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Title Page:

ATLANTIC DIP: High prevalence of abnormal glucose tolerance postpartum is reduced by breast-feeding in women with prior gestational diabetes mellitus

Abbreviated title: Lactation and postpartum glycemia

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Disclosure statement – Please find attached:

Objective

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

Design

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

Methods

Postpartum OGTT results were classified as normal [fasting plasma glucose (FPG) <5.6mmol/l, 2-h<7.8mmol/l] and abnormal [impaired fasting glucose (IFG), FPG 5.6-6.9mmol/l; impaired glucose tolerance (IGT), 2-h glucose 7.8-11mmol/l; IFG+IGT; T2DM, FPG≥7mmol/l ± 2h glucose ≥11.1mmol/l]. Binary logistic regression was used to identify factors predictive of persistent hyperglycemia.

Results

520 women were tested; 6 (2.7%) with NGT in pregnancy had postpartum dysglycemia compared to 57 (19%) with GDM in index pregnancy (p<0.001). Non-European ethnicity (OR 3.40, 95% 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 versus bottle-fed postpartum (8.2% v 18.4%, p<0.001).

Conclusions

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

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 (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 to 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 7-35%. [4]. The current literature suggests that the rate of uptake of postpartum diabetes screening is low, and that a fasting plasma glucose alone may miss up to 72% of cases of postpartum dysglycemia [5, 6]. To date studies on persistent postpartum hyperglycemia have shown inconsistent results. Some authors have suggested that breast-feeding may offer a protective effect against postpartum 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 postpartum glucose tolerance in a predominantly European population. We hypothesise that breast-feeding improves early postpartum glucose tolerance after GDM. The primary objectives of this study were to identify the prevalence of persistent pre-diabetes (impaired fasting glucose or impaired glucose tolerance), diabetes and metabolic syndrome in the early postpartum period (up to 12 weeks), the maternal factors associated with these states, and to examine the effect of breast-feeding on postpartum 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 centres along the Irish Atlantic seaboard, with

11,000 deliveries annually, covering a geographical area of 7,338 square miles [8]. This partnership advocates universal screening for GDM using 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 postpartum and repeated a 75g 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 Pregnacy Outcome (HAPO) trial [10]. Participants with incomplete results were excluded from final analysis. The control group also received a 75g OGTT at 12 weeks postpartum. 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 postpartum. Diabetes clinical nurse specialists coordinating postpartum 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 4 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 immunisations.

Women were categorised in pregnancy as having normal glucose tolerance (NGT) or GDM according to IADPSG criteria (fasting glucose ≥5.1mmol/l *or* 1-hour value ≥10.0mmol/l *or* 2-hour value ≥8.5mmol/l). Post partum OGTT results were classified as normal (NGT; fasting plasma glucose <5.6mmol/l; 2-h value <7.8mmol/l) or abnormal (dysglycemia) according to the following cut-off values: (i) impaired fasting glucose (IFG; fasting glucose 5.6-6.9mmol/l; 2-h glucose value <7.8mmol/l), (ii) impaired glucose tolerance (IGT; fasting glucose <5.6mmol/l; 2-h glucose value 7.8-11.0mmol/l), (iii) IFG *and* IGT (fasting glucose 5.6-6.9mmol/l *and* 2-h glucose value 7.8-11.0mmol/l) and (iv) type 2 diabetes (T2DM; fasting glucose ≥7.0mmol/l *or* 2-h glucose value ≥11.1mmol/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, body mass index (BMI) at 20-24 weeks gestation, and breast-feeding.

Finally we measured the prevalence of postpartum 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 (89cm); plasma triglycerides ≥1.7mmol/l; plasma HDL ≤1.27mmol/l; blood pressure >130/85; fasting plasma glucose >6.1mmol/l [11].

Age and BMI were analysed as continuous variables. BMI was also categorised into groups for demographic assessment as normal (BMI ≤24.9kg/m²), overweight (25.0-29.9kg/m²) and obese (≥30.0kg/m²). Binary logistic regression analysis was used to identify maternal factors predictive of persistent postpartum 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. Statistical significance was reached at $p < 0.05$.

Results:

564 women were tested postpartum. Complete ante- (IADPSG criteria) and postpartum data for analysis were available on 520 women. Three hundred women had GDM in the index pregnancy in 2006-07 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 ± 4.7 years compared to 32.7 ± 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 (PIH). Within the GDM group, 75 were treated with insulin in pregnancy and 225 were managed with dietary measures alone. All glucose-lowering interventions were stopped at delivery.

Mean BMI was higher in the GDM group compared to NGT controls (30.7 v 27.8 kg/m², p<0.001). There was a significantly greater number of non-European women in the GDM group (17.0% v 9.1%, p=0.009). Only 6 of 220 (2.7%) of NGT women went on to develop postpartum dysglycemia. By comparison 57 of 300 (19.0%) women with GDM remained glucose intolerant postpartum, with the remaining 243 (81%) reverting to normal glucose metabolism. None of the NGT cohort developed T2DM postpartum; 9 women with GDM were subsequently diagnosed with T2DM postpartum (3.0%) (Table 2). Only 44 of 63 (69.8%) women with

persistent hyperglycemia on postpartum OGTT would have been identified with a fasting plasma glucose 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 week postpartum 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 to 56.7%, P<0.001). The rate of postpartum hyperglycemia was significantly lower in women who breast-fed their babies (n=26, 8.2%) compared to 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 postpartum (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 postpartum pre-diabetes/diabetes; non-European women were 3.4 times more likely to remain hyperglycemic compared to Europeans (adjusted OR 3.40; 95% CI 1.45-8.02, p=0.005). Family history of diabetes and insulin treatment both more than doubled the odds of persistent postpartum 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 postpartum glucose intolerance (adjusted OR 1.08; 95% CI 1.03-1.14, p=0.03). Breast-feeding at time of postpartum OGTT significantly reduced the odds of persistent dysglycemia compared to bottle-feeding (adjusted OR 0.418; 95% CI 0.199-0.888, p=0.022).

When European women were analysed separately, family history of diabetes and insulin requirement in pregnancy significantly raised the odds of postpartum glucose abnormalities,

while lactation again had a protective effect (Table 5). BMI had a trend towards 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 postpartum dysglycemia, compared to 25.5% of women in the overweight group and 61.7% of women in the obesity group (p=0.049). The prevalence of postpartum glucose intolerance was 17.9% in European women compared to 30.6% in women of other ethnicities (p=0.041). Glycosylated haemoglobin (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 postpartum, compared to 12 (48.0%) and 7 (70.0%) with HbA1c of 6.0-6.4% and ≥6.4% respectively, p<0.001. A glycosylated HbA1c value at term of ≥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 criteria for postpartum metabolic syndrome. Women with GDM had an increased risk of metabolic syndrome compared to women with NGT in pregnancy (10.4% v 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 postpartum (n=57), 15 (26.3%) had metabolic syndrome compared to 17 of 243 (6.9%) of women with GDM who reverted to normal glucose tolerance postpartum (p<0.001). Women with metabolic syndrome postpartum were more likely to have had pre-eclamptic toxaemia (PET) in the index pregnancy compared to those without (adjusted OR 2.77; 95% CI 1.18-6.48, p=0.01). This subgroup with postpartum metabolic syndrome were 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 postpartum metabolic syndrome and polyhydramnios or ante- or postpartum haemorrhage, but a trend towards significance on a composite of poor maternal outcomes (p=0.08). The incidence of postpartum metabolic syndrome

increased as the degree of postpartum 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 postpartum 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 upon 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 postpartum period. While our study was not a randomised 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 to the non-lactating group. Previous studies have also suggested that breast-feeding may confer a protective role on maternal glucose regulation in the early postpartum period [15, 16]. Kjos et al studied glucose tolerance in 809 primarily Latina women with previous GDM at 4-12 weeks postpartum. 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 postpartum 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 studied the long-term metabolic health benefits of breast-feeding in a cohort of 1,828 women aged 40-78 years [19], and noted an increased risk of future diabetes when term pregnancy was followed by less than 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 2 large prospective cohorts found that duration of lactation was inversely associated with risk of type 2 diabetes 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 postpartum 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 found that lactating women handle oral carbohydrate loads normally, but have increased insulin sensitivity [21]. During ingestion of identical amounts of glucose, plasma glucose concentrations in lactating women were identical to those of non-lactating women, but insulin levels were lower in the lactating group. Diniz has 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 postpartum glucose intolerance compared to 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 postpartum 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 postpartum [26].

Raised BMI at booking visit (20-24 weeks) was associated with subsequent postpartum 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 to controls, independent of pregnancy glucose status [29]. Elevated HbA1c at term was also predictive of persistent hyperglycemia. Seventy percent of those with a HbA1c ≥6.5% at term remained glucose intolerant at 12 weeks postpartum, emphasising the importance of tight glycemic control throughout pregnancy.

Metabolic syndrome was present in over 25% of those who remained glucose intolerant postpartum. 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 coronary heart disease (CHD) compared to 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 postpartum 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 (≥5.6mmol/l) in our study identified less than 70% of women with persistent glucose abnormalities on postpartum OGTT. These results are similar to

recent data from McClean et al [6], who found that an FPG cut-off value of ≥6.1mmol/l identified abnormal glucose tolerance in 199 of 272 cases (sensitivity 0.73). Interestingly, of these 272 women, 109 had frank diabetes, of whom 11 (10%) had a fasting plasma glucose ≤6.0mmol/l. Kwong et al found that up to 72% of women with postpartum hyperglycemia would have been missed if only an FPG (≥6.1mmol/l) was performed [5]. Clearly measurement of FPG alone lacks sensitivity, rendering it unacceptable as a screening test for postpartum glucose abnormalities in comparison with an OGTT. The ADA recommends a 75g OGTT at 12 weeks postpartum after GDM, and this is currently implemented in our 5 regional centers. Women with GDM who have normal glucose tolerance on testing at 12 weeks postpartum 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 postpartum 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 postpartum period [2]. In addition, most work on the effects of lactation on early postpartum glycemia has focused primarily on Asian and Latino populations [15, 16]. Some recent studies on breast-feeding and postpartum 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 postpartum testing, and early pharmacotherapy with insulin-sensitizing agents may be appropriate. Women with normal glucose tolerance postpartum 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 postpartum 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 postpartum 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 postpartum 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.

