ORIGINAL ARTICLE

Risk of development of diabetes mellitus in Chinese women with persistently impaired glucose tolerance after gestational diabetes

KF Lee 李家輝
Maria WH Mak 麥慧嫻
KO Lau 劉建安
Harriet HY Chung 鍾巧儀

Objectives To estimate the cumulative incidence for the development of diabetes mellitus in Chinese women with persistently impaired glucose tolerance after gestational diabetes, and evaluate putative risk factors.

Design Historical cohort study.

Setting A regional hospital in Hong Kong.

Patients Women with postpartum impaired glucose tolerance (as confirmed by a 75-gram oral glucose tolerance test 6 weeks after delivery) seen between January 2000 and December 2006.

Results After a mean follow-up period of 52 (standard deviation, 22; range, 12-106) months, 47 (20%) of the 238 women converted to diabetes mellitus. Concomitant postpartum impaired fasting plasma glucose levels increased the risk of future diabetes mellitus by 3.5-fold (95% confidence interval, 1.7-7.0; P=0.001) when compared to those with postpartum impaired glucose tolerance only. Based on multivariate analysis, only antepartum and postpartum fasting plasma glucose levels predicted future development of diabetes mellitus. At 1 year after delivery in 95/159 (60%) of the women, glucose tolerance regressed to normal, while in only 9/159 (6%) it progressed to diabetes mellitus. At this stage, 29% of those with impaired glucose regulation (impaired glucose tolerance, impaired fasting glucose or both) compared to 2% of those whose glucose tolerance reverted to normal developed diabetes mellitus upon subsequent follow-up (P<0.001). In all, 24/159 (15%) fulfilled the definition of metabolic syndrome and its presence was associated with 4.7-fold increased risk of future diabetes mellitus (95% confidence interval, 1.7-13.4; P=0.004).

Conclusions Women with persistent postpartum impaired glucose tolerance after gestational diabetes have a high risk of developing diabetes mellitus. However, a significant proportion of these women regress to normal glucose tolerance 1 year after delivery, and their risk of progression to diabetes mellitus is lower than those with persistent impaired glucose regulation. Therefore, women with a history of gestational diabetes, particularly those with persistent glucose intolerance 6 weeks and 1 year after delivery, should have regular surveillance for the development of diabetes mellitus.

Key words
Diabetes, gestational; Glucose intolerance; Metabolic syndrome; Pregnancy in diabetics; Prevalence

Hong Kong Med J 2011;17:195-201

Department of Medicine and Geriatrics, Kwong Wah Hospital, 25 Waterloo Road, Hong Kong
KF Lee, FRCP, FHKAM (Medicine)
MWH Mak, MRCP, FHKAM (Medicine)
KO Lau, MBA, APN (DM)
HHY Chung, MSc, NS (DM)

Correspondence to: Dr KF Lee
Email: leekf1@ha.org.hk

Introduction

Depending on the prevalence of type 2 diabetes in a given population or ethnic group, gestational diabetes mellitus (GDM) is present in 0.6 to 15% of subjects, and has been shown to increase the risk of later diabetes mellitus (DM).[1,2] However, the reported rates of progression to DM vary widely from 3 to 70%, which were probably related to differences in GDM and DM definitions, tests for glucose tolerance, length of follow-up, retesting rates, selection biases, and ethnicity.[3] Although the local incidence of GDM was high (14% per year, based on 1998 World Health Organization [WHO] criteria) as reported by Ko et al,[4] reported incidence estimates of subsequent DM were limited.[5-7] As there is a growing body of

