

Plenary Session / EC – US Workshop: Early life programming of obesity

Lecture 4: Gestational Diabetes, A risk factor for obesity and diabetes in later life

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Abstract

Background: Data from animal models and human clinical and epidemiological follow-up studies have provided strong evidence that exposure to the metabolic environment of pre-existing diabetes or gestational diabetes mellitus (GDM) increases the risk of obesity and altered glucose metabolism in adolescence and adulthood (diabetes begets diabetes). It has been estimated that such exposure has been a major contributor to the continued increase in the prevalence of type 2 diabetes in the Pima Indians. Furthermore, the risk of obesity and/or diabetes in the offspring is higher when mother's glucose levels during pregnancy are higher. However, the extent to which intrauterine exposure to maternal diabetes or GDM contributes to the overall risk of diabetes and obesity in other populations is not known. Fetal hyperinsulinism has been identified as a risk factor, but studies examining perinatal risk factors are limited. This is addressed in the Hyperglycemia & Adverse Pregnancy Outcome (HAPO) study.

HAPO Study: 25,505 pregnant women (15 centers, 9 countries) underwent 75 gm oral glucose tolerance tests (OGTTs) at 24-32 weeks gestation. Results remained blinded if fasting plasma glucose (FPG) was no greater than 105 mg/dL (5.8 mmol/L) and 2-hr plasma glucose (2-hrPG) no greater than 200 mg/dL (11.1 mmol/L). Primary outcomes were: birthweight above the 90th percentile; primary cesarean delivery; clinical neonatal hypoglycemia; cord C-peptide above the 90th percentile. Secondary outcomes were: premature delivery (<37 weeks); shoulder dystocia/birth injury; intensive neonatal care; hyperbilirubinemia and preeclampsia. Among 23,316 blinded participants, adjusted odds ratios (OR) (95% confidence intervals [CI]) for glucose higher by one standard deviation (SD) were respectively 1.38 (1.32-1.44) for FPG (SD - 6.9 mg/dL), 1.46 (1.39-1.53) for 1-hr PG (SD - 30.9 mg/dL), and 1.38 (1.32-1.44) for 2-hr PG (SD - 23.5 mg/dL) for birthweight above the 90th percentile; 1.55 (1.47-1.64), 1.46 (1.38-1.54), and 1.37 (1.38-1.44) for cord C-peptide above the 90th percentile; 1.11 (1.06-1.15), 1.10 (1.06-1.15), and 1.08 (1.03-1.12) for primary cesarean delivery; and 1.08 (0.98-1.19), 1.13 (1.03-1.26), and 1.10 (1.00-1.12) for neonatal hypoglycemia. There were no obvious thresholds at which risks increased. Significant associations were also observed for secondary outcomes, although these tended to be weaker, with OR (CI) 1.21 (1.13 - 1.29), 1.28 (1.20 - 1.37), and 1.28 (1.20 - 1.37) for preeclampsia; 1.18 (1.04 - 1.33), 1.23 (1.09 - 1.38), and 1.22 (1.09 - 1.37) for shoulder dystocia or birth injury; 1.05 (0.99 - 1.11), 1.18 (1.12 - 1.25), and 1.16 (1.10 - 1.23) for premature delivery; 1.00 (0.95 - 1.05), 1.11 (1.05 - 1.17), and 1.08 (1.02 - 1.13) for hyperbilirubinemia; and 0.99 (0.94 - 1.05), 1.07 (1.02 - 1.13), and 1.09 (1.03 - 1.14) for intensive neonatal care. These results that are adjusted for potential confounders (including field center, age and BMI), in general, show slight to moderate attenuation when compared to the unadjusted associations, and the associations do not differ among field centers. This means that the results of the HAPO study are applicable to all of the centers.

Conclusions: The HAPO Study results indicate strong continuous associations of maternal glucose levels below those diagnostic of diabetes with birthweight, cord C-peptide levels and with preeclampsia. Efforts are currently being made to use these associations and results of other studies to develop outcome based criteria for the diagnosis and classification of disturbances in glucose metabolism during pregnancy. The risks for obesity and altered metabolism in childhood remain to be determined.