Disclosure:

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Table 1: Baseline characteristics of women with GDM and NGT

	GDM (IADPSG criteria) N=300	**NGT in pregnancy N=220**
Age in years (mean ± SD; range)	33.5±4.7 (20-44)	32.7±5.5 (18-45)
Persistent positivity**	Dysglycemia = 57 (19%)*	Dysglycemia = 6 (2.7%)
Mean BMI (kg/m²) at booking	30.7±6.7*	27.8±4.4
Metabolic syndrome postpartum	Present = 31 (10.3%)	Present = 18 (8.2%)
Ethnicity	Non-European = 51 (17%)*	Non-European = 20 (9.1%)
Family history T2DM	Yes = 148 (49.3%) *	Yes = 87 (39.5%)

*P<0.05

BMI, body mass index; GDM, gestational diabetes mellitus; IADPSG, International Association of Diabetes in Pregnancy Study Group; NGT, normal glucose tolerance; SD, standard deviation; T2DM, type 2 diabetes mellitus

**Persistent positivity (dysglycemia) based on oral glucose tolerance test results at 12 weeks postpartum:

(i) IFG, FPG5.6-6.9mmol/l, 2-h <7.8mmol/l (ii) IGT, FPG <5.6mmol/l, 2-h 7.8-11.0mmo/l (iii) IFG *and* IGT and (iv) T2DM, FPG≥7.0mmol/l or 2-h ≥11.1mmol/l

Table 2: Pregnancy and postpartum glucose status in study population

Pregnancy glucose status (IADPSG criteria)	**Postpartum glucose status**				
	Normal	**IFG**	**IGT**	**IFG+IGT**	**T2DM**
NGT (n=220)	214 (97.3%)	2 (0.9%)	2 (0.9%)	2 (0.9%)	0
GDM (n=300)	243 (81.0%)	24 (8.0%)	14 (4.7%)	10 (3.3%)	9 (3.0%)

Abbreviations: 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

Table 3: Baseline characteristics of breast-feeding and bottle-feeding women

	Breast-feeding (n=319)	**Bottle-feeding alone (n=201)**
Age in years (mean±SD)	33.3±5.3	32.9±5.1
BMI (kg/m²) at booking visit 24-28 weeks gestation	29.2±6.3	30.1±6.2
Ethnicity	Non-European = 64 (90.1%) European = 255 (56.7%)*	Non-European = 7 European = 194
Persistent positivity postpartum**	26 (8.2%)*	37 (18.4%)
Postpartum metabolic syndrome	30 (9.4%)	19 (9.5%)

*P<0.05

**Persistent positivity (dysglycemia) based on oral glucose tolerance test results at 12 weeks postpartum:
(i) IFG, FPG 5.6-6.9mmol/l, 2-h <7.8mmol/l (ii) IGT, FPG <5.6mmol/l, 2-h 7.8-11.0mmo/l
(iii) IFG *and* IGT and (iv) T2DM, FPG≥7.0mmol/l or 2-h ≥11.1mmol/l

Table 4: Maternal predictors of persistent postpartum dysglycemia **

Variable	OR*	CI 95% lower	CI 95% upper	P-value
Age	1.03	0.95	1.10	0.333
Non-European	**3.40**	1.45	8.02	**0.005**
Family history	**2.14**	1.06	4.32	**0.034**
Gestational insulin	**2.62**	1.17	5.87	**0.019**
BMI	**1.08**	1.03	1.14	**0.03**
Breast-feeding	**0.418**	0.199	0.888	**0.022**

Abbreviations: BMI, body mass index; CI, confidence interval; FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; T2DM, type 2 diabetes mellitus; OR, odds ratio

*Binary logistic regression analysis with OR adjusted for age, BMI, ethnicity, insulin use, positive family history, presence of metabolic syndrome, and breast-feeding

**Persistent positivity (dysglycemia) based on oral glucose tolerance test results at 12 weeks postpartum:

(i) IFG, FPG 5.6-6.9mmol/l, 2-h <7.8mmol/l (ii) IGT, FPG <5.6mmol/l, 2-h 7.8-11.0mmo/l (iii) IFG *and* IGT and (iv) T2DM, FPG≥7.0mmol/l or 2-h ≥11.1mmol/l

Table 5: Predictive factors of persistent dysglycemia in European women

	OR*	**Lower**	**Upper**	**P-value**
Age	1.006	0.928	1.09	0.893
BMI	1.062	0.991	1.138	0.09
Gestational insulin	**3.118**	1.32	7.36	**0.009**
Family history	**3.187**	1.34	7.54	**0.008**
Breast-feeding	**0.409**	0.158	0.786	**0.011**

Abbreviations: BMI, body mass index; OR, odds ratio

*Binary logistic regression analysis with OR adjusted for age, BMI, ethnicity, insulin use, positive family history, presence of metabolic syndrome, and breast-feeding