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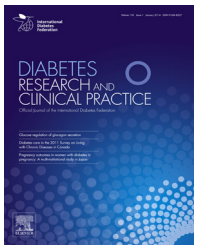

Gestational diabetes: Glycaemic predictors for fetal macrosomia and maternal risk of future diabetes

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ABSTRACT

Aims: To investigate how glucose levels at diagnosis of gestational diabetes (GDM) are associated with infant birth weight and long-term risk of manifest diabetes mellitus in the mother.

Methods: In a case control study GDM pregnancies ($n = 2085$) were compared with non-GDM pregnancies matched for day of delivery and obstetric unit ($n = 3792$). GDM was defined as capillary blood glucose (cB-glucose) ≥9.0 mmol/l (plasma glucose ≥10.0 mmol/l) after a 75 g oral glucose tolerance test (OGTT). The GDM cohort were followed up 8.5–13.5 yrs after initial diagnosis with a questionnaire, answered by 1324 GDM women (65%).

Results: GDM women had higher mean infant birth-weight compared with controls (3682 g vs. 3541 g, $P < 0.001$). In multiple linear regression analysis, birth weight was positively correlated to fasting cB-glucose at GDM diagnosis ($P < 0.001$), increased week of gestation ($P < 0.001$) and BMI before pregnancy ($P < 0.003$), while 2 h OGTT cB-glucose values ≥9.0 mmol/l were not related. Infants born to mothers with fasting cB-glucose ≤4.5 mmol/l had no increased mean birth-weight or macrosomia (≥4500 g) compared to controls. In the follow up 334/1324 women (25%) of the GDM women had developed diabetes, 215 type 2 diabetes, 46 type 1 diabetes and 72 unclassified diabetes. In logistic regression fasting cB-glucose and 2 h OGTT cB-glucose at diagnosis of GDM as well as BMI >25 and origin outside Europe were risk factors for manifest diabetes.

Conclusions: Fasting blood glucose at diagnosis of GDM gives important information besides 2 h OGTT glucose about pregnancy outcome and future risk for maternal diabetes.

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1. Introduction

Gestational diabetes mellitus (GDM) is associated with greatly increased risks for various perinatal complications like preeclampsia, fetal macrosomia, shoulder dystocia and cesarean section. In addition the mother runs a much increased risk of developing overt diabetes later in life [1]. A number of studies have been published aiming at defining the best predictor of adverse maternal, fetal and neonatal morbidity [2–7] and/or subsequent development of diabetes [8–12] and various criteria for the diagnosis of GDM have been presented. In the WHO technical report 1980 the 75 g OGTT, which is now universally used, was introduced and it was recommended that the same diagnostic levels should be used for IGT in pregnant and non-pregnant women [13]. In Sweden the criteria given by the Diabetic Pregnancy Study Group (DPSG) of EASD (European Association for the Study of Diabetes), which takes into account physiological changes during pregnancy, have been used for many years [14,15]. Recently WHO and ADA has recommended the IADPSG criteria [16] which are based on data from the HAPO (Hyperglycemia Adverse Pregnancy Outcome) study [6].

It must be emphasized that it is difficult for several reasons to compare results of different studies [17]. Some of the reasons include factors such as differences in GDM screening method, family history of diabetes, maternal age, ethnicity, BMI, amount of glucose administrated (100, 75 or 50 g),blood sampling site, glucose analysis, classification criteria employed in determining perinatal outcome and length of follow-up time after the index pregnancy.

The aim of the present study was to validate the DPSG diagnostic criteria [14,15] in a large cohort of pregnancies by analyzing adverse pregnancy outcome variables and the future risk of developing diabetes in the mother. The results are clinically important and can be expected to provide care givers and women with GDM and their families with reliable information on the short and long term consequences of the condition.

2. Materials and methods

The study includes two parts: (1) a case control study and (2) a prospective cohort study of cases with previous GDM (Fig. 1).

Study 1: All maternal health care clinics in Sweden were invited to prospectively register women diagnosed with GDM during the period January 1, 1995 to December 31 1999. A registration form was used which included: Indication for performing an OGTT, date for OGTT, fasting and 2 h cB-glucose levels, civic number, name, address, country of birth, height, pre-pregnancy weight, estimated day for delivery. Registration forms were collected at the Department of Public Health and Clinical Medicine, Umeå University. For registered women data on gestational age at delivery and birth weight were collected from the Swedish Medical Birth Registry (MBR) [18]. Total number of deliveries in Sweden 1995 to 1999 and country of birth of the mother were also obtained from MBR.

For each woman with GDM, anonymous data was obtained from the MBR for two controls without GDM given birth the day before and the day after the registered woman at the same obstetric unit. Data obtained as described above was used for the case control study.

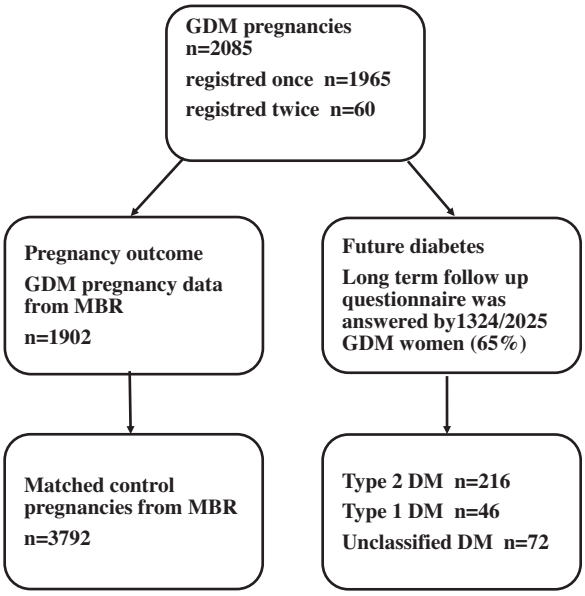

Fig. 1 – *Study flow chart*. Between 1995 and 1999, incident cases with GDM were reported on a nationwide base and in total 2085 pregnancies were reported in 2025 unique individuals. Pregnancy outcome was available for 1902 of these GDM women in the Swedish Medical Birth Registry (MBR). For comparison anonymous data from controls (*n* = 3792) without GDM given birth before and after the registered woman at the same obstetric unit was also collected from MBR. In the follow-up study 1324 (65% of the entire cohort) answered the questionnaire and 334/1324 (25%) women reported they had been diagnosed with diabetes mellitus.

Study 2: Using the 10 digit personal civic number it was possible to obtain addresses to women with previous GDM (Fig. 1). Questionnaires were sent during 2008 to these women, with questions including which treatment they had during pregnancy, breastfeeding, follow-up after pregnancy, diabetes diagnosis, current diabetes treatment, other diseases, smoking, any concomitant medication, later pregnancies, heredity for diabetes and their own birth weight.

2.1. *Screening and diagnosis of GDM*

The major screening criteria to perform a diagnostic OGTT at the maternal health care clinics was in 79% a combination of random blood glucose (4–6 samples of non-fasting cB-glucose during pregnancy) with risk factors, while 9% tested all pregnant women with OGTT around gestational week 28, 6% used random cB-glucose only and 6% used risk factors only.

For diagnosis of GDM, a 75 g oral glucose load was used and a 2 h cB-glucose value ≥9.0 mmol/l was required for diagnosis [14,15]. GDM was defined as any degree of glucose intolerance with onset or first recognition during pregnancy. A few cases (*n* = 52) were diagnosed directly without OGTT by having a

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