

## **NZSSD EXPERT OPINION**

### **Comment on the HAPO Study**

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The diagnostic criteria for gestational diabetes (GDM) were originally formulated for their ability to predict the later development of type 2 diabetes in the mothers, rather than adverse pregnancy outcomes. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study<sup>1</sup> was designed to determine the impact on a number of pregnancy outcomes of varying degrees of glycaemia, up to a fasting blood glucose  $<5.8$  and 2 hr values  $<11.1$  mmol/l on a 75g GTT performed at 24-32 weeks' gestation. The strengths of the study include its very large size (24,505 pregnant women took part) and that it involved individual centres from four continents. Clinicians were blinded as to the result of the GTT.

The most important finding was that there was no association between perinatal mortality and higher blood glucose levels. A number of neonatal morbidities (such as shoulder dystocia and premature delivery) were associated with higher blood glucose, but the rate of such complications was generally low. Admissions to neonatal special care facilities were also related to blood glucose levels, but there was striking between-centre variation (the rates of admission varied from 3 to 29%), suggesting that local practice, rather than blood glucose is the main determinant of this particular outcome. The study did find a continuous relationship between birth weight and maternal blood glucose (both fasting and post glucose load). There was also some association between higher maternal blood glucose and the occurrence of neonatal hypoglycaemia, but this relationship disappeared when a variety of other maternal characteristics, including body mass index, were taken into account; as did the relationship between higher blood sugar and the need for primary caesarean section. A surrogate measure of uncertain significance, the cord blood C-peptide level, was strongly associated with maternal blood glucose measures.

Overall, the results confirm earlier findings that birth weight is related in a continuous fashion to maternal blood glucose<sup>2</sup>. The relationships between maternal glycaemia and primary caesarean section are confounded by maternal body mass. Perinatal mortality and morbidity were low. Whilst some of the morbidities were associated with maternal glucose, it is impossible to assess from the paper the 'number-needed-to-treat' to avoid such outcomes (even assuming that treatment is effective). The HAPO data do not provide compelling reasons for reducing the diagnostic thresholds for GDM. Indeed, the continuous nature of all the relationships argues indicates that there is no particular blood glucose threshold for the development of perinatal morbidity.

1. HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, Hadden DR, McCance DR, Hod M, McIntyre HD, Oats JJ, Persson B, Rogers MS, Sacks DA. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med* 2008; 358:1991-2002.
2. Naylor CD, Sermer M, Chen E, Sykora K. Cesarean delivery in relation to birthweight and gestational glucose tolerance: pathophysiology or practice style? *JAMA* 1996; 275: 1165-1170