

## CLINICAL STUDY

# Atlantic DIP: high prevalence of abnormal glucose tolerance *post partum* is reduced by breast-feeding in women with prior gestational diabetes mellitus

Michael W O'Reilly, Gloria Avalos, Michael C Denny, Eoin P O'Sullivan and Fidelma Dunne

Atlantic DIP Investigators, Department of Endocrinology and Diabetes Mellitus, University College Hospital/National University of Ireland, Galway, Republic of Ireland

(Correspondence should be addressed to M W O'Reilly; Email: micilino@hotmail.com)

## Abstract

**Objective:** Gestational diabetes (GDM) is associated with adverse fetal and maternal outcomes, and identifies women at risk of future type 2 diabetes mellitus (T2DM). Breast-feeding may improve *post partum* maternal glucose tolerance. Our objective was to identify the prevalence of *post partum* dysglycemia after GDM, to delineate associated factors and to examine the effect of lactation on *post partum* glucose tolerance.

**Design:** We compared *post partum* 75 g oral glucose tolerance test (OGTT) results from 300 women with GDM and 220 controls with normal gestational glucose tolerance (NGT) in five regional centers. Breast-feeding data was collected at time of OGTT.

**Methods:** *Post partum* OGTT results were classified as normal (fasting plasma glucose (FPG) <5.6 mmol/l, 2 h <7.8 mmol/l) and abnormal (impaired fasting glucose (IFG), FPG 5.6–6.9 mmol/l; impaired glucose tolerance (IGT), 2 h glucose 7.8–11 mmol/l; IFG+IGT; T2DM, FPG  $\geq 7$  mmol/l  $\pm$  2 h glucose  $\geq 11.1$  mmol/l). Binary logistic regression was used to identify factors predictive of persistent hyperglycemia.

**Results:** Five hundred and twenty women were tested; six (2.7%) with NGT in pregnancy had *post partum* dysglycemia compared with 57 (19%) with GDM in index pregnancy ( $P < 0.001$ ). Non-European ethnicity (odds ratio (OR) 3.40; 95% confidence interval (CI) 1.45–8.02,  $P = 0.005$ ), family history of T2DM (OR 2.14; 95% CI 1.06–4.32,  $P = 0.034$ ), and gestational insulin use (OR 2.62; 95% CI 1.17–5.87,  $P = 0.019$ ) were associated with persistent dysglycemia. The prevalence of persistent hyperglycemia was significantly lower in women who breast-fed vs bottle-fed *post partum* (8.2 vs 18.4%,  $P < 0.001$ ).

**Conclusions:** Non-European ethnicity, gestational insulin use, family history of T2DM, and elevated body mass index were associated with persistent dysglycemia after GDM. Breast-feeding may confer beneficial metabolic effects after GDM and should be encouraged.

European Journal of Endocrinology 165 953–959

## Introduction

Gestational diabetes (GDM) is associated with adverse fetal and maternal outcomes (1). GDM is also associated with an increased risk of persistent dysglycemia and development of type 2 diabetes mellitus (T2DM) in later life (2). Pre-diabetes and T2DM are associated with a two- to four-fold increased risk of coronary heart disease (CHD) compared with the risk in the non-diabetic population (3). Early recognition of pre-diabetes and diabetes with appropriate and cost-effective screening is advocated to allow early interventions for this high risk group and consequently reduce the risk of future vascular disease. Reported prevalence of pre-diabetes and T2DM following GDM ranges from 7 to 35% (4). The current literature suggests that the rate of uptake of

*post partum* diabetes screening is low, and that a fasting plasma glucose (FPG) alone may miss up to 72% of cases of *post partum* dysglycemia (5, 6). To date studies on persistent *post partum* hyperglycemia have shown inconsistent results. Some authors have suggested that breast-feeding may offer a protective effect against *post partum* hyperglycemia in women with GDM in an index pregnancy (7). Further work is needed because there are few studies on the effects of lactation on early *post partum* glucose tolerance in a predominantly European population. We hypothesize that breast-feeding improves early *post partum* glucose tolerance after GDM. The primary objectives of this study were to identify the prevalence of persistent pre-diabetes (impaired fasting glucose (IFG) or impaired glucose tolerance (IGT)), diabetes and metabolic syndrome in

the early *post partum* period (up to 12 weeks), the maternal factors associated with these states, and to examine the effect of breast-feeding on *post partum* glucose tolerance after GDM.

## Materials and methods

The Atlantic Diabetes in Pregnancy (Atlantic DIP) partnership was set up in 2005 and serves a population of 500 000 in five regional centers along the Irish Atlantic seaboard, with 11 000 deliveries annually, covering a geographical area of 7338 square miles (8). This partnership advocates universal screening for GDM by a 2 h 75 g oral glucose tolerance test (OGTT) at 24–28 weeks gestation using International Association of Diabetes in Pregnancy Study Group (IADPSG) criteria.

We recalled women with GDM in the index pregnancy at 12 weeks *post partum* and repeated a 75 g OGTT. All women diagnosed with GDM in an index pregnancy between January 1st 2006 and December 31st 2007 ( $n=323$ ) were invited to participate in this study, which is a substudy of GDM patients from the ongoing Atlantic DIP collaboration (8). We also recalled a control group of women who had normal glucose tolerance (NGT) during an index pregnancy during the same time period in the same location. Women were originally classified as GDM/IGT or NGT in pregnancy according to WHO criteria, but IADPSG criteria were retrospectively applied to the database (9) after the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) trial (10). Participants with incomplete results were excluded from final analysis. The control group also received a 75 g OGTT at 12 weeks *post partum*. This study was approved by the Research Ethics Committee in each participating hospital. Written consent was obtained from all participants.

Breast-feeding data was collected from all women participating in the study at the time of OGTT at 12 weeks *post partum*. Diabetes clinical nurse specialists coordinating *post partum* OGTTs collected data on lactation by means of maternal questionnaire. Women were classified as lactating or non-lactating according to the following criteria, all of which were required: i) ongoing feeding (at least four times per day) at time of OGTT, ii) meeting maternal expectations, iii) duration >8 weeks, iv) infant reaching developmental milestones, in particular gaining weight, and v) infant receiving scheduled immunizations.

Women were categorized in pregnancy as having NGT or GDM according to IADPSG criteria (fasting glucose  $\geq 5.1$  mmol/l or 1 h value  $\geq 10.0$  mmol/l or 2 h value  $\geq 8.5$  mmol/l). *Post partum* OGTT results were classified as normal (NGT; FPG <5.6 mmol/l; 2 h value <7.8 mmol/l) or abnormal (dysglycemia) according to the following cut off values: i) IFG (fasting glucose 5.6–6.9 mmol/l; 2 h glucose value <7.8 mmol/l), ii) IGT (fasting glucose <5.6 mmol/l; 2 h glucose value

7.8–11.0 mmol/l), iii) IFG and IGT (fasting glucose 5.6–6.9 mmol/l and 2 h glucose value 7.8–11.0 mmol/l), and iv) T2DM (fasting glucose  $\geq 7.0$  mmol/l or 2 h glucose value  $\geq 11.1$  mmol/l). Weight from booking visit at 20–24 weeks gestation, body mass index (BMI), waist circumference, total cholesterol, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), and triglycerides were also measured. Contributing associated maternal factors included in the analysis were age, ethnicity (European or non-European), family history of T2DM, insulin use in pregnancy, BMI at 20–24 weeks gestation, and breast-feeding.

Finally, we measured the prevalence of *post partum* metabolic syndrome as a further positive predictor of future cardiovascular disease using the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guidelines based on the presence of three of the following five risk factors: waist circumference >35 inches (89 cm); plasma triglycerides  $\geq 1.7$  mmol/l; plasma HDL  $\leq 1.27$  mmol/l; blood pressure >130/85; and FPG >6.1 mmol/l (11).

Age and BMI were analyzed as continuous variables. BMI was also categorized into groups for demographic assessment as normal (BMI  $\leq 24.9$  kg/m<sup>2</sup>), overweight (25.0–29.9 kg/m<sup>2</sup>), and obese ( $\geq 30.0$  kg/m<sup>2</sup>). Binary logistic regression analysis was used to identify maternal factors predictive of persistent *post partum* dysglycemia, with adjustment for age, BMI, ethnicity, insulin use, positive family history, presence of metabolic syndrome, and breast-feeding. Statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS), version 15.0 (Chicago, IL, USA). Statistical significance was reached at  $P < 0.05$ .

## Results

Five hundred and sixty-four women were tested *post partum*. Complete ante- (IADPSG criteria) and *post partum* data for analysis were available on 520 women. Three hundred women had GDM in the index pregnancy in 2006–2007 according to IADPSG criteria and 220 had NGT (Table 1). The mean age of the whole group was 33.2 years (range 18–45), greater in women with previous GDM at  $33.5 \pm 4.7$  years compared with  $32.7 \pm 5.5$  years in the NGT group ( $P=0.10$ ). The majority of women were of European ethnicity (449, 86.4%). Specifically, the ethnic breakdown of non-European women (71, 13.6%) was as follows: Asian (Indian/Pakistani/Bangladeshi),  $n=25$  (35.2%); Black African,  $n=22$  (30.9%); Asian (other, including Chinese),  $n=11$  (15.5%); Mixed race,  $n=3$  (4.2%); and any other ethnicity,  $n=10$  (14.2%). Seventy-two women (13.8%) had pregnancy-induced hypertension. Within the GDM group, 75 were treated with insulin in pregnancy and 225 were managed with dietary

**Table 1** Baseline characteristics of women with GDM<sup>†</sup> and NGT. Data are presented as mean  $\pm$  s.d. or as *n* (%).