分娩後呈持續性葡萄糖耐受不良的妊娠期糖尿病華籍婦女的糖尿病風險

目的 估計分娩後呈持續性葡萄糖耐受不良的妊娠期糖尿病華籍婦女，其糖尿病風險的累積發病率，以及評估其假定風險因素。

設計 歷史性隊列研究。

安排 香港一所分區醫院。

患者 2000年1月至2006年12月期間，於分娩後六星期接受75克口服葡萄糖耐受試驗而確診為葡萄糖耐受不良的婦女。

結果 隨訪期平均為52個月（標準差22個月；介乎12至106個月）。結果發現238名婦女中，47名（20%）患上糖尿病。與分娩後只呈葡萄糖耐受不良的婦女比較，同時有分娩後空腹血糖高的婦女日後患糖尿病的風險高出3.5倍（95%置信區間：1.7-7.0；P=0.001）。多元分析顯示，只有分娩前及分娩後的空腹血糖水平可以預計日後的糖尿病風險。於分娩一年後接受檢查的婦女共159人，其中95人（60%）已回復正常耐糖狀態，另9人（6%）發展至糖尿病。在此階段，葡萄糖調節不良（包括葡萄糖耐受不良、高空腹血糖水平、或者兩者兼備）的婦女中有29%最終會發展至糖尿病，而回復正常耐糖狀態的婦女中則只有2%最終會發展至糖尿病（P<0.001）。159人中，24人（15%）附合代謝症候群的定義，有此症候群的婦女日後患糖尿病的風險要高出4.7倍（95%置信區間：1.7-13.4；P=0.004）。

結論 分娩後呈持續性葡萄糖耐受不良的妊娠期糖尿病華籍婦女，日後患有糖尿病的風險較高。可是，亦有大部分婦女於分娩一年後回復正常耐糖狀態；與呈持續性葡萄糖耐受不良的婦女比較，回復正常耐糖狀態的婦女日後患糖尿病的風險相對較低。因此，有妊娠期糖尿病的婦女，尤其是那些於分娩後六個星期及一年仍然有持續性葡萄糖耐受不良的人，應定期接受糖尿病檢查。

evidence suggesting effective treatment—including lifestyle and pharmacological intervention—can delay the development of DM in women with previous GDM,[8] it is important to determine the cumulative incidence of DM accurately by following up patients over a longer period of time. Moreover, identification of multiple antepartum and postpartum predictors for future DM development is also important for the selection of high-risk women undergoing more intensive surveillance.[9] In view of high local prevalence of GDM, this seems to be a more cost-effective approach for screening. We therefore conducted a local study on a cohort of Chinese women with postpartum impaired glucose tolerance (IGT), aiming to estimate the cumulative incidence of DM and evaluate risk factors for its development.

Methods

Subjects

The study population was derived from a cohort of 388 patients with postpartum IGT after GDM, being followed up (from January 2000 to December 2006) in the Diabetes Centre of Kwong Wah Hospital. In Kwong Wah Hospital, women with GDM or gestational IGT, as defined by WHO 1998 criteria,[10] were advised to return for a 75-gram oral glucose tolerance test (OGTT) between 4 and 8 weeks after delivery in the Department of Obstetrics and Gynaecology postnatal clinic. Women diagnosed to have DM were referred to the medical diabetes clinic, while those diagnosed to have IGT were referred to the diabetes nurse clinic for standard diabetes education and regular follow-up. The latter women were advised to return annually for a 75-gram OGTT and metabolic assessment including sitting blood pressure (BP) measurement, anthropometric measurement (body mass index [BMI] and waist circumference [WC]), and biochemical measurements (fasting lipid profile, glycosylated haemoglobin [HbA1c], electrolyte and serum creatinine, and liver enzymes). Due to limited resources, women with normal postpartum glucose tolerance were discharged after standard diabetes education but no subsequent follow-up was arranged.

Of the 388 women, 238 (61%) had returned to the diabetes nurse clinic at least once before December 2008 and were included in the analysis. The women were followed up until their last visit before December 2008, or until they reached the study endpoint, diabetes, as defined by WHO 1998 criteria.[10] For patients who developed GDM in subsequent pregnancies during the follow-up period, for the purpose of analysis, the first pregnancy was regarded as the index pregnancy.

Demographic data including age, family history of diabetes, smoking and drinking history were retrieved from clinical records. Antepartum variables including parity, insulin use during pregnancy, neonatal birth weight, and gestation were also retrieved from clinical records during their first postpartum visit. The glucose tolerance test result at 28 weeks of gestation was taken as the antepartum glycaemic variable.

Definitions

Antepartum and postpartum 75-gram OGTT results were defined by WHO (1998) criteria[10]; DM was defined as a fasting blood glucose (FBG) ≥7.0 mmol/L and/or a 2-hour post-load glucose ≥11.1 mmol/L, and IGT was defined as a FBG <7.0 mmol/L and a 2-hour post-load glucose of 7.8 to 11.1 mmol/L. Impaired fasting glucose (IFG) was defined according to American Diabetes Association criteria[11] as a FBG ≥5.6

mmol/L but <7.0 mmol/L. A normal glucose tolerance (NGT) was defined as a FBG <5.6 mmol/L and 2-hour post-load glucose <7.8 mmol/L. Metabolic syndrome was defined according to International Diabetes Federation criteria,[12] as central obesity (defined as WC ≥80 cm for Chinese women) plus any two of the following four features. They were: (1) raised blood triglyceride level >1.7 mmol/L, or specific treatment for this lipid abnormality; (2) reduced high-density lipoprotein level <0.9 mmol/L in males and <1.1 mmol/L in females, or specific treatment for this lipid abnormality; (3) raised BP with systolic BP ≥130 or diastolic BP ≥85 mm Hg, or treatment of previously diagnosed hypertension; and (4) a FBG ≥5.6 mmol/L, or previously diagnosed type 2 diabetes. As all women had undergone 75-gram OGTT, those with IFG (≥5.6 mmol/L) and/or IGT (2-hour post-OGTT plasma glucose of 7.8 to 11.1 mmol/L) were included as criteria for the metabolic syndrome.

Statistical analysis

Cohort characteristics were described for categorical variables by n (%) and for continuous variables using mean ± standard deviation (SD) or median (interquartile range) according to their distribution. Group comparisons of continuous variables were by the Student's *t*-test or the Mann Whitney *U* test, where appropriate. Group comparisons of categorical data entailed Chi squared or Fisher's exact tests, as appropriate. The Cox proportional hazards regression analysis was used to examine the relationship between demographic, antepartum, postpartum and metabolic variables and the development of diabetes during follow-up. As the exact time of DM development was not ascertainable (due to irregular follow-up), it was estimated as the mid-point in time between the date of diagnosis (by 75-gram OGTT) and the date of the preceding test (by 75-gram OGTT) that yielded no DM. The date of first postpartum 75-gram OGTT was chosen as the point of entry for calculation of follow-up duration.

A separate analysis was performed for women who had their first nurse clinic visit about 1 year after their postpartum 75-gram OGTT, in order to assess the association of various metabolic and anthropometric variables at this time and the subsequent development of diabetes. All analyses were performed with Statistical Package for the Social Sciences (Windows version 13.0; SPSS Inc, Chicago [IL], US). All reported P values were two-sided.

Results

Main cohort

After a mean ± SD follow-up of 52 ± 22 (range, 11-106) months, 47 (20%) out of 238 women (mean age at delivery, 34 ± 4 years) with postpartum IGT developed type 2 DM. The cumulative incidence was 7.5% (14 out of 186 women) after a mean follow-up of 19 ± 14 months. Regarding these women, 93% had a follow-up period exceeding 2 years and 82% had more than one visit after their 6-week postpartum OGTT. Of these 238 women who had postpartum IGT, 47 (20%) also had concomitant IFG; 18 (38%) of these 47 converted to DM while only 29 (15%) of the 191 women with only IGT developed DM eventually. Therefore, the co-existence of postpartum IFG on top of IGT further increased the risk of future DM by 3.5-fold (unadjusted odds ratio; 95% confidence interval, 1.7-7.0; P=0.001).

Table 1 shows a comparison of antepartum and postpartum characteristics in those who developed DM and those remained non-diabetic at the end of the study, using univariate analysis. Most of the metabolic variables were not measured because only a postpartum 75-gram OGTT was performed in the busy postnatal clinic. Apart from the antepartum and postpartum glycaemic variables, older age, higher parity and higher BMI were associated with the development of DM. Insulin use during pregnancy, representing the extent of underlying glucose disturbance, also yielded a significant predictive value. Based on multivariate regression analysis using the Cox proportional hazard model, only antepartum and postpartum fasting plasma glucose remained statistically significant predictors of DM (Table 2).

TABLE 1. Antepartum and postpartum risk factors for the development of diabetes mellitus (DM) in 238 women with postpartum impaired glucose tolerance

Variable*	DM (n=47)†	Non-DM (n=191)†	P value
Age at delivery (years)	34.1 ± 5.1	33.6 ± 3.9	0.05
Parity	1.83 ± 1.01	1.52 ± 0.72	0.02
Positive family history of DM	24 (51%)	74 (39%)	0.13
Smoking	2 (4%)	10 (5%)	0.78
Alcohol	2 (4%)	5 (3%)	0.56
Insulin use during pregnancy	8 (17%)	10 (5%)	0.01
Antepartum fasting plasma glucose (mmol/L)	5.4 (4.8-6.2)	4.6 (4.3-5.0)	<0.001
Antepartum 2-hour post–75-gram OGTT plasma glucose (mmol/L)	10.3 (9.6-11.2)	9.0 (8.4-9.7)	<0.001
Birth weight (kg)	3.19 ± 0.59	3.22 ± 0.54	0.77
BMI at postpartum OGTT (kg/m^2)	25.6 ± 4.0	24.1 ± 3.2	0.02
Postpartum fasting plasma glucose (mmol/L)	5.4 (5.0-5.9)	4.9 (4.6-5.3)	<0.001
Postpartum 2-hour post–75-gram OGTT plasma glucose (mmol/L)	9.3 (8.6-10.0)	8.8 (8.2-9.5)	0.001

* OGTT denotes oral glucose tolerance test, and BMI body mass index

† Data are shown as mean ± standard deviation, No. (%), or median (interquartile range)

Subgroup analysis

Glycaemic variables

Of these 238 women with postpartum IGT, 159 (67%) had their first diabetic nurse clinic visit about 1 year (mean duration, 1.1 ± 0.4 years) after delivery. Their demographic, antepartum and postpartum characteristics were not statistically different from those of other women not turning up during that period (data not shown). Of these 159 women with postpartum IGT, glucose tolerance status of 95 (60%) had regressed to NGT, while only 9 (6%) progressed to diabetes. As shown in Table 3, glycaemic variables except HbA1c (fasting plasma glucose and 2-hour post–75-gram OGTT plasma glucose) measured during this period still showed a significant association with DM development at the end of the study. In fact, the glycaemic status during this time determined the probability of developing future DM as shown in the Figure. Only two (2%) of the 95 women with NGT 1 year post-delivery converted to DM, while five of 13 (38%) with IFG and IGT 1 year post-delivery developed DM during subsequent follow-up (P<0.001 by Fisher's exact test). Six (23%; n=26) of the women with IGT only, and five (31%; n=16) with IFG only at this stage eventually developed DM (P=0.001 for both when compared to women having NGT by Fisher's exact test). Overall, 16 (29%; n=55) of women with abnormal glucose regulation (IGT, IFG, or both) eventually developed DM (P=0.001 vs women with NGT, by Fisher's exact test).

TABLE 2. Multivariate regression analysis of antepartum and postpartum variables in predicting the development of diabetes in 238 women with postpartum impaired glucose tolerance

Variable	Adjusted hazard ratio* (95% confidence interval)	P value
Antepartum fasting plasma glucose (mmol/L)	1.93 (1.42-2.63)	<0.001
Postpartum fasting plasma glucose (mmol/L)	1.69 (1.05-2.71)	0.03

* Adjusted hazard ratio from time-dependent Cox proportional hazard models using stepwise regression analysis—independent variables entered for analysis included age at delivery, parity, insulin use during pregnancy, antepartum and postpartum fasting plasma glucose and 2-hour post–75-gram oral glucose tolerance test (OGTT) plasma glucose, and post-delivery body mass index. The time of diabetes development was estimated as the mid-point in time between the diagnosis (by OGTT) and the date of the immediate past OGTT

TABLE 3. Metabolic risk factors at 1 year post-delivery for the development of diabetes in a subgroup of 150 women with persistent impaired glucose tolerance after gestational diabetes mellitus (DM)

Variable*	DM (n=18)†	Non-DM (n=132)†	P value
BMI (kg/m^2)	23.6 ± 3.6	22.7 ± 3.2	0.28
WC (cm)	76.5 ± 8.7	75.7 ± 7.4	0.68
Systolic BP (mm Hg)	114.9 ± 9.6	115.6 ± 17.2	0.87
Diastolic BP (mm Hg)	69.4 ± 8.8	71.0 ± 10.6	0.56
Fasting plasma glucose (mmol/L)	5.6 ± 0.7	5.0 ± 0.5	<0.001
2-hour post–75-gram OGTT plasma glucose (mmol/L)	8.1 ± 1.6	6.7 ± 1.5	0.001
HbA1c (%)	5.5 ± 0.4	5.3 ± 0.4	0.096
Plasma triglyceride (mmol/L)	1.3 (0.8-1.8)	0.9 (0.6-1.2)	0.37
Plasma LDL-C (mmol/L)	2.6 ± 0.5	2.8 ± 0.7	0.49
Plasma HDL-C (mmol/L)	1.3 (1.1-1.6)	1.4 (1.1-1.6)	0.49
Aspartate transaminase (IU/L)	17.0 (14.0-20)	17.5 (15.0-23.0)	0.38
Alanine transaminase (IU/L)	15.0 (12.0-25.5)	16.5 (12.0-22.0)	0.55
Metabolic syndrome	6 (33%)	9 (7%)	0.003

* BMI denotes body mass index, WC waist circumference, BP blood pressure, OGTT oral glucose tolerance test, HbA1c glycosylated haemoglobin, LDL-C low-density lipoprotein cholesterol, and HDL-C high-density lipoprotein cholesterol

† Data are shown as mean ± standard deviation, No. (%), or median (interquartile range)

Metabolic syndrome

All women in this subgroup had full metabolic assessments as already described. Within this subgroup, 24 (15%; n=159) fulfilled the definition of metabolic syndrome. All nine women who developed DM at this stage also had metabolic syndrome. As shown in Table 3, apart from the glycaemic variables, the presence of metabolic syndrome at this stage increased the risk of future DM by 4.7-fold (unadjusted odds ratio; 95% confidence interval, 1.7-13.4; P=0.004). However, individual metabolic parameters such as BMI, WC, systolic BP, diastolic BP, liver transaminase levels, plasma triglycerides, plasma low-density-lipoprotein–cholesterol and high-density-lipoprotein–cholesterol showed no significant association in the univariate analysis. Using multivariate regression analysis with the Cox proportional hazard model, only fasting plasma glucose and the 2-hour post–75-gram OGTT plasma glucose at 1 year after delivery remained statistically significant predictors of DM (Table 4).

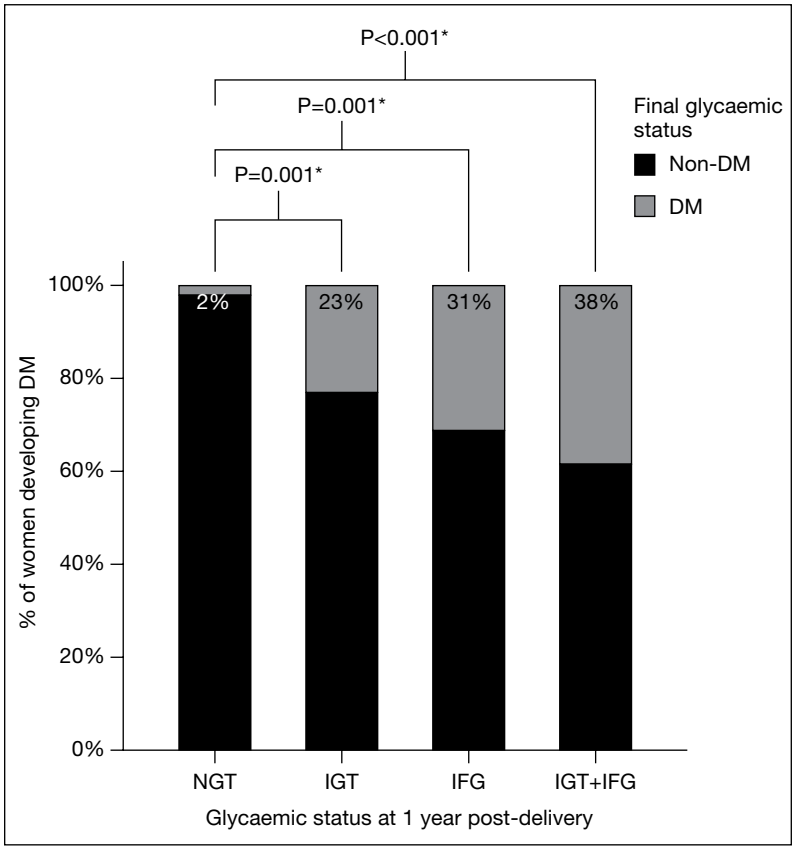
Discussion

Incidence of type 2 diabetes

Gestational diabetes mellitus, defined as glucose intolerance first detected during pregnancy, is recognised as a risk factor for adverse perinatal outcome and later development of type 2 diabetes. A recent meta-analysis confirmed that women with GDM had approximately a 7-fold increased risk of developing type 2 diabetes compared to those without GDM.[2] Furthermore, the Diabetes Prevention Program found that women with a self-reported history of GDM and IGT had a 74% increased risk of developing type 2 diabetes compared to a cohort of women with IGT but no history of GDM, even after adjusting for age.[8] The reported cumulative incidence of DM in women with a history of GDM varies from 3% to 70%. The difference in rates of progression between different ethnic groups was probably due

to the different definition of GDM and DM, different tests for glucose tolerance, different lengths of follow-up, different retesting rates and selection biases.[3] Using the WHO (1998) criteria, 7.5% and 20% of Chinese women with GDM and postpartum IGT in our study developed DM after a mean follow-up of 1.6 years and 4.3 years, respectively. This finding seems comparable to a study on 671 Latino women,[13] in which 22% with GDM developed type 2 diabetes after 5 to 7 years' follow-up. However, their study included women with normal and abnormal glucose tolerance at the 4 to 16 weeks' postpartum examination. In these Latino women with postpartum IGT and NGT as defined by WHO criteria, the respective 5-year unadjusted cumulative rates for the incidence of DM were 80% and 12%. Therefore we expected a lower cumulative incidence in our study if women with GDM and postpartum NGT were included. When compared with the Caucasian population,[14] they had a lower cumulative incidence of DM (19% nine years after delivery), though the reported rate might be an underestimate as the development of DM was based on self-reporting or hospital records. Although it is difficult to compare the risk of DM development with another local prospective study[7] because of different inclusion criteria and methods of analysis, our GDM patients seem to have a higher conversion rate to DM. The cumulative incidence of DM in our patients was 20% after a mean follow-up of 4.3 years, while 9.0% of their patients converted to DM within 8 years of delivery related to the index pregnancy. This was possibly because our study was limited to patients with postpartum IGT only.

Due to limitations posed by our study design, a significant proportion of women might have had a delayed diagnosis of DM conversion, because they did not turn up regularly for testing. As a result, our cumulative incidence might be an underestimate. Selection bias were also possible; only 238 (61%) of 388 of eligible women turned up for at least one visit after their postpartum examination, but there were even lower turnout rates in similar studies.[13,15]



* Comparison between different groups was tested by Chi squared or Fisher's exact test, where appropriate

FIG. Glycaemic status at 1 year post-delivery and its association with final diabetes mellitus (DM) development

NGT denotes normal glucose tolerance, IGT impaired glucose tolerance, and IFG impaired fasting glucose

TABLE 4. Multivariate regression analysis of metabolic risk factors at 1 year post-delivery for the development of diabetes in a subgroup of 150 women with persistent impaired glucose tolerance after gestational diabetes mellitus

Variable	Adjusted hazard ratio* (95% confidence interval)	P value
Fasting plasma glucose at 1 year post-delivery (mmol/L)	3.25 (1.61-6.55)	0.001
2-Hour post–75-gram OGTT plasma glucose at 1 year post-delivery (mmol/L)	1.36 (1.02-1.82)	0.04

* Adjusted hazard ratio from time-dependent Cox proportional hazard models using stepwise regression analysis—independent variables entered for analysis included age at delivery, parity, fasting plasma glucose and 2-hour post–75-gram oral glucose tolerance test (OGTT) plasma glucose at 1 year post-delivery, and the presence of metabolic syndrome. The time of diabetes development was estimated as the mid-point in time between the diagnosis (by OGTT) and the date of the immediate past OGTT

Risk factors for type 2 diabetes

Factors associated with long-term development of type 2 diabetes have been examined in various studies using univariate or multivariate analysis.[3,5,9,13,15-17] The fasting plasma glucose encountered with an OGTT during pregnancy was the strongest independent predictive factor in the majority of studies. Other factors such as the degree of antepartum and postpartum glucose intolerance, HbA1c level during pregnancy, gestational age at the diagnosis of GDM, maternal BMI (before, during, or after pregnancy), maternal age, parity, insulin use during pregnancy, family history of diabetes, prior history of GDM, and specific measure for β-cell function such as HOMA-β (homeostasis model assessment of β-cell function), insulinogenic index and disposition index were also associated with DM development. Notably, most associations were lost upon multivariate analysis. Similarly, our study also showed that antepartum and the 6-week postpartum fasting plasma glucose were the only independent risk factors for DM development. As expected, insulin use during pregnancy, which reflected the

degree of glucose intolerance at this stage, was predictive in DM development in the univariate analysis. Furthermore, the concomitant presence of IFG at this stage increased the risk of future DM in our patients (3.5-fold). Therefore, we think that the postpartum glucose tolerance test is important not only for diagnosing women with pre-existing DM, but also as a means of selecting high-risk subjects for more intensive DM screening. Due to limited referral criteria and hence the inclusion criteria, in the present study, women with IFG only were not followed up and hence their natural history could not be delineated. Because of the significant predictive power of fasting plasma glucose, we recommend that women with postpartum IFG only should be followed up like those with postpartum IGT.

As in another local study,[5] 60% of our patients with initial postpartum IGT reverted to NGT and only 6% progressed to diabetes within 1 year of delivery. This interesting finding suggests that the exaggerated insulin resistance of pregnancy takes time to abate. Assessing the glucose tolerance level 1-year post-delivery may provide additional information for later development of type 2 diabetes. This was shown in our study that women with IGT, IFG or both 1-year post-delivery had a higher conversion rate to type 2 diabetes than those who regressed to NGT at the same stage. Metabolic assessment at this stage revealed that 15% of the women had metabolic syndrome, and its presence was associated with 4.7-fold increased risk of developing DM. Since individual metabolic parameters were not associated with the development of DM, the predictive power of the syndrome was largely attributable to glucose intolerance. This was confirmed by the loss of significant predictive power of metabolic syndrome upon multivariate analysis with other independent variables such as fasting and 2-hour post–75-gram OGTT plasma glucose levels. Nevertheless, women with metabolic syndrome constitute another high-risk group deserving intensive screening. These findings were comparable to a local study of 801 Chinese women with a history of GDM.[6] The latter study found that women with a GDM history had more adverse cardiovascular risk factors, including higher BP, dysglycaemia and dyslipidaemia than controls, even after adjustment for age, BMI, and smoking history.

As only 48 (of 238) and 18 (of 150) patients in the main and subgroup analyses developed DM respectively, our study was not sufficiently powered to examine independent effects of multiple risk factors for DM by multivariate regression analysis. Therefore, our findings need to be confirmed in a larger prospective study with regular follow-up.

Implication for postpartum screening

Although our study focused only on women with GDM and postpartum IGT and excluded those with GDM but NGT postpartum, our findings support recommendations for metabolic assessments after GDM, as suggested in the Fifth International Workshop-Conference on GDM.[18] The panel recommended a 75-gram OGTT early postpartum, 1 year postpartum and at a minimum, every 3 years thereafter. Based on our findings, metabolic assessment 1 year postpartum is pivotal in further refining a screening strategy. We recommend that women with persistent glucose intolerance 1 year postpartum should have more intensive metabolic screening (possibly every year), while women with NGT at this stage can be screened every 3 years. As women with IGT and previous GDM were 50% less likely to progress to type 2 diabetes when treated with metformin,[8] vigorous metabolic screening is mandatory.

Although a well-defined and structured screening protocol is available, its success largely depends on public awareness and attendance rates. When co-ordinated with postpartum visits, the default rate for immediate postpartum glucose tolerance testing can be minimised.[18] As in our study however, the attendance rate for subsequent follow-up drops off significantly. Measures should be formulated to enhance compliance to the screening programme. A nurse-led clinic provides a one-stop service involving education, metabolic assessment, and screening could be a cost-effective way to enforce the screening programme. With better co-ordination with obstetricians, more public awareness promotion and automated re-call systems, screening rates can be improved.

Conclusions

In this cohort study, 20% of Chinese women with GDM and postpartum IGT developed type 2 diabetes after a mean follow-up of 4.3 years. Fasting plasma glucose levels during and 6 weeks after pregnancy were the strongest independent risk factor for DM development. Even though a significant proportion of these women reverted to NGT 1 year after delivery, those retaining persistent glucose intolerance had a particularly high rate of conversion to type 2 diabetes. The presence of metabolic syndrome at this stage was also associated with future DM development. Therefore, repeating the OGTT and metabolic assessment at 1 year after delivery are strongly recommended in the follow-up programme, in order to provide more cost-effective surveillance for future DM. As the use of lifestyle modification and pharmacological interventions for preventing diabetes are gaining more evidence, systematic postpartum surveillances of women with GDM represents a golden opportunity for improving the diagnosis and prevention of type 2 diabetes.

References

1. Diabetes and impaired glucose tolerance in women aged 20-39 years. World Health Organization Ad Hoc Diabetes Reporting Group. World Health Stat Q 1992;45:321-7.
2. Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet 2009;373:1773-9.
3. Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. Diabetes Care 2002;25:1862-8.
4. Ko GT, Tam WH, Chan JC, Rogers M. Prevalence of gestational diabetes mellitus in Hong Kong based on the 1998 WHO criteria. Diabet Med 2002;19:80.
5. Lam KS, Li DF, Lauder IJ, Lee CP, Kung AW, Ma JT. Prediction of persistent carbohydrate intolerance in patients with gestational diabetes. Diabetes Res Clin Pract 1991;12:181-6.
6. Ko GT, Chan JC, Tsang LW, Li CY, Cockram CS. Glucose intolerance and other cardiovascular risk factors in Chinese women with a history of gestational diabetes mellitus. Aust N Z J Obstet Gynaecol 1999;39:478-83.
7. Tam WH, Yang XL, Chan JC, et al. Progression to impaired glucose regulation, diabetes and metabolic syndrome in Chinese women with a past history of gestational diabetes. Diabetes Metab Res Rev 2007;23:485-9.
8. Ratner RE, Christophi CA, Metzger BE, et al. Prevention of diabetes in women with a history of gestational diabetes: effects of metformin and lifestyle intervention. J Clin Endocrinol Metab 2008;93:4774-9.
9. Ratner RE. Prevention of type 2 diabetes in women with previous gestational diabetes. Diabetes Care 2007;30 Suppl 2:S242-5. Erratum in: Diabetes Care 2007;30:3154.
10. World Health Organization. Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO consultation. Geneva: WHO; 1999.
11. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2006;29 Suppl 1:S43-8.
12. IDF worldwide definition of metabolic syndrome. International Diabetes Federation website: http://www.idf.org/metabolic_syndrome. Accessed Dec 2010.
13. Kjos SL, Peters RK, Xiang A, Henry O, Montoro M, Buchanan TA. Predicting future diabetes in Latino women with gestational diabetes. Utility of early postpartum glucose tolerance testing. Diabetes 1995;44:586-91.
14. Feig DS, Zinman B, Wang X, Hux JE. Risk of development of diabetes mellitus after diagnosis of gestational diabetes. CMAJ 2008;179:229-34.
15. Steinhart JR, Sugarman JR, Connell FA. Gestational diabetes is a herald of NIDDM in Navajo women. High rate of abnormal glucose tolerance after GDM. Diabetes Care 1997;20:943-7.
16. Ekelund M, Shaat N, Almgren P, Groop L, Berntrop K. Prediction of postpartum diabetes in women with gestational diabetes mellitus. Diabetologia 2010;53:452-7.
17. Schaefer-Graf UM, Buchanan TA, Xiang AH, Peters RK, Kjos SL. Clinical predictors for a high risk for the development of diabetes mellitus in the early puerperium in women with recent gestational diabetes mellitus. Am J Obstet Gynecol 2002;186:751-6.
18. Metzger BE, Buchanan TA, Coustan DR, et al. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. Diabetes Care 2007;30 Suppl 2:S251-60. Erratum in: Diabetes Care 2007;30:3154.