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The Relative Contribution of Ethnicity, Overweight and Gestational Diabetes Severity to Postpartum Abnormal Glucose Tolerance

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Abstract

Aim: To analyze the influence of ethnicity, body mass index (BMI) and gestational diabetes (GDM) severity on abnormal glucose metabolism at the early postpartum.

Methods: Glucose tolerance (WHO criteria) was evaluated at 3-9 months after delivery in a group of 71 GDM women (NDDG criteria) coming from Latin America, 43 from Africa and 14 from Asia or Pacific Islands. Their glucose tolerance was compared to 1,948 European control women by prepregnancy and postpartum BMI and by GDM severity. The effect of these parameters was adjusted for age, family history of diabetes, previous gestational diabetes, gestational age at GDM diagnosis and excess gestational weight gain.

Results: Postpartum glucose tolerance was abnormal in 37.3% of women. Asian-Pacific Islanders (64.3%), Latinas (62.8%) and African (50.4%) had glucose metabolism abnormalities more frequently than European (35.5%) mothers (P<0.001).

There was an effect of being overweight (AOR 1.38, 95% CI 1.12-1.71, P<0.001), obese (2.10, 1.56-2.83, P<0.001) prepregnancy and of non-European geographic origin (1.80, 1.2-2.7, P=0.004) on postpartum impaired glucose metabolism in the adjusted analysis. The main predictors of postpartum dysglycemia were prepregnancy obesity and GDM fasting glycemia in both non-European and European groups. The effect of ethnicity disappeared when the effect of postpartum BMI (2.14, 1.61-2.84, P<0.001 of overweight; 2.31, 1.60-3.32, P<0.001 of obesity) was considered.

Conclusion: The effect of body weight is stronger than that of ethnicity on postpartum dysglycemia in women with recent gestational diabetes.

Keywords

Gestational diabetes mellitus, Race/ethnicity, Body mass index, Overweight, Obesity

Abbreviations

GDM: Gestational Diabetes, T2DM: Type 2 Diabetes, BMI: Body Mass Index, OGTT: Oral Glucose Tolerance Test, WHO: World Health Organization.

Introduction

Gestational diabetes (GDM) is considered as a precursor of type 2 diabetes (T2DM) that is first identified during pregnancy. Up to 60% of GDM mothers will develop T2DM at 5-10 years after delivery [1]. This risk was 7.5-fold increased in women with previous GDM at a variable follow-up time, as compared to women with normal glucose tolerance pregnancies, in a meta-analysis of observational studies [2].

Obesity is the main predisposing factor to GDM and T2DM. Beyond pregnancy, O'Sullivan [3] described that obesity markedly enhanced the proclivity to T2DM at the postpartum of GDM women. The link between obesity, GDM and T2DM is a situation of insulin resistance, which is induced by obesity and pregnancy, on a background of an impaired β cell function [4].

Ethnicity may modify the association between body mass index (BMI) and GDM [5]. In this regard, ethnicity may have an influence stronger than that of BMI in Asian, Pacific Islanders and Latinas, while BMI may predominate over ethnic group in Caucasian and African women [5,6]. Otherwise, the concept of overweight may not be comparable between ethnic groups. Over time, the risk of T2DM after GDM may be differentially influenced by ethnicity and by BMI.

In women with recent gestational diabetes, this study objective was to assess the relative effect of ethnicity, body mass index and GDM severity to predict an impairment of glucose tolerance at the early postpartum period. This information may be relevant for medical counselling and to schedule an adequate follow-up after delivery.

Methods

All consecutive women with singleton pregnancies diagnosed with gestational diabetes and managed at a Diabetes and Pregnancy Unit in Madrid (Spain) were eligible for this retrospective cohort study. Women who completed a postpartum 2-hour glucose tolerance test were included. Exclusion criteria were multiple pregnancies, pregestational diabetes, secondary causes of hyperglycemia (e.g. steroids treatment), maternal morbidity relevant for the analyses and

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Table 1: Characteristics of ethnic groups of women with gestational diabetes.

	Asia/Pacific Islands (N=14)	Latin America (N=71)	Africa (N=43)	Europe (N=1,948)	P value
Age	34 ± 5	32 ± 5	34 ± 4	33 ± 4	0.055
Family history of GDM or type 2 diabetes	33.3	58.0	31.4	59.0	<0.001
GDM in a previous pregnancy	5.6	6.2	15.7	11.8	0.276
Gestational age at GDM diagnosis	28 ± 5	26 ± 4	26 ± 5	27 ± 5	0.598
GDM 100g-OGTT fasting glycemia (mg/dl)	104.6 ± 29.9	93.6 ± 16.6	100.2 ± 15.6	89.2 ± 13.6	<0.001
GDM 100g-OGTT area under the curve (mg/dl·min⁻¹)	553.1 ± 114.5	520.0 ± 58.5	526.5 ± 57.7	511.2 ± 50.7	0.001
Prepregnancy BMI (kg/m²)	21.7 ± 3.1	26.5 ± 5.8	28.1 ± 5.6	24.6 ± 4.6	<0.001
Prepregnancy overweight or obese (BMI ≥25)	18.8	55.8	73.3	37.1	<0.001
Prepregnancy obesity (BMