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# Comparison of pregnancy outcomes between women with gestational diabetes and overt diabetes first diagnosed in pregnancy: A retrospective multi-institutional study in Japan

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## ABSTRACT

**Aims:** To determine differences in pregnancy outcomes including diabetic complications, maternal and perinatal complications between gestational diabetes mellitus and overt diabetes in pregnancy in Japan.

**Methods:** A multi-institutional retrospective study compared pregnancy outcomes between gestational diabetes mellitus and overt diabetes in pregnancy. We examined pregnant women who met the former criteria for gestational diabetes mellitus and received dietary intervention with self-monitoring of blood glucose with or without insulin. Overt diabetes in pregnancy was defined as  $\geq 2$  abnormal values on 75-g oral glucose tolerance test, fasting

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glucose  $\geq 126$  mg/dl (7.0 mmol/l) and 2-h postprandial glucose  $\geq 200$  mg/dl (11.1 mmol/l), or glycated hemoglobin levels  $\geq 6.5\%$  (48 mmol/mol).

**Results:** Data were collected on 1267 women with gestational diabetes and 348 with overt diabetes in pregnancy. Pregestational body mass index was higher ( $26.2 \pm 6.1$  vs.  $24.9 \pm 5.7$  kg,  $P < 0.05$ ) and gestational age at delivery was earlier ( $37.8 \pm 2.5$  weeks vs.  $38.1 \pm 2.1$  weeks,  $P < 0.05$ ) in overt diabetes than in gestational diabetes. Glycated hemoglobin ( $6.8 \pm 1.1\%$  [51 mmol/mol] vs.  $5.8 \pm 0.5\%$  [40 mmol/mol],  $P < 0.05$ ) and glucose on 75-g oral glucose tolerance test and prevalence of retinopathy (1.2% vs. 0%,  $P < 0.05$ ) and pregnancy-induced hypertension (10.1% vs. 6.1%,  $P < 0.05$ ) were higher in overt diabetes than in gestational diabetes. Pregnancy-induced hypertension was associated with pregestational body mass index, gestational weight gain, chronic hypertension, and nulliparity but not with 75-g oral glucose tolerance test.

**Conclusions:** Overt diabetes in pregnancy is significantly associated with maternal complications such as retinopathy and pregnancy-induced hypertension.

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## 1. Introduction

Gestational diabetes mellitus (GDM) is associated with maternal complications such as pregnancy-induced hypertension (PIH) and cesarean section, and neonatal complications, such as macrosomia, hypoglycemia, jaundice, and respiratory distress syndrome [1,2]. GDM is significantly associated with large-for-gestational age (LGA) infants [3,4], and mean glucose concentration is strongly associated with neonatal birth weight in women with GDM [5]. The Hyperglycemia Adverse Pregnancy Outcome (HAPO) study showed a positive correlation between maternal hyperglycemia level and adverse maternal, fetal, and/or neonatal outcomes [3]. The International Association of Diabetes in Pregnancy Study Group (IADPSG) recently proposed new criteria for diagnosing GDM [6]. The new criteria are based primarily on glucose levels that are associated with a 1.75-fold increased risk of giving birth to a LGA infant according to the HAPO study [1].

GDM is defined as glucose intolerance that first occurs or is first identified during pregnancy [7]. The possibility that unrecognized glucose intolerance antedated the pregnancy is therefore not excluded, and this has become a more significant problem as the prevalence of obesity and subsequent development of type 2 diabetes in young women has increased worldwide [8]. Furthermore, ethnicity is associated with risk factors for GDM [8]. For instance, Asian people have a high risk of developing GDM. We previously reported that more than 50% of GDM cases in Japan are diagnosed in the first trimester of pregnancy [9]. The IADPSG proposed the following definition for overt diabetes during pregnancy (ODM): pregnant women who meet the criteria for diabetes in the non-pregnant state but were not previously diagnosed with diabetes. Thus, 2 types of glucose intolerance are identified in pregnancy: GDM and ODM. The clinical significance of ODM has been reported. The risk of congenital malformations and of maternal complications such as retinopathy and nephropathy is increased in diabetes. Rapid management and follow-up may also be required during pregnancy [10,11].

Our hypothesis is that overt diabetes would have a more severe glycemic disturbance and increased risk of both maternal and neonatal complications; however, little has

been reported regarding differences in pregnancy outcomes between these groups. Therefore, the Japan Diabetes and Pregnancy Study (JDPS) Group conducted a multi-institutional retrospective review to assess and compare pregnancy outcomes between ODM and GDM in Japan.

## 2. Materials and methods

### 2.1. Study design

The present retrospective study was conducted in 40 general hospitals in Japan from 2003 to 2009. The individual ethics committees at each of the 40 collaborating centers approved the protocol. All women with singleton pregnancy and no prior diagnosis of diabetes mellitus were included. Women with multiple fetal gestations, pre-gestational diabetes, history of previous treatment for gestational diabetes, active chronic systemic disease other than chronic hypertension, and those with the second of 2 pregnancies within the same year were excluded. All women underwent a universal 2-step screening for GDM, i.e. a casual glucose test or 50-g glucose challenge test (GCT) between 24 and 30 weeks of gestation. Women who had random plasma glucose  $\geq 100$  mg/dl (5.5 mmol/l) or plasma glucose  $\geq 140$  mg/dl (7.8 mmol/l) on GCT were then scheduled for a diagnostic 75-g 2-h oral glucose tolerance test (OGTT) after an overnight fast, using JSOG criteria (fasting, 100 mg/dl [5.5 mmol/l]; 1 h, 180 mg/dl [10 mmol/l]; 2 h, 150 mg/dl [8.3 mmol/l]) [12]. GDM was diagnosed when at least 2 plasma glucose measurements were the same as or higher than the cut-off points. Overweight or obese pregnant women are recommended to undergo a 75-g OGTT at any time during gestation. HbA1c measurements was shown in NGSP units (%).

Overt diabetes first diagnosed in pregnancy (ODM) was defined as  $\geq 2$  abnormal values on 75-g oral glucose tolerance test, fasting glucose  $\geq 126$  mg/dl (7.0 mmol/l) and 2-h postprandial glucose  $\geq 200$  mg/dl (11.1 mmol/l), glycated hemoglobin levels  $\geq 6.5\%$  (48 mmol/mol), random glucose  $\geq 200$  mg/dl (11.1 mmol/l), or diabetic retinopathy recognized in pregnancy.

Collected data included maternal age; parity; pre-pregnancy BMI; chronic hypertension; pregnancy-induced hypertension

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