Reviewer's report

Title: Growth factor concentrations and their placental mRNA expression are modulated in gestational diabetes mellitus: possible interactions with macrosomia

Version: 2 Date: 21 February 2009

Reviewer: Robert Lindsay

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Grissa et al Growth factor concentrations and their placental mRNA expression...

The authors have examined a number of growth factors in serum of mothers with gestational diabetes and their offspring at birth. This is an important area. They present a large number of changes in serum growth factors - predominantly with an increase in women with gestational diabetes and their babies. This looks like an interesting data collection and would merit more detailed analysis to try to tease out the factors that are most closely associated with fetal overgrowth in GDM.

Major Compulsory Revisions

1) methods: the main criticism is that the hypothesis is not clearly stated. Two groups have been selected – control women and women with GDM with really very marked macrosomia (2SD above population mean). It would appear to have made sense to have included macrosmic offspring of normal glucose tolerant women and less marked degree of fetal overgrowth in the GDM women. It is impossible to pick out what is simply response to maternal hyperglycaemia and what is central to fetal overgrowth. It is assumed that the authors wished to determine what factors were most closely associated with fetal overgrowth. Again many of the growth factors may be correlated (data not given on this) and it would make sense to perform multivariate analysis to try to distinguish this - although I accept that the study may be too small to investigate this efficiently.

2) How were these growth factors and binding proteins selected for example did the authors consider measurement of other IGF binding proteins?

3) There is no account of maternal obesity. Data on this should be included in table 1. Maternal obesity may be an independent risk factor (beyond glycaemia) for macrosomia in their sample and it would be of interest to know which fetal growth factors might correspond to maternal obesity rather than glycaemia. The authors should consider analysis of this.

4) The description of gestational diabetes diagnosis is incomplete. Brief description of diagnostic criteria used and management should be included. HbA1c measurement is surprisingly high for a treated population.

5) We need normal range for HbA1c for their assay.
6) Blood sample collection- it is stated that all samples were taken fasting. Further details on maternal management at the time of delivery is important. For example were these all vaginal deliveries? Were mothers treated with intravenous glucose and insulin at the time of delivery?

7) Discussion- again there is a lack of focus. And much of the review of literature is selective. For example not all studies of offspring of women with diabetes find an increase in IGF-1 but only references finding an increase are given.

Minor Essential Revisions
Page 5 line 4: “apolipoproteines”

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

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests