 diabetes during the OGTT between 24 and 28 weeks of gestation that could be attributable to sample size'. How did you assess this? Is this conclusion based on the glucose levels (i.e. diabetes in pregnancy as per WHO 2013 criteria) or based on sustained hyperglycaemia after delivery or how?

R: We asses this affirmation based on OGTT results and in the incidence of pregestacional diabetes that is 1 in 1000 pregnant women.

Overall:

C: There are a number of typos and spelling errors in the corrected version, which should be checked.

R: The corrected manuscript was edited by Scribendi a Professional Editing Service.

Reviewer: 3

Major comments

C: 1. My major concern about how the data was collected is still disconcerting. We need to be reassured that the patients were not collected at random and many of them were not missed out. In three years, there were 620 adolescents with OGTT at 24-28 weeks. Please let us know how large was your hospital and how many deliveries are conducted each year. If 11% of the deliveries are in adolescents, the hospital should have around 6500 deliveries during this period. Furthermore, in any hospital anywhere in the world (tertiary or otherwise), patients (self or physician referred) come during any trimester. So, there must be patients who were picked up in 24-28 weeks by the OGTT who had diabetes. The data on how many women had pregestational DM, (and with other exclusion criteria) and not used in the study must be provided in much more detail. If data was obtained from maternal and neonatal records, was the data was presumably from electronic records (which is more robust). We need more details about how these adolescent women identified? From age of patients? Please clarify all these points in the paper.

R: We clarify how large is our hospital and how many deliveries are conducted each year, we report the number of women with pregestacional diabetes and describe in much more detail how adolescent women were included or excluded. Data was obtained of non-electronic records

C: 2. The entire literature on FPG confirms that at sensitivities of 80- 90%, the specificities are around 60%- 70% (Gestational diabetes mellitus: Screening with fasting plasma glucose. World Journal of Diabetes. 2016; 7:279-289). Even Perucchini's (BMJ. 1999; 319:812–815) well known study at sensitivity of 81% showed specificity of 76%. At higher sensitivities, the specificity would be even lower. Understandably, the population is different as well as the criteria. However, even with IADPSG, a) The study from Brazil (ref 32) showed that at a sensitivity of 92.5%, the specificity was 78.4 and b) The study from UAE (ref 18) at a sensitivity of 88.9%, the specificity was just 60.1%. This is a population where DM is among the highest (second highest for many years) in the world. How is the FPG performing much better in a Mexican adolescent population? Though not many figures are available on adolescents (which makes this paper attractive), one can only speculate about FPG from the available literature from other populations. In general, we go by probabilities, not possibilities: anything is possible. Thus, once it is shown that the data collection is robust, the authors must be able to speculate further at the reasons for this super performance of the FPG.

R: We agree with your commentary, however to our knowledge there is no studies in adolescent women using IADPSG criteria, additionally this is a retrospective analysis and we need to probe this finding in a prospective study, we speculate that the diagnostic capacity of FPG could be explain by maternal age and diagnostic criteria, as we point off in the discussion section. We report with more detail data collection.

Minor comments

1. Page 7, procedure: The laboratory is certified by ISO 9001:2115—this is a management certification program and not specific to laboratories. Incidentally, ISO 15189 is for laboratories. Is the lab certified by a local Mexican laboratory authority? Or by an international agency like College of American Pathologists. This is critical as even a simple test like glucose can vary 10- 25% from the correct target value (i.e., the bias).

R: We have no certification by international agency. The laboratory fulfils the Official Mexican Norm, NOM-007-SSA3-2011, for the organization and functioning of clinical laboratories in Mexico and is certified by the Global Certification Bureau for quality management systems in concordance with the ISO 9001:2015 norm.

C. 2. The coefficient of variation (CV) must also have the corresponding glucose values. This is because the relationship between analyte is usually a reversed J shaped curve. As the glucose values increase, the CV will decrease and then rise again.

R: We agree with the comment, unfortunately during the study period the equipment to measure glucose was in lending. The provider and the equipment were changed in January 2016, so we have not the data requested.

C.3. The authors persist that Table 2 is needed. It is copied 'at verbatim' from SPSS. SPSS reports values as 64.5 mg/dl and not 64.0 (and so on) mg/dl. When one converts small increments in mg/dl to mmol/l, one lands up with 2-3 similar numbers in mmol/l (due to rounding). The results are about the same and do not matter. It only clutters the table and confuses the lay reader. Thus, in my view, it

would be better to add few more FPG values in Table 3 and delete Table 2 completely. It would be much more informative to add more values to table 3 with all the details of PPV, NPV, LR+, LR-.If you read similar studies, almost none give all possible values—and for a reason. I would omit it.

C: We delete table 2, and added 2 glucose values to table 3.

VERSION 3 – REVIEW

REVIEWER	Mukesh M Agarwal California University of Science and Medicine, School of Medicine, USA
REVIEW RETURNED	05-Sep-2017

GENERAL COMMENTS	Reyes-Munoz et al. have submitted a second revised version of their manuscript on screening Mexican adolescents for gestational diabetes mellitus (GDM) by fasting glucose (FPG) using the 75-g OGTT (IADPSG criteria) as gold standard. Major comments: 1. The major problem with this paper remains what one always suspected: data collection. This is obvious after the authors have elucidated details of women included in the study (in their second revision). In the total study period, 1315 adolescent girls underwent the OGTT in weeks 0-24, 24-28 and 28-39, as follows: 331 adolescents,620 adolescents and 364 adolescents respectively. The authors initially included only 493 (of 620) girls from 24-28 weeks; of these, 331 (i.e., only 25% of the entire cohort) were used leaving out another 127 girls for a variety of reasons. Then, the authors back titrate and apply their findings to all 1315 adolescents undergoing OGTT anytime in pregnancy as mentioned throughout the manuscript (e.g., 'Conclusion' in abstract and 'Strength and limitations of this research'). Furthermore, if data was missing with incomplete records in 72 women, how can table 1 & 3 include these women without bias. 2. The error committed by the authors is very common: applying findings of the "sickest of the sick" to the "wellest of the well" (Evidence-Based Diagnosis: Thomas B. Newman, Michael A). In other words, the test population and the population to which the test is applied must be exactly similar. The authors' test population is too selective, but applied generally (more examples, Page 15 the first line of discussion and Page 18, line 46: A fasting glucose of 90 mg/dl could be a useful screening test in Mexican adolescents). If a patient walks in at say 29 weeks gestation, these findings cannot be applied. When evaluating tests for sensitivity/specificity, etc., for correct interpretations this mistake cannot be made. 3. The authors' efforts are not lost. They should include all the women with OGTT complete data (with some exceptions for obvious reasons) irrespective of the trimester. This will increase their numbers and show a more realistic picture. Despite recommendations of expert committees, this is how data is applied in all hospitals and would be more realistic and more useful. I know of no hospital which restricts OGTT to 24-28 weeks gestation only as it is not only unrealistic but almost impossible to follow. Thus, they need to redo Table 2 and Figure 1 with this new information. The outcome can be restricted to the select patient cohort as they have done.

	Minor comments: 1. Abstract, Results: Page 2, line 42. Rephrase in this format: GDM was present in 31 (6.3%) women. The numbers may change when they include more women in the cohort (major comment 1). 2. Introduction. Page 6, lines 15-21. Paraphrase. … recommend that the fasting plasma glucose can be used to decide if the OGTT is needed or not. This would ease the burden on the laboratory and save resources as the IADPSG recommendation to make every pregnant woman undergo the 75-g OGTT is too demanding. 3. Page 6, line 31. Delete Our hypothesis is that …..GDM. 4. Page 17, lines 32-37. Remove We did not include…….GDM. 5. Page 5, Lines28-35. Include acronyms for organizations which will be repeated later in MS. Eg WHO. All organizations are repeated on page 18, lines 8-17. There is no need to do so. Once the authors fix these obvious errors, this paper should provide useful data on GDM in adolescents.