	GDM ( <i>n</i> =300)	NGT ( <i>n</i> =220)
Age in years (range)	33.5 $\pm$ 4.7 (20–44)	32.7 $\pm$ 5.5 (18–45)
Persistent positivity <sup>a</sup>	57 (19%)*	6 (2.7%)
BMI (kg/m <sup>2</sup> ) at booking	30.7 $\pm$ 6.7*	27.8 $\pm$ 4.4
MS <i>post partum</i>	31 (10.3%)	18 (8.2%)
Ethnicity (non-European)	51 (17%)*	20 (9.1%)
Family history of T2DM	148 (49.3%)*	87 (39.5%)

BMI, body mass index; GDM, gestational diabetes mellitus; IADPSG, International Association of Diabetes in Pregnancy Study Group; NGT, normal glucose tolerance; T2DM, type 2 diabetes mellitus; MS, metabolic syndrome. \**P*<0.05.

<sup>a</sup>Persistent positivity (dysglycemia) based on oral glucose tolerance test results at 12 weeks *post partum*: i) IFG, FPG 5.6–6.9 mmol/l, 2 h <7.8 mmol/l, ii) IGT, FPG <5.6 mmol/l, 2 h 7.8–11.0 mmol/l, iii) IFG and IGT and iv) T2DM, FPG  $\geq$  7.0 mmol/l or 2 h  $\geq$  11.1 mmol/l. <sup>†</sup>IADPSG criteria for GDM.

measures alone. All glucose-lowering interventions were stopped at delivery.

Mean BMI was higher in the GDM group compared with NGT controls (30.7 vs 27.8 kg/m<sup>2</sup>, *P*<0.001). There was a significantly greater number of non-European women in the GDM group (17.0 vs 9.1%, *P*=0.009). Only six of the 220 (2.7%) of NGT women went on to develop *post partum* dysglycemia. By comparison 57 of the 300 (19.0%) women with GDM remained glucose intolerant *post partum*, with the remaining 243 (81%) reverting to normal glucose metabolism. None of the NGT cohort developed T2DM *post partum*; nine women with GDM were subsequently diagnosed with T2DM *post partum* (3.0%) (Table 2). Only 44 of the 63 (69.8%) women with persistent hyperglycemia on *post partum* OGTT would have been identified with FPG alone.

Breast-feeding data was available on all 520 women. Three hundred and nineteen (61.3%) women were breast-feeding successfully at time of 12 weeks *post partum* OGTT. Age and BMI did not differ significantly between lactating and non-lactating women (Table 3). Non-European women were more likely to breast-feed than European women (90.1% compared with 56.7%, *P*<0.001). The rate of *post partum* hyperglycemia was significantly lower in women who breast-fed their babies (*n*=26, 8.2%) compared with those who bottle-fed alone (*n*=37, 18.4%), *P*<0.001.

Binary logistic regression analysis was used to identify maternal factors predictive of persistent dysglycemia *post partum* (Table 4). Ethnicity, family history of diabetes, elevated BMI in pregnancy, and requirement for insulin treatment during pregnancy were all significant predictors of persistent glucose intolerance. Non-European ethnicity was the strongest risk factor for *post partum* pre-diabetes/diabetes; non-European women were 3.4 times more likely to remain hyperglycemic compared with Europeans (adjusted odds ratio (OR) 3.40; 95% confidence interval (CI) 1.45–8.02, *P*=0.005). Family history of diabetes and insulin

treatment both more than doubled the odds of persistent *post partum* dysglycemia (adjusted OR 2.14; 95% CI 1.06–4.32, *P*=0.034 and OR 2.62; 95% CI 1.17–5.87, *P*=0.019 respectively). Elevated BMI conferred a small but statistically significant increased risk of *post partum* glucose intolerance (adjusted OR 1.08; 95% CI 1.03–1.14, *P*=0.03). Breast-feeding at time of *post partum* OGTT significantly reduced the odds of persistent dysglycemia compared with bottle-feeding (adjusted OR 0.418; 95% CI 0.199–0.888, *P*=0.022).

