Using the 100-g Oral Glucose Tolerance Test to Predict Fetal and Maternal Outcomes in Women with Gestational Diabetes Mellitus

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Background: This 5-year cohort study investigated gestational diabetes mellitus (GDM) using new diagnostic criteria and predictive factors for maternal and fetal outcomes.

Methods: From March 2001 to February 2006, 8557 pregnant women underwent a 50-g glucose challenge test (GCT) at 24 to 28 weeks of gestation. A diagnosis of GDM was based on a a one-hour plasma glucose level ≧ 140 mg/dl on the 50 g GCT, followed by at lease two abnormal values on a 100-g oral glucose tolerance test (OGTT), according to the Carpenter and Coustan modification of the National Diabetes Data Group (NDDG) criteria. Maternal and fetal outcomes were compared with women with normal glucose tolerance (NGT).

Results: The incidence of GDM was 7.4%. After excluding women with twin pregnancies, 617 women with GDM and 1250 women with NGT were enrolled for comparison. Older age (33.7 ± 4.1 vs. 32.2 ± 4.1, $p < 0.001$), lower weight gain during pregnancy (13.2 ± 4.4 vs. 14.6 ± 4.0 kg, $p < 0.001$), and higher rates of caesarean section (43.8% vs. 32.7%, $p < 0.001$) occurred in women with GDM compared to those in the NGT group. The rates of macrosomia and neonatal death were higher in the GDM group than the NGT group (7.0% vs. 1.9%, $p < 0.001$ and 0.6% vs. 0.0%, $p = 0.005$ respectively). The fasting glucose on the 100-g OGTT was positively correlated with birth weight in the GDM group (r = 0.117, 95% CI 0.038-0.194, $p = 0.004$). A value exceeding 90 mg/dl was 80% sensitive and 50% specific for macrosomia.

Conclusions: The incidence of GDM in Taiwan is increasing more than before based on current diagnostic criteria. The fasting glucose on the 100-g OGTT correlates closely with birth weight and is also an independent risk factor for macrosomia. Focusing on women with fasting blood glucose concentrations > 90 mg/dL is anticipated to improve outcomes effectively.

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Key words: gestational diabetes mellitus, oral glucose tolerance test, outcome, risk factor

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Gestational diabetes mellitus (GDM) is associated with increased risks of maternal and perinatal complications.[1-3] Various criteria exist for diagnosing this disease. The most widely accepted diagnostic test is the 100-g oral glucose tolerance test (OGTT) proposed by O'Sullivan and Mahan in 1964[4] and modified in 1973.[5] Subsequently, in 1979, the National Diabetes Data Group (NDDG) recommended conversion of the O'Sullivan criteria from whole blood to plasma or serum values.[6] In 1982, Carpenter and Coustan hypothesized that the NDDG conversion of the O'Sullivan and Mahan values from the original Somogyi-Nelson determinations may have resulted in values that were high by about 5 mg/dl. Carpenter and Coustan proposed new cutoff values for plasma glucose that appeared to more accurately represent the original O'Sullivan and Mahan determinations.[7] Recommendations from the Fourth International Workshop-Conference on Gestational Diabetes Mellitus, held by the American Diabetes Association (ADA) in March 1997 supported the use of the Carpenter and Coustan diagnostic criteria. The ADA began to recommend the new diagnostic criteria by Carpenter and Coustan in their position statement released in 2000.[8] The widespread use of these new diagnostic criteria will significantly increase the incidence of GDM. Intervention at a lower blood glucose level in the prevention of major complications of GDM, particularly macrosomia, was evaluated based on different criteria.[9] This study examined the current incidence of GDM in Taiwan based on these new diagnostic criteria and determined the predictors of fetal and maternal outcomes using the 100-g OGTT.

METHODS

From March 2001 to February 2006, a total of 8557 women were screened using the 50-g glucose challenge test (GCT) at 24 to 28 weeks of gestation. Diagnosis of GDM was based on a one-hour plasma glucose level ≧ 140 mg/dl on the 50-g GCT, followed by at least two abnormal values on a 100-g OGTT. All women diagnosed with GDM fulfilled the Carpenter and Coustan modification of the NDDG criteria which required at least two of the following blood glucose levels: fasting glucose ≧ 95 mg/dL, 1-hour ≧ 180 mg/dL, 2-hour ≧ 155 mg/dL, and 3-hour ≧ 140 mg/dl.[7,8]

The women diagnosed with GDM were referred immediately to our multidisciplinary team for aggressive management. Women with GDM were given medical nutrition counseling and instructed to restrict caloric intake to 1500-1800 Kcal/day with carbohydrate 180-250 g/day divided into three meals with snacks between.[10] The educators sought to modify patient lifestyle to achieve an optimal body weight. Self-monitoring of blood glucose was performed at least twice daily, with weekly reports to the team. If blood glucose exceeded the standard, patients were asked to undergo biweekly follow- ups at our metabolism clinic. Insulin therapy with premeal short-acting insulin and bedtime intermediate-acting insulin was recommended if the fasting blood glucose ≧ 105 mg/dl or 1-hour glucose ≧ 155 mg/dl. Diabetic educators and diabetologists performed clinical evaluations biweekly with monitoring by an obstetrician.

Patient age, parity, and weight gain during pregnancy were recorded. Moreover, pregnancy outcomes including preeclampsia, polyhydramnios, infant birth weight, and neonatal death were analyzed. Women with normal glucose tolerance (NGT) were matched for comparison. Birth weights were correlated with the results of the 100-g OGTT. Macrosomia (≧ 4000 g) was the primary outcome in this study. Informed consent was obtained from each subject.

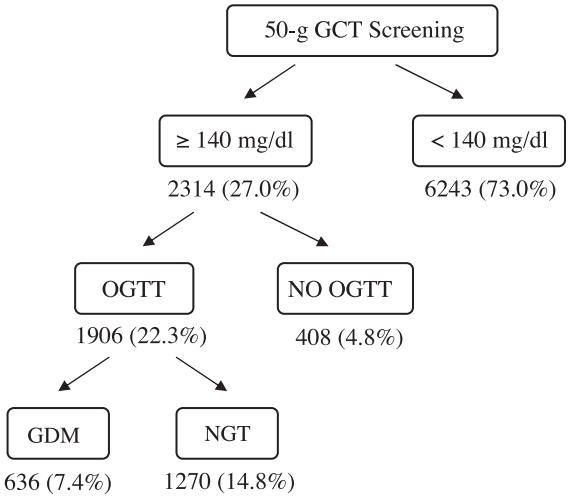
Differences between groups in continuous variables were tested using independent-samples Student's *t*-test. Differences in proportions were assessed by the chi-square test or Fisher's exact test. Pearson's correlation coefficient was used to test the correlation between the 100-g OGTT results and birth weight. Multiple linear regression models were used to predict birth weight. Multiple logistic regression analysis with backward selection was applied to identify independent risk factors for maternal and fetal outcomes. Results were expressed as means ± SD or %. The level of statistical significance was set at a *p*-value of 0.05 or less.

RESULTS

Among the 8557 pregnant women undergoing the 50-g glucose challenge test, 2314 (27%) tested positive and 1906 (22.3%) received a 100-g OGTT. Among this latter group, 636 were diagnosed with

GDM. The incidence of GDM in the study population thus was at least 7.4% (Fig.1).

After excluding women with twin pregnancies, 617 women with GDM and 1250 with NGT were enrolled to compare maternal and fetal morbidity. Table 1 reveals that women with GDM were older than women with NGT (33.7 ± 4.1 vs. 32.2 ± 4.1, $p < 0.001$), and gained less weight during pregnancy (13.2 ± 4.4 vs. 14.6 ± 4.0 kg, $p < 0.001$). Furthermore, the rate of caesarean section was considerably higher in women with GDM than in those with NGT (43.8% vs. 32.7%, $p < 0.001$ respectively). The rate of preeclampsia was not significantly different after adjustment for maternal age (4.5% vs. 2.6%, $p = 0.063$). Polyhydramnios, known as a maternal complication in GDM, did not differ between two groups. The newborns in the GDM group were markedly heavier than those in the NGT group (3265.3 ± 491.6 vs. 3194.2 ± 425.9 g, $p = 0.007$) (Table 2). The rates of macrosomia and neonatal death were higher in the GDM than the NGT group (7.0% vs. 1.9%, $p < 0.001$ and 0.6% vs. 0.0%, $p = 0.005$ respectively).



Abbreviations: GCT: glucose challenge test; OGTT: oral glucose tolerance test; GDM: gestational diabetes mellitus; NGT: normal glucose tolerance.

Fig. 1 Enrollment and Outcomes.

Table 1. Comparison of Maternal Outcomes between Women with GDM and NGT

	GDM	NGT	*p* value*
Number	617	1250	–
Age (years)	33.7 ± 4.1	32.2 ± 4.1	< 0.001
Weight gain (kg)	13.2 ± 4.4	14.6 ± 4.0	< 0.001
Polyhydramnios	2 (0.3%)	4 (0.3%)	0.878
Preeclampsia	28 (4.5%)	33 (2.6%)	0.063
Cesarean delivery	270 (43.8%)	409 (32.7%)	< 0.001

Abbreviations: GDM: gestational diabetes mellitus; NGT: normal glucose tolerance; *: Values were adjusted for maternal age.

Correlations between the 100-g OGTT results and neonatal birth weight were analyzed in the GDM group. There were no significant correlations among the 1-hour, 2-hour, and 3-hour glucose values and the area under curve (AUC). A significant positive correlation was found only for fasting glucose (r = 0.117, 95% CI 0.038-0.194, $p = 0.004$) (Fig. 2). The multiple linear regression models demonstrated that every 1 mg/dl increase in fasting glucose on the 100-g OGTT predicted a 5.781 g increase in birth weight (95% CI 3.333-8.229, $p < 0.001$) following adjustments for age, cesarean delivery, weight gain during pregnancy, 50-g GCT and the other three 100-g OGTT values. A value exceeding 90 mg/dl was 80% sensitive and 50% specific for macrosomia. Furthermore, multiple logistic regression analysis demonstrated that the fasting glucose value on the 100-g OGTT in women with GDM and weight gain during pregnancy were independent risk factors for infant macrosomia (odds ratio 1.036, 95% CI 1.019-1.053, $p < 0.001$ and 1.160, 95% CI 1.076-1.250, $p < 0.001$ respectively) (Table 3).

Table 2. Comparison of Fetal Outcomes between GDM and NGT Groups

	GDM	NGT	*p* value
Number	617	1250	–
Neonatal birth weight (g)	3265.3 ± 491.6	3194.2 ± 425.9	0.007
Macrosomia (≧ 4000 g)	43 (7.0%)	24 (1.9%)	< 0.001
Neonatal death	4 (0.6%)	0 (0.0%)	0.005

Abbreviations: GDM: gestational diabetes mellitus; NGT: normal glucose tolerance.

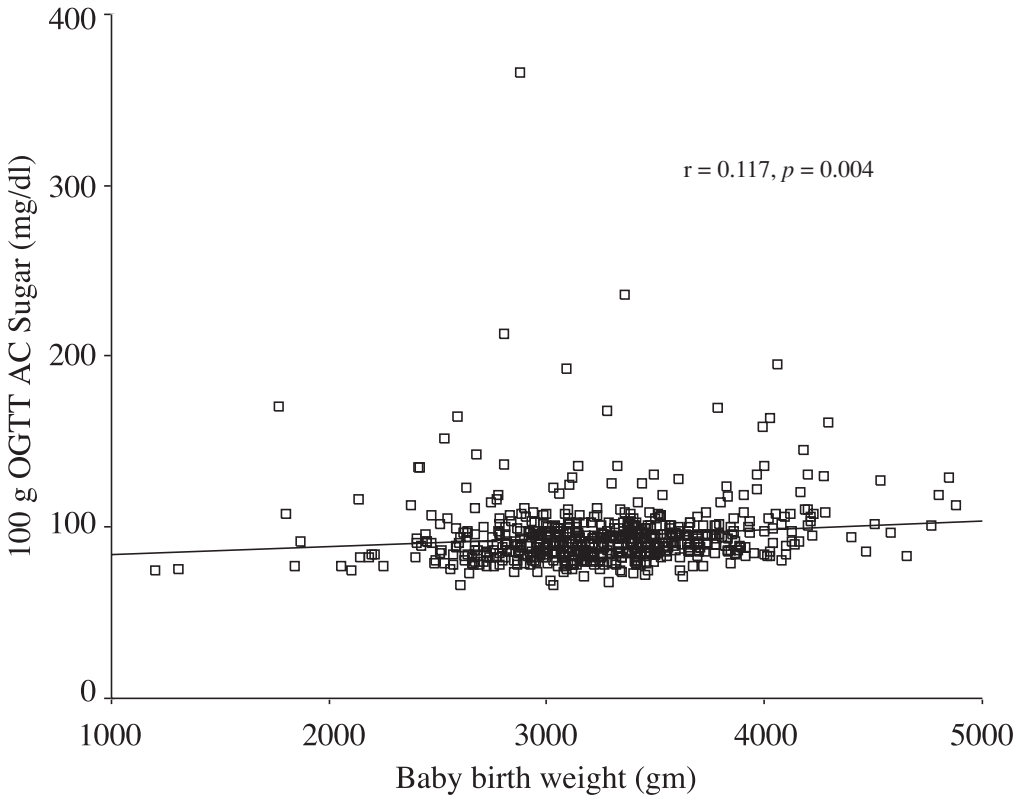


Fig. 2 Correlation between fasting (AC) glucose values on the 100-g oral glucose tolerance test (OGTT) and neonatal birth weight in 617 women with gestational diabetes mellitus.

Table 3. Independent Predictive Factors of Macrosomia in Women with GDM Based on Multiple Logistic Regression Analysis

	Logistic coefficient	Odds ratio	95% CI	*p* value
Fasting glucose on the 100-g OGTT (mg/dl)	0.036	1.036	1.019-1.053	< 0.001
Weight gain (kg)	0.148	1.160	1.076-1.250	< 0.001
Intercept	–8.559			

Abbreviations: GDM: gestational diabetes mellitus; OGTT: oral glucose tolerance test.

DISCUSSION

This prospective cohort investigation represents the most recent project evaluating women with GDM in Taiwan. The incidence of GDM in this investigation was up to 7.4%, higher than the 2.03% previously reported in Taiwan.[11] The reasons for this significant increase are the new diagnostic criteria set at lower glucose levels[8] and younger population in the previous report.[11] Of women with a positive 50-g glucose screening test in this study, 82.4% (1906/2314) underwent a subsequent 100-g OGTT. Women with GDM could effectively be identified by the screening system used in this study.

Since the change in diagnostic criteria, this was the first cohort investigation based on intervention at a lower blood glucose level in Taiwan. The women with GDM were older on average than those with NGT (Table 1). Age thus is an important consideration in risk assessment for GDM.[8,12] The lower weight gain in the GDM group compared with the NGT group was a positive result of intervention.

This phenomenon was attributed to a program of lifestyle modification and diet control. Although this study found a higher rate of preeclampsia among women with GDM than women with NGT, the rate was lower than those in other Taiwanese studies (16.1-19.7%).[11] The rate of cesarean delivery associated with GDM has been reported to be approximately 30% for all indications.[2,3] In this investigation, an increased rate of cesarean delivery in the GDM group was related to the obstetrician attitudes toward a diagnosis of GDM in Taiwan. The rate of polyhydramnios was similar in the two groups. The mechanism of polyhydramnios associated with diabetes is unclear and an increased glucose concentration in the amniotic fluid may play a role.[13] However, Biggio et. al. demonstrated that polyhydramnios caused by diabetes is generally mild and does not considerably increase the risk of an adverse outcome.[14]

Casey et al. estimated that approximately one in eight women with GDM delivers a large for gestational age (LGA) infant.[2] A major fetal effect of GDM is macrosomia. A continuous relationship has been documented between glucose concentration and fetal growth, even in normoglycemic women.[15-18] The incidence of macrosomia can be reduced by controlling glucose.[3] However, effective education and achieving control of glucose is difficult in most women with GDM. In Table 2, the rate of macrosomia in the GDM group was still higher than that in the NGT group. Although multidisciplinary care was provided as possible to the women with GDM surveyed in the present cohort, newborn outcomes were not identical in the GDM and NGT groups. The increasing number of women with GCM and the shortage of clinical practitioners are reasons why active glycemic control failed to achieve any improvement in the study population. Consequently, it is necessary to identify high risk women and develop cost-effective and labor-saving strategies to reduce macrosomia. Schrader et al raised the concept of correlations between the fasting blood glucose on the 100-g OGTT and infant birth weight in women who do not meet the criteria for GDM.[15] This cohort study demonstrated a positive correlation between glucose concentration and fetal growth in women with GDM. Multiple logistic regression models further documented that the fasting blood glucose on the 100-g OGTT was an independent risk factor for macrosomia. Therefore, women with GDM with fasting glucose values exceeding 90 mg/dl in the 100-g OGTT are candidates for intensive blood glucose control to prevent adverse perinatal outcomes.