VERSION 3 – AUTHOR RESPONSE

Reviewer: 3

Reviewer Name: Mukesh M Agarwal

Institution and Country: California University of Science and Medicine, School of Medicine, USA

Please state any competing interests or state 'None declared': None

Please leave your comments for the authors below

Reyes-Munoz et al. have submitted a second revised version of their manuscript on screening Mexican adolescents for gestational diabetes mellitus (GDM) by fasting glucose (FPG) using the 75-g OGTT (IADPSG criteria) as gold standard.

Major comments:

C. 1. The major problem with this paper remains what one always suspected: data collection. This is obvious after the authors have elucidated details of women included in the study (in their second revision). In the total study period, 1315 adolescent girls underwent the OGTT in weeks 0-24, 24-28 and 28-39, as follows: 331 adolescents,620 adolescents and 364 adolescents respectively. The authors initially included only 493 (of 620) girls from 24-28 weeks; of these, 331 (i.e., only 25% of the entire cohort) were used leaving out another 127 girls for a variety of reasons. Then, the authors back titrate and apply their findings to all 1315 adolescents undergoing OGTT anytime in pregnancy as mentioned throughout the manuscript (e.g., 'Conclusion' in abstract and 'Strength and limitations of this research'). Furthermore, if data was missing with incomplete records in 72 women, how can table 1 & 3 include these women without bias?

R: We excluded women before 24 and after 28 weeks of gestation following the recommendations of most international associations regarding to the optimal time to perform a screening of GDM. However, we agree with the reviewer and in the revised version of the manuscript, we are including all adolescent with OGTT during the study period irrespective of the trimester that fulfill the inclusion criteria (1061 of 1315), because we considered that is most appropriate to the "real" clinical practice.

C. 2. The error committed by the authors is very common: applying findings of the "sickest of the sick" to the "wellest of the well" (Evidence-Based Diagnosis: Thomas B. Newman, Michael A). In other words, the test population and the population to which the test is applied must be exactly similar. The authors' test population is too selective, but applied generally (more examples, Page 15 the first line of discussion and Page 18, line 46: A fasting glucose of 90 mg/dl could be a useful screening test in Mexican adolescents). If a patient walks in at say 29 weeks gestation, these findings cannot be applied. When evaluating tests for sensitivity/specificity, etc., for correct interpretations this mistake cannot be made.

R: As we mentioned before, we agree with the reviewer, so we decided to include all the women with OGTT that fulfill the inclusion criteria.

C. 3. The authors' efforts are not lost. They should include all the women with OGTT complete data (with some exceptions for obvious reasons) irrespective of the trimester. This will increase their numbers and show a more realistic picture. Despite recommendations of expert committees, this is how data is applied in all hospitals and would be more realistic and more useful. I know of no hospital which restricts OGTT to 24-28 weeks gestation only as it is not only unrealistic but almost impossible to follow. Thus, they need to redo Table 2 and Figure 1 with this new information. The outcome can be restricted to the select patient cohort as they have done.

R: In the corrected manuscript we analyzed 1061 of 1315 women. Figure 1 and tables 1, 2 and 3 were corrected according with the new information.

Minor comments:

1. Abstract, Results: Page 2, line 42. Rephrase in this format: GDM was present in 31 (6.3%) women. The numbers may change when they include more women in the cohort (major comment 1).

R. The line was rephrased, according with the reviewer recommendation.

2. Introduction. Page 6, lines 15-21. Paraphrase. … recommend that the fasting plasma glucose can be used to decide if the OGTT is needed or not. This would ease the burden on the laboratory and

save resources as the IADPSG recommendation to make every pregnant woman undergo the 75-g OGTT is too demanding.

R: We attended the reviewer recommendation.

3. Page 6, line 31. Delete Our hypothesis is that …..GDM.

R: We attended the reviewer recommendation.

4. Page 17, lines 32-37. Remove We did not include…….GDM.

R: We attended the reviewer recommendation.

5. Page 5, Lines 28-35. Include acronyms for organizations which will be repeated later in MS. Eg WHO. All organizations are repeated on page 18, lines 8-17. There is no need to do so.

R: We now included acronyms for each organization in the corrected manuscript.