When European women were analyzed separately, family history of diabetes and insulin requirement in pregnancy significantly raised the odds of *post partum* glucose abnormalities, while lactation again had a protective effect (Table 5). BMI had a trend toward statistical significance (adjusted OR 1.062; 95% CI 0.991–1.138, *P*=0.09). In the study group as whole, however, only 12.8% of women with normal BMI in pregnancy had *post partum* dysglycemia, compared with 25.5% of women in the overweight group and 61.7% of women in the obesity group (*P*=0.049). The prevalence of *post partum* glucose intolerance was 17.9% in European women compared with 30.6% in women of other ethnicities (*P*=0.041). HbA1c results at term were available in 316 women. Of those women with a HbA1c of <6% at delivery, 32 (11.4%) remained glucose intolerant *post partum*, compared with 12 (48.0%) and seven (70.0%) with HbA1c of 6.0–6.4 and  $\geq$  6.4%, respectively, *P*<0.001. A glycosylated HbA1c value at term of  $\geq$  6.5% significantly increased the odds of persistent hyperglycemia at 12 weeks (adjusted OR 18.156; 95% CI 4.47–73.752, *P*<0.001).

Forty-nine women met the criteria for *post partum* metabolic syndrome. Women with GDM had an increased risk of metabolic syndrome compared with women with NGT in pregnancy (10.4 vs 8.2%) but this increased risk did not reach statistical significance (OR 1.12; 95% CI 0.59–2.16, *P*=0.4). On further analysis of women with GDM who remained glucose intolerant *post partum* (*n*=57), 15 (26.3%) had metabolic syndrome compared with 17 of the 243 (6.9%) of

**Table 2** Pregnancy and *post partum* glucose status in study population. Data are presented as *n* (%).

Post partum glucose status	Pregnancy glucose status <sup>a</sup>	
	NGT ( <i>n</i> =220)	GDM ( <i>n</i> =300)
Normal	214 (97.3)	243 (81.0)
IFG	2 (0.9)	24 (8.0)
IGT	2 (0.9)	14 (4.7)
IFG+IGT	2 (0.9)	10 (3.3)
T2DM	0	9 (3.0)

GDM, gestational diabetes mellitus; IADPSG, International Association of Diabetes in Pregnancy Study Group; NGT, normal glucose tolerance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; T2DM, type 2 diabetes mellitus.

<sup>a</sup>According to IADPSG criteria.

**Table 3** Baseline characteristics of breast- and bottle-feeding women. Data are presented as mean  $\pm$  s.d. or as *n* (%).

	Breast-feeding ( <i>n</i> =319)	Bottle-feeding ( <i>n</i> =201)
Age in years	33.3 $\pm$ 5.3	32.9 $\pm$ 5.1
BMI (kg/m <sup>2</sup> ) <sup>a</sup>	29.2 $\pm$ 6.3	30.1 $\pm$ 6.2
Ethnicity		
Non-European	64 (90.1%)	7
European	255 (56.7%)*	194
Persistent positivity <sup>b</sup>	26 (8.2%)*	37 (18.4%)
Post partum MS	30 (9.4%)	19 (9.5%)

\**P*<0.05. MS, metabolic syndrome.

<sup>a</sup>At booking visit 24–28 weeks gestation.

<sup>b</sup>Persistent positivity (dysglycemia) based on oral glucose tolerance test results at 12 weeks *post partum*: i) IFG, FPG 5.6–6.9 mmol/l, 2 h <7.8 mmol/l, ii) IGT, FPG <5.6 mmol/l, 2 h 7.8–11.0 mmol/l, iii) IFG and IGT and iv) T2DM, FPG  $\geq$ 7.0 mmol/l or 2 h  $\geq$ 11.1 mmol/l.

women with GDM who reverted to NGT *post partum* (*P*<0.001). Women with metabolic syndrome *post partum* were more likely to have had pre-eclamptic toxemia in the index pregnancy compared with those without (adjusted OR 2.77; 95% CI 1.18–6.48, *P*=0.01). This subgroup with *post partum* metabolic syndrome was also more likely to have had an operative or instrumental delivery (C-section, ventouse or forceps, adjusted OR 2.15; 95% CI 1.11–4.20, *P*=0.02). There was no significant association between *post partum* metabolic syndrome and polyhydramnios or ante- or *post partum* hemorrhage, but a trend toward significance on a composite of poor maternal outcomes (*P*=0.08). The incidence of *post partum* metabolic syndrome increased as the degree of *post partum* glucose intolerance increased: NGT, *n*=34 (7.4%); IFG, *n*=26 (23.1%); IGT, *n*=16 (18.8%); T2DM, *n*=5 (55.6%), *P*<0.001.

## Discussion

GDM is associated with adverse fetal and maternal outcomes in the index pregnancy and an increased risk of diabetes in future years (12, 13). Our study highlights the importance of early *post partum* testing and quantifies the considerable disease burden of persistent hyperglycemia after GDM. Risk estimates of T2DM after GDM vary from 17 to 63% within 5–16 years after the index pregnancy depending on the ethnic background of the study population and the detection method for GDM and glucose intolerance (2, 14). We have demonstrated a possible protective effect on glucose metabolism conferred by breast-feeding in the immediate *post partum* period. While our study was not a randomized controlled trial, it suggests potentially beneficial metabolic effects in women who breast-feed after adjustment for confounding variables. Lactation reduced the odds of persistent dysglycemia by 60% compared with the non-lactating group. Previous studies have also suggested that breast-feeding may

confer a protective role on maternal glucose regulation in the early *post partum* period (15, 16). Kjos *et al.* (16) studied glucose tolerance in 809 primarily Latino women with previous GDM at 4–12 weeks *post partum*. Breast-feeding women had improved glucose tolerance, lower fasting glucose levels and higher HDL cholesterol levels than women who were bottle-feeding. However, these findings are not supported in a recent South Korean study (17).

In addition to reducing immediate *post partum* dysglycemia after GDM, lactation may have sustained benefits on maternal glucose metabolism years after weaning. Compared with nulliparous women, child-bearing women who do not breast-feed have about a 50% increased risk of T2DM in later life (18). Schwarz *et al.* (19) studied the long-term metabolic health benefits of breast-feeding in a cohort of 1828 women aged 40–78 years, and noted an increased risk of future diabetes when term pregnancy was followed by <1 month of lactation, independent of physical activity and BMI in later life. Other studies have also noted an association between increased duration of lactation and a reduction in future dysglycemia. An analysis of two large prospective cohorts found that duration of lactation was inversely associated with risk of T2DM in young and middle-aged women, independent of other diabetes risk factors such as BMI (20). In our study, follow-up of patients with prior GDM was discontinued in the event of a normal *post partum* OGTT. Follow-up studies are necessary to confirm if the beneficial effects of lactation on glycemia persisted at 6 months, 12 months, and beyond after weaning in our cohort.

The mechanism underlying a possible preventative role of breast-feeding for maternal diabetes is unclear. Tigas *et al.* (21) found that lactating women handle oral carbohydrate loads normally, but have increased insulin sensitivity. During ingestion of identical amounts of glucose, plasma glucose concentrations in lactating women were identical to those of non-lactating women,

**Table 4** Maternal predictors of persistent *post partum* dysglycemia<sup>a</sup>. Binary logistic regression analysis with odds ratio (OR) adjusted for age, BMI, ethnicity, insulin use, positive family history, presence of metabolic syndrome, and breast-feeding. Data are presented as OR (95% CI lower–upper limit).

Variable	OR (95% CI)	<i>P</i> value
Age	1.03 (0.95–1.10)	0.333
Non-European	<b>3.40</b> (1.45–8.02)	<b>0.005</b>
Family history	<b>2.14</b> (1.06–4.32)	<b>0.034</b>
G insulin	<b>2.62</b> (1.17–5.87)	<b>0.019</b>
BMI	<b>1.08</b> (1.03–1.14)	<b>0.03</b>
Breast-feeding	<b>0.418</b> (0.199–0.888)	<b>0.022</b>

BMI, body mass index; CI, confidence interval; FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; T2DM, type 2 diabetes mellitus; G insulin, gestational insulin.

<sup>a</sup>Persistent positivity (dysglycemia) based on oral glucose tolerance test results at 12 weeks *post partum*: i) IFG, FPG 5.6–6.9 mmol/l, 2 h <7.8 mmol/l, ii) IGT, FPG <5.6 mmol/l, 2 h 7.8–11.0 mmol/l, iii) IFG and IGT and iv) T2DM, FPG  $\geq$ 7.0 mmol/l or 2 h  $\geq$ 11.1 mmol/l. Bold values denote statistical significance, *P*<0.05

**Table 5** Predictive factors of persistent dysglycemia in European women. Data are presented as OR (lower–upper limit). Data are binary logistic regression analysis with OR adjusted for age, BMI, ethnicity, insulin use, positive family history, presence of metabolic syndrome, and breast-feeding.

	OR	P value
Age	1.006 (0.928–1.09)	0.893
BMI	1.062 (0.991–1.138)	0.09
G insulin	<b>3.118</b> (1.32–7.36)	<b>0.009</b>
Family history	<b>3.187</b> (1.34–7.54)	<b>0.008</b>
Breast-feeding	<b>0.409</b> (0.158–0.786)	<b>0.011</b>

BMI, body mass index; OR, odds ratio; G insulin, gestational insulin. Bold values denote statistical significance,  $P < 0.05$

but insulin levels were lower in the lactating group. Diniz & Da Costa have also suggested that breast-feeding women have improved insulin sensitivity that persists after childbirth (22), but further research is needed to understand the associations observed here.

Previous studies have shown that the risk of diabetes following GDM increases with the degree of carbohydrate intolerance in pregnancy, the need for insulin therapy and early diagnosis of GDM during the index pregnancy (23). High rates of persistent glucose intolerance in Indo-Asian women may reflect undiagnosed diabetes pre-dating pregnancy (5, 24, 25). We have also shown that GDM patients who required insulin therapy during the index pregnancy had significantly increased odds of *post partum* glucose intolerance compared with those managed with dietary measures alone. This is not surprising as these women have a more profound degree of insulin resistance and  $\beta$ -cell decompensation necessitating exogenous insulin treatment. The  $\beta$ -cell defect in women with GDM is still present in the *post partum* period. Recent data suggest that subsequent further deterioration of  $\beta$ -cell function is a very early event in women with GDM and IGT of pregnancy, taking place within the first year *post partum* (26).

Raised BMI at booking visit (20–24 weeks) was associated with subsequent *post partum* hyperglycemia, particularly in non-European women; this corroborates some but not all previous studies (27, 28). Glucose-tolerant overweight and obese women also need to be targeted aggressively, however, as recent data show that these women have greater adverse fetal and maternal outcomes compared with controls, independent of pregnancy glucose status (29). Elevated HbA1c at term was also predictive of persistent hyperglycemia. Seventy percent of those with HbA1c  $\geq 6.5\%$  at term remained glucose intolerant at 12 weeks *post partum*, emphasizing the importance of tight glycemic control throughout pregnancy.

Metabolic syndrome was present in over 25% of those who remained glucose intolerant *post partum*. GDM predicts later manifestation of the metabolic syndrome including T2DM, both associated with vascular

dysfunction and atherogenesis, and so these two metabolic abnormalities may be intimately connected (30). Women with a history of GDM have a markedly elevated risk of CHD compared with women without a history of same (31). It is likely that this risk is mediated in part by the presence of the metabolic syndrome and its component cardiovascular risk factors. Breast-feeding did not lower the incidence of *post partum* metabolic syndrome in our study; however the sample size may be too small to draw meaningful conclusions from this result.

Measurement of an abnormal FPG ( $\geq 5.6$  mmol/l) in our study identified  $< 70\%$  of women with persistent glucose abnormalities on *post partum* OGTT. These results are similar to recent data from McClean *et al.* (6), who found that an FPG cut off value of  $\geq 6.1$  mmol/l identified abnormal glucose tolerance in 199 of the 272 cases (sensitivity 0.73). Interestingly, of these 272 women, 109 had frank diabetes, of whom 11 (10%) had an FPG  $\leq 6.0$  mmol/l. Kwong *et al.* (5) found that up to 72% of women with *post partum* hyperglycemia would have been missed if only an FPG ( $\geq 6.1$  mmol/l) was performed. Clearly measurement of FPG alone lacks sensitivity, rendering it unacceptable as a screening test for *post partum* glucose abnormalities in comparison with an OGTT. The ADA recommends a 75 g OGTT at 12 weeks *post partum* after GDM, and this is currently implemented in our five regional centers. Women with GDM who have NGT on testing at 12 weeks *post partum* may still have a significant risk of becoming hyperglycemic within 12 months (32), and ideally require a follow-up OGTT at 6 and 12 months.

Our data are novel because other authors have not studied the impact of lactation on early *post partum* glycemia in women with GDM and in glucose-tolerant controls in a predominantly European cohort. The majority of controlled studies to date have looked at long-term risk of diabetes after GDM, rather than in the early *post partum* period (2). In addition, most work on the effects of lactation on early *post partum* glycemia has focused primarily on Asian and Latino populations (15, 16). Some recent studies on breast-feeding and *post partum* diabetes have had conflicting results (17), and further work was necessary.

There is clear evidence that addressing the long-term consequences of diabetes early in the course of the disease is of benefit (33). Aggressive intervention should be offered to those women who test positive on *post partum* testing, and early pharmacotherapy with insulin-sensitizing agents may be appropriate. Women with NGT *post partum* who are identified as high risk based on ethnicity, gestational insulin use, obesity or positive family history should also be encouraged to breast-feed, as large population-based studies have shown that the beneficial metabolic effects of lactation may persist for years after weaning (19). Our study supports a growing body of evidence that lactation may improve *post partum* glucose tolerance after GDM.

Breast-feeding must be strongly encouraged by health-care providers after GDM. The rate of lactation is low in European women, and this needs to be addressed. Similarly, uptake rates of *post partum* OGTT after GDM remain low internationally (5, 34). Electronic alerts via text message or email, automated letters, and nurse phone contact may increase uptake. Where such a facility is not in place, those at highest risk should be particularly targeted. Patients at high risk of *post partum* hyperglycemia need further glucose measurement at 6 and 12 months, and ideally annually thereafter. It is crucial that funding for this screening process is provided by health strategists and politicians, and supported at a regional and national level.

### Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

### Funding

This research was funded by the Health Research Board (HRB) of Ireland (HRB Grant HS/005/19).

### References

- American Diabetes Association. Standards of medical care in diabetes. (Position Statement). *Diabetes Care* 2005 **28** (Supplement 1) S4–S36.
- Cheung NW & Byth K. Population health significance of gestational diabetes. *Diabetes Care* 2003 **26** 2005–2009. (doi:10.2337/diacare.26.7.2005)
- Laasko M. Hyperglycemia and cardiovascular disease in type 2 diabetes. *Diabetes* 1993 **48** 937–942.
- Ogonowski J & Miazgowski T. The prevalence of 6 weeks *postpartum* abnormal glucose tolerance in Caucasian women with gestational diabetes. *Diabetes Research and Clinical Practice* 2009 **84** 239–244. (doi:10.1016/j.diabres.2009.04.003)
- Kwong S, Mitchell RS, Senior PA & Constance LC. *Postpartum* diabetes screening. *Diabetes Care* 2010 **32** 2242–2244. (doi:10.2337/dc09-0900)
- McClellan S, Farrar D, Kelly A, Tuffnell DJ & Whitelaw DC. The importance of *postpartum* glucose tolerance testing after pregnancies complicated by gestational diabetes. *Diabetic Medicine* 2010 **27** 650–654. (doi:10.1111/j.1464-5491.2010.03001.x)
- Lawrence JM, Black MH, Hsu JW, Chen W & Sacks DA. Prevalence and timing of *postpartum* glucose testing and sustained glucose dysregulation after gestational diabetes mellitus. *Diabetes Care* 2010 **33** 569–576. (doi:10.2337/dc09-2095)
- Dunne FP, Avalos G, Durkan M, Mitchell Y, Gallacher T, Keenan M, Hogan M, Carmody LA & Gaffney G. The Atlantic DIP collaborators: pregnancy outcome for women with pregestational diabetes along the Irish Atlantic seaboard. *Diabetes Care* 2009 **32** 1205–1206. (doi:10.2337/dc09-1118)
- O'Sullivan EP, Avalos G, O'Reilly M, Denny MC, Gaffney G & Dunne F & Atlantic DIP collaborators. Atlantic diabetes in pregnancy (DIP): the prevalence and outcomes of gestational diabetes mellitus using new diagnostic criteria. *Diabetologia* 2011 **54** 1670–1675. (doi:10.1007/s00125-011-2150-4)
- HAPO Study Cooperative Research Group. Hyperglycemia and adverse pregnancy outcomes. *New England Journal of Medicine* 2008 **358** 991–2002. (doi:10.1056/NEJMoa0707943)
- Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *Journal of the American Medical Association* 2001 **285** 2486–2497. (doi:10.1001/jama.285.19.2486)
- American Diabetes Association. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 1997 **20** 1183–1197.
- O'Sullivan JB. Diabetes after GDM. *Diabetes* 1991 **40** 131–135.
- Ben-Haroush A, Yogev Y & Hod M. Epidemiology of gestational diabetes mellitus and its association with type 2 diabetes. *Diabetic Medicine* 2004 **21** 103–113. (doi:10.1046/j.1464-5491.2003.00985.x)
- Villegas R, Gao YT, Yang G, Li HL, Elasy T, Zheng W & Shu XO. Duration of breast-feeding and the incidence of type 2 diabetes mellitus in the Shanghai Women's Health Study. *Diabetologia* 2008 **51** 258–266. (doi:10.1007/s00125-007-0885-8)
- Kjos SL, Henry O, Lee RM, Buchanan TA & Mishell DR Jr. The effects of lactation on glucose and lipid metabolism in women with recent gestational diabetes. *Obstetrics and Gynecology* 1993 **82** 451–455.
- Kim SH, Kim MY, Yang JH, Park SY, Yim CH, Han KO, Yoon HK & Park S. Nutritional risk factors of early development of *postpartum* prediabetes and diabetes in women with gestational diabetes mellitus. *Nutrition* 2010 **27** 782–788. (doi:10.1016/j.nut.2010.08.019)
- Liu B, Jorm L & Banks E. Parity, breastfeeding and the subsequent risk of maternal type 2 diabetes. *Diabetes Care* 2010 **33** 1239–1241. (doi:10.2337/dc10-0347)
- Schwarz EB, Brown JS, Creasman JM, Stuebe A, McClure CK, Van den Eeden SK & Thom D. Lactation and maternal risk of type 2 diabetes: a population-based study. *American Journal of Medicine* 2010 **123** 863.e1–863.e6. (doi:10.1016/j.amjmed.2010.03.016)
- Stuebe AM, Rich-Edwards JW, Willett WC, Manson JE & Michels KB. Duration of lactation and incidence of type 2 diabetes. *Journal of the American Medical Association* 2005 **294** 2601–2610. (doi:10.1001/jama.294.20.2601)
- Tigas S, Sunehag A & Haymond MW. Metabolic adaptation to feeding and fasting during lactation in humans. *Journal of Clinical Endocrinology and Metabolism* 2002 **87** 302–307. (doi:10.1210/jc.87.1.302)
- Diniz JM & Da Costa TH. Independent of body adiposity, breast-feeding has a protective effect on glucose metabolism in young adult women. *British Journal of Nutrition* 2004 **92** 905–912. (doi:10.1079/BJN20041288)
- Dornhorst A, Bailey PC, Anyaoku V, Elkeles RS, Johnston DG & Beard RW. Abnormalities of glucose tolerance following gestational diabetes mellitus. *Quarterly Journal of Medicine* 1990 **284** 1219–1228.
- Sinha B, Brydon P, Taylor RS, Hollins A, Munro A, Jenkins D & Dunne F. Maternal ante-natal parameters as predictors of persistent postnatal glucose intolerance: a comparative study between Afro-Caribbeans, Asians and Caucasians. *Diabetic Medicine* 2003 **20** 382–386. (doi:10.1046/j.1464-5491.2003.00941.x)
- Benjamin E, Winters D, Mayfield J & Gohdes D. Diabetes in pregnancy in Zuni Indian women: prevalence and subsequent development of clinical diabetes after gestational diabetes. *Diabetes Care* 1991 **16** 1231–1235. (doi:10.2337/diacare.16.9.1231)
- Retnakaran R, Ying Q, Sermer M, Connelly PW, Hanley AJG & Zinman B. Declining beta cell function in 1st year *postpartum*. *Diabetes Care* 2010 **33** 1798–1804. (doi:10.2337/dc10-0351)
- Lobner K, Knopff A, Baumgarten A, Mollenhauser U, Marienfeld S, Garrido-Franco M, Bonifacio E & Ziegler A. Predictors of *postpartum* diabetes in women with gestational diabetes mellitus. *Diabetes* 2006 **55** 792–797. (doi:10.2337/diabetes.55.03.06.db05-0746)
- Aberg AE, Jonsson EK, Eskilsson I, Landin-Olsson M & Frid A. Predictive factors of developing diabetes mellitus in women with gestational diabetes. *Acta Obstetrica et Gynecologica Scandinavica* 2002 **81** 11–16. (doi:10.1046/j.0001-6349.2001.00000.x)

- 29 Owens LA, O'Sullivan EP, Kirwan B, Avalos G, Gaffney G & Dunne F. Atlantic DIP: the impact of obesity on pregnancy outcome in glucose-tolerant women. *Diabetes Care* 2010 **33** 577–579. (doi:10.2337/dc09-0911)
- 30 Carpenter MW. Gestational diabetes, pregnancy hypertension, and late vascular disease. *Diabetes Care* 2007 **30** (Supplement 2) S246–S250. (doi:10.2337/dc07-s224)
- 31 Shah BR, Retnakaran R & Booth GL. Increased risk of cardiovascular disease in young women following gestational diabetes. *Diabetes Care* 2008 **31** 1668–1669. (doi:10.2337/dc08-0706)
- 32 Lauenborg J, Hansen T, Jensen DM, Vestergaard H, Molsted-Pedersen L, Hornnes P, Locht H, Pedersen O & Damm P. Increasing incidence of diabetes after gestational diabetes: a long-term follow-up in a Danish population. *Diabetes Care* 2004 **27** 1194–1199. (doi:10.2337/diacare.27.5.1194)
- 33 Holman RR, Paul SK, Bethel MA, Matthews DR & Neil HAW. 10-Year follow-up of intensive glucose control in type 2 diabetes. *New England Journal of Medicine* 2008 **359** 1577–1589. (doi:10.1056/NEJMoa0806470)
- 34 Schaefer-Graf UM, Klavehn S, Hartmann R, Kleinwechter H, Demandt N, Sorger M, Kjos SL, Vetter K & Abou-Dakn M. How do we reduce the number of cases of missed *postpartum* diabetes in women with recent gestational diabetes mellitus? *Diabetes Care* 2009 **32** 1960–1964. (doi:10.2337/dc09-0627)

---

Received 28 July 2011

Revised version received 26 August 2011

Accepted 20 September 2011