Women with GDM have a non significantly higher rate of preeclampsia than women with NGT in this study. Preeclampsia is recognized as a state of proinflammatory changes and is closely related to insulin resistance.[19] The incidence of preeclampsia is reported about three times higher in pregnant women with diabetes than in those without diabetes.[20] The non significantly different rates of preeclampsia between two groups reflect the effect of glucose control in women with GDM in this study.

A fasting glucose value on the 100-g OGTT was also identified as an independent risk factor in predicting postpartum diabetes or abnormal glucose tolerance.[21] Both perinatal outcome and postpartum metabolic status are key concerns in women with GDM. Using this simple indicator, it is possible to easily identify high risk women with GDM and provide care.

Intensive treatment of GDM has been well documented to reduce serious perinatal morbidity in Caucasians.[3] But the outcomes in women with GDM in this study were not significantly improved when compared to women with NGT, even after active control of blood glucose. Infrequent self-monitoring of blood glucose (twice daily on average) and a low percentage of good control were possible factors. This is an important topic which we need to explore in further study of Taiwanese GDM care.

In conclusion, the incidence of GDM in Taiwan has increased after applying current diagnostic criteria. Older age, less weight gain during pregnancy, and higher rates of cesarean section are characteristics of the GDM population with the multidisciplinary medical management examined in this study. The fasting glucose on the 100-g OGTT correlates closely with birth weight and is also an independent risk factor for macrosomia. This study recommends active medical and nutritional therapy for women with GDM with fasting blood glucose concentrations > 90 mg/dL. Through selection of high risk women, it is anticipated that maternal and fetal outcomes will effectively improve.

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以 100 公克葡萄糖耐受試驗來評估妊娠糖尿病婦女及胎兒之預後

林嘉鴻 溫世芬 吳雅慧 黃妙珠

背 景： 本篇是以新的診斷標準，對妊娠糖尿病 (gestational diabetes mellitus, GDM) 的婦女，進行爲期 5 年的世代研究，並評估其影響母親及胎兒預後的相關性。

方 法： 從 2001 年 3 月到 2006 年 2 月，共 8557 位懷孕 24 到 28 週的婦女，接受 50 公克葡萄糖初步試驗。GDM 的診斷標準是以 1 小時的血糖 ≧ 140 mg/dl，並且接受 100 公克葡萄糖耐受試驗時，達到 Carpenter and Coustan 修正過 NDDG 的標準。母親和胎兒的預後是和葡萄糖耐受正常 (NGT) 的婦女作比較。

結 果： 妊娠糖尿病的比率爲 7.4%，共有 617 位 GDM 和 1250 位 NGT 的單胎次婦女進入比較。GDM 和 NGT 的婦女相比之下，有年齡較大 (33.7 ± 4.1 vs. 32.2 ± 4.1 歲，$p < 0.001$)，懷孕期間體重增加較少 (13.2 ± 4.4 vs. 14.6 ± 4.0 kg, $p < 0.001$)，以及較高比率的剖腹產 (43.8% vs. 32.7%, $p < 0.001$) 的特徵。巨嬰症和死產的比率也是 GDM 高於 NGT 的婦女 (分別是 7.0% vs. 1.9%, $p < 0.001$ 和 0.6% vs. 0.0%, $p = 0.005$)。在 GDM 的婦女，其 100 公克葡萄糖耐受試驗中的空腹血糖數值 (AC) 和胎兒出生體重呈現正相關 (r = 0.117, 95% CI 0.038-0.194, $p = 0.004$)。以 AC 超過 90 mg/dl，可提供一個敏感度爲 80% 及特異度爲 50%，用來預測巨嬰症的方法。

結 論： 以目前新的診斷標準爲根據，GDM 在台灣的比率是增加的。100 公克葡萄糖耐受試驗中的空腹血糖數值和胎兒出生體重呈現正相關，並且是一個獨立危險預測因子。以 AC 超過 90 mg/dl 的 GDM 婦女作爲積極控制的重點族群，期望可以更有效改善預後結果。

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關鍵詞：妊娠糖尿病，葡萄糖耐受試驗，預後，危險因子

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