Gestational diabetes mellitus: consequence and inheritance

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ABSTRACT

This PhD dissertation comprises a review and three original papers. The research was carried out at the Centre for Diabetes and Pregnancy, Department of Obstetrics, Rigshospitalet and at Steno Diabetes Centre in 2000-02.

The aims were 1) to study the incidence of diabetes, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) in two cohorts of women with a history of diet-treated gestational diabetes (GDM), 2) to search for predictive factors for the long-term development of diabetes in these women, 3) to study the prevalence of the metabolic syndrome, a well-known risk factor for cardiovascular disease, and 4) to examine some aspects of the genetic background for GDM and later development of type 2 diabetes. The study population consisted of two cohorts, the *old cohort* with diet-treated GDM during 1978-85 and the *new cohort* with GDM during 1987-96. Sixty-four per cent (n=481) of the total cohort participated in the follow-up. Median age at follow-up was 43 years. Women without known diabetes at follow-up had a 75g oral glucose tolerance test. Cardiovascular risk factors were evaluated in all subjects and compared to an age-matched control group (n=1000). Historical data were collected from medical records.

Forty per cent of the women with previous GDM had diabetes and 26% IFG/IGT. Independent predictors for overt diabetes were: IGT 2 months after delivery, pre-pregnancy overweight, diagnosis of GDM early in pregnancy and a high fasting blood glucose at GDM diagnosis. The prevalence of diabetes was similar in the two cohorts although the *old cohort* was followed for 11 years longer after pregnancy. This could primarily be ascribed the fact that the *new cohort* was substantially more overweight. However, our data also indicate that the *new cohort* was at increased risk independently of the other tested variables. We speculate that this is caused by a change towards a less healthy lifestyle in the *new cohort* compared to the *old cohort*. Overall the prior GDM women had a more severe cardiovascular health profile with a prevalence of the metabolic syndrome at 38%, which was three fold increased compared to a control group.

A polymorphism with a known interaction with glucose stimulated insulin secretion, the Ala/Val98 of the hepatocyte nuclear factor-1α gene, was examined for the association with GDM and for the physiological effect on serum insulin and C-peptide secretion during an OGTT. No association was shown but a significantly reduced secretion of insulin and C-peptide was found in a glucose tolerant control group.

Women with prior GDM have a high risk of developing glucose intolerance and the metabolic syndrome. They should be offered regular control of glucose metabolism and cardiovascular risk profile together with intervention to delay or stop the progression to cardiovascular disease.