VERSION 4 – REVIEW

REVIEWER	Mukesh M Agarwal California University of Science and Medicine, California, USA
REVIEW RETURNED	18-Jan-2018

GENERAL COMMENTS	Reyes-Munoz et al. have submitted another revision of their manuscript on screening Mexican adolescents for GDM. Major comments: The manuscript has reached a scientifically acceptable stage; however, the authors need major revisions in language. They need to consult a language editing service/colleagues to rephrase major portions of the manuscript. 1. The authors should spell out in the conclusions (in abstract and or manuscript): A FPG threshold of 80 mg/dl would miss n (%) women with GDM, pick up n (%) women without GDM and avoid n(%) OGTTs. 2. Please do not use first person (we, our) in the writing, but third person. 3. In conclusions (page 18, line 33), please do not do not talk about costs as that in not something that you have worked out. For the sake of argument, -if one misses women in screening, these women could have abnormal babies and to take care of them could increase overall costs.

	4. The number of references should be cut down. 5. I have tried to work on their abstract and strengths and limitations as I would have presented it. ABSTRACT Objective: To evaluate fasting plasma glucose (FPG) as a screening test for gestational diabetes mellitus (GDM) in Mexican adolescents using the International Association of Diabetes and Pregnancy Study Groups criteria. Design: Retrospective cohort study Setting: Level-three medical institution in Mexico City. Participants: The study population comprised of 1061 adolescent women, aged 12 to 19 years with singleton pregnancy, who underwent a 75-g oral glucose tolerance test (OGTT) between 11 and 35 weeks of gestation. Primary and secondary outcome measures: The sensitivity(Sn), specificity(Sp), positive and negative predictive values (PPV and NPV, respectively), and positive and negative likelihood ratios (LR(+) and LR(-), respectively) with 95% confidence intervals for selected FPG cut-offs were compared. Secondary measures were perinatal outcomes in women with and without GDM. Results: GDM was present in 71 (6.7%) women. The performance of FPG at thresholds of ≥ 80 (4.5 mmol/L), 85 (4.7 mmol/L), and 90 mg/dL (5.0 mmol/L) was as follows, respectively: Sn: 97%, 94%, and 91%; Sp: 50%, 79%, and 97%; PPV: 12%, 23%, and 64%; NPV: 99% for all three cut-offs; LR (+): 1.9, 4.3, and 26.7; and LR (-): 0.06, 0.07, and 0.09, respectively. No significant differences in perinatal outcomes were found between adolescents with and without GDM. Conclusions: A FPG cut-off of ≥90 mg/dL (5.0 mmol/L) is ideal for GDM screening in Mexican adolescent women. Strengths and limitations of this research • A fasting glucose cut-off of ≥90 mg/dL (5.0 mmol/L) is ideal for GDM screening in Mexican adolescent women. • This is the first study in Mexico and Latin America addressing the prevalence of GDM in adolescent women using IADPSG criteria. • The study was retrospective, with findings applicable to only Mexican, and, potentially, Latin women. • The diagnostic validity of the test was not confirmed in a second independent population. • The sample size is limited to compare perinatal outcomes. In summary, since there is a paucity of data on adolescents with GDM, this study would add to the world's literature. Finally, one must commend the authors on their tenacity ; indeed, it is remarkable.

VERSION 4 – AUTHOR RESPONSE

Editorial Requests:
Editors comments to Author:

1. C. Please ensure that you improve the quality of language in your manuscript, either with the assistance of an English-speaking colleague or with a professional copyediting agency.
R. A professional copyediting agency edited the corrected manuscript. We thank Audrey Holmes, MA, from Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

2. C. Along with your revised manuscript, please include a copy of the STARD checklist indicating the page/line numbers of your manuscript where the relevant information can be found (http://www.stard-statement.org/)
R. A copy of the STARD checklist was included.

3. C. Please improve the reporting of the statistics throughout your manuscript. For example, please include the 95% CI for the reporting of all likelihood ratios including those in the abstract.
R. The reporting of the statistics was improved

4. C. Please include a statement relating to the ethical approval obtained for your study.
R. We included a statement relating to the ethical approval obtained for this study.

Reviewer(s)' Comments to Author:

Reviewer: 1
Reviewer Name: Mukesh M Agarwal

Institution and Country: California University of Science and Medicine, California, USA

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
Reyes-Munoz et al. have submitted another revision of their manuscript on screening Mexican adolescents for GDM.

Major comments:
C. The manuscript has reached a scientifically acceptable stage; however, the authors need major revisions in language. They need to consult a language editing service/colleagues to rephrase major portions of the manuscript.
R. A professional copyediting agency edited the corrected manuscript. We thank Audrey Holmes, MA, from Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

1. C. The authors should spell out in the conclusions (in abstract and or manuscript): A FPG threshold of 80 mg/dl would miss n (%) women with GDM, pick up n (%) women without GDM and avoid n(%) OGTTs.
R: The paragraph "A FPG cut-off of ≥90 mg/dL (5.0 mmol/L) is ideal for GDM screening in Mexican adolescent women. A FPG threshold of 90 mg/dl would miss 6 (8.5%) women with GDM, pick up 34 (3.4%) women without GDM and avoid 962 (90.7%) OGTTs" was added to the corrected manuscript.

2. C. Please do not use first person (we, our) in the writing, but third person.
R: This change was performed in the revised manuscript.

3. C. In conclusions (page 18, line 33), please do not do not talk about costs as that in not something that you have worked out. For the sake of argument, -if one misses women in screening, these women could have abnormal babies and to take care of them could increase overall costs.
R: The paragraph about cost was eliminated.

4. C. The number of references should be cut down.
R: References were cut down from 40 to 34.

5. C. I have tried to work on their abstract and strengths and limitations as I would have presented it.
R: Thanks very much. The suggested abstract was included in the corrected manuscript.

ABSTRACT
Objective: To evaluate fasting plasma glucose (FPG) as a screening test for gestational diabetes mellitus (GDM) in Mexican adolescents using the International Association of Diabetes and Pregnancy Study Groups criteria.
Design: Retrospective cohort study
Setting: Level-three medical institution in Mexico City.
Participants: The study population comprised of 1061 adolescent women, aged 12 to 19 years with singleton pregnancy, who underwent a 75-g oral glucose tolerance test (OGTT) between 11 and 35 weeks of gestation.
Primary and secondary outcome measures: The sensitivity(Sn), specificity(Sp), positive and negative predictive values (PPV and NPV, respectively), and positive and negative likelihood ratios (LR(+) and LR(-), respectively) with 95% confidence intervals for selected FPG cut-offs were compared. Secondary measures were perinatal outcomes in women with and without GDM.
Results: GDM was present in 71 (6.7%) women. The performance of FPG at thresholds of ≥ 80 (4.5 mmol/L), 85 (4.7 mmol/L), and 90 mg/dL (5.0 mmol/L) was as follows, respectively: Sn: 97%, 94%, and 91%; Sp: 50%, 79%, and 97%; PPV: 12%, 23%, and 64%; NPV: 99% for all three cut-offs; LR (+): 1.9, 4.3, and 26.7; and LR (-): 0.06, 0.07, and 0.09, respectively. No significant differences in perinatal outcomes were found between adolescents with and without GDM.
Conclusions: A FPG cut-off of ≥90 mg/dL (5.0 mmol/L) is ideal for GDM screening in Mexican adolescent women.

Strengths and limitations of this research
• A fasting glucose cut-off of ≥90 mg/dL (5.0 mmol/L) is ideal for GDM screening in Mexican adolescent women.
• This is the first study in Mexico and Latin America addressing the prevalence of GDM in adolescent women using IADPSG criteria.
• The study was retrospective, with findings applicable to only Mexican, and, potentially, Latin women.
• The diagnostic validity of the test was not confirmed in a second independent population.
• The sample size is limited to compare perinatal outcomes.

C. In summary, since there is a paucity of data on adolescents with GDM, this study would add to the world's literature. Finally, one must commend the authors on their tenacity ; indeed, it is remarkable.
R: Thanks.

FORMATTING AMENDMENTS (if any)
Required amendments will be listed here; please include these changes in your revised version:
R: We included these changes in the revised version.