Reviewer's report

**Title:** Elevated maternal lipids in early pregnancy are not associated with risk of intrapartum caesarean in overweight and obese nulliparous women

**Version:** 1  **Date:** 20 February 2013

**Reviewer:** Eleazar Soto

**Reviewer's report:**

This is a secondary analysis of the SCOPE study which is a multicentre prospective cohort study intended to develop screening tests for prediction of preeclampsia, spontaneous preterm birth and small for gestational age neonates. For this analysis, the authors evaluated the effect of serum cholesterol in the early second trimester (14-16 weeks) and the effect of failure to progress during labor and requiring a cesarean delivery. The authors reported that serum cholesterol concentrations at 14-16 weeks of gestation were not higher among overweight and obese women who had a first stage caesarean for failure to progress multivariable analysis that provided risk factors associated with arrest of labor that required a cesarean delivery.

This manuscript is well written, short and easy to follow. The primary result of the study (association between cholesterol levels and arrest of labor) was not significant. However, there are several limitations of the study. For example, the use of any maternal blood marker (cholesterol) in the early second trimester to predict arrest of labor is quite challenging. Could the authors add to the discussion section of the manuscript any marker in the second or third trimester that could predict arrest of labor (or be associated with cesarean delivery)? The authors acknowledged in the discussion section that perhaps a closer cholesterol serum evaluation to the delivery period could provide additional information but thus far their testing hypothesis was not valid. Another important limitation of the study is the definition of arrest of labor provided by the authors (see below); this will limit the extrapolation of their results to other similar cohorts and should be acknowledge by the authors. Before this manuscript is accepted for publication several issues should be addressed:

**Abstract:**

1. Please specify at the conclusion section what other risk factors have been identified. (Minor Essential Revisions)

2. Key words: Please use different keywords not present in the title (Minor Essential Revisions)

**Background**

1. Can the authors provide a reference for the following statement (page 2, 2nd
paragraph): “The relative hyperlipidaemia of normal pregnancy is exaggerated in obese women (REF)...” It appears that the reference 7 supports only the subsequent statement in the sentence “and it has been speculated that obesity related dyslipidaemia may contribute to altered myometrial cell signalling, dysfunctional labour and increased caesarean delivery for failure to progress” but not the first part of the sentence. (Minor Essential Revisions)

Methods

1. Can the authors mention that this is a secondary analysis of the SCOPE study and provide a citation at the beginning of the methods section? (Minor Essential Revisions)

2. Which maternal BMI was used for the analysis: Pre-pregnancy BMI or current BMI at the time of evaluation during pregnancy? Please specify. (Major Compulsory Revisions)

3. Can the authors provide the formula for BMI calculation that was used? (Major Compulsory Revisions)

4. Please provide under what circumstances the serum cholesterol was measured at 14-16 weeks. Was the serum cholesterol measured in regular prenatal clinic appointments or in patients who were evaluated at the ER? Was the information available for clinical care? (Minor Essential Revisions)

5. Please provide (briefly) which technique was used to measure the cholesterol profile in the study population? What are the characteristics of the test used (sensitivity, accuracy, variability etc)? (Major Compulsory Revisions)

6. Was the serum cholesterol measured the same day of the blood draw or the analysis was performed using stored samples at a later day. Please specify. (Minor Essential Revisions)

7. Please spell out GP (page 4) (Minor Essential Revisions)

8. Please provide the original reference for the definition of preeclampsia used in reference 8 and not reference 8. (Minor Essential Revisions)

9. The definition used by the authors for active labor appears to be quite aggressive (>3cm). If patients are labeled in active labor at > 3 cm of dilatation a proportion of patients will be called arrest of dilatation in the active phase while they are actually in the latent phase of labor, this is major issue of the study regarding the extrapolation of the authors results to other populations. The classic definition of active labor is 4 cm (Reviewed by Ling M. et al. Clin Obstet Gynecol. 2006 Sep;49(3):585-93); however, most recent evidence suggests that perhaps for primiparous women the active phase of labor does not start after 6 cm of dilatation (Zhang J. et al. Obstet Gynecol. 2010 Dec;116(6):1281-7). Therefore, the diagnosis of arrest disorder should not be made before the patient has entered into the active phase which appears to be early before 6 cm. (Major Compulsory Revisions)
10. Was the diagnosis of arrest of labor during the first stage of labor made after an adequate attempt to allow the patient to labor (use of oxytocin, rupture of membranes, use of intra-uterine catheter to assess adequate contractions, etc). This information is not provided in the methods section and is essential for the description of the study, otherwise, without standardization the results are difficult to interpret. (Major Compulsory Revisions)

11. How many patients had combined indications for cesarean delivery? (Major Compulsory Revisions)

12. Regarding the inclusion of diabetic patients; how many were pre-gestational diabetes and of those with gestational diabetes how many were on medical therapy (i.e insulin or glyburide).

13. Regarding the sample size calculation. Can the authors justify the use of a difference of 0.2 mmol/L of total cholesterol to be clinically meaningful? Normal cholesterol values should be below 5.2 mmol/L therefore, a difference of 0.2 mmol/L does not appear to have any major significance. (Major Compulsory Revisions)

Results

1. Perhaps including the cholesterol values in the first paragraph of the result section would be useful to the reader. (Minor Essential Revisions)

2. Please refer to table 1 the following statement (page 6, 2nd paragraph): “There were also no differences in other lipid parameters.” (Minor Essential Revisions)

3. Can the authors provide the cervical dilatation at the time when it was decided to perform a cesarean delivery for failure to progress? (Major Compulsory Revisions)

4. Can the author perform a sub-analysis dividing overweight from obese women? Are there any differences between the groups? Moreover, do the authors have enough patients to perform another analysis with the different class of morbidity obesity (I, II and III). This information will enhance the manuscript. (Major Compulsory Revisions)

5. Can the authors explain why triglycerides were not measured? (Minor Essential Revisions)

6. Was an estimated fetal weight (either by ultrasound or Leopold maneuvers) available to the clinician? This information could create a bias, as those with larger estimated fetal weight may be more prone for cesarean delivery due to the potential diagnosis of “macrosomia”.

7. Can the authors provide the cholesterol levels at 14-16 weeks of gestation in the normal BMI group? This information would be interesting and could provide useful information to the author’s hypothesis. (Discretionary Revisions)

Discussion
1. Please mention in this section the limitations of the study (i.e secondary analysis, definition of arrest of labor etc) (Major Compulsory Revisions)

2. Can the authors comment regarding the difference in birth weight between the groups as well as increase rate of induction in the group who had “failure to progress”? (Major Compulsory Revisions)

Table 1.
Of the patients diagnosed with gestational diabetes, how many required medical therapy (insulin, glyburide)? (Major Compulsory Revisions)

Can the authors provide the head circumference and cord pH of the neonates for each group? (Discretionary Revisions)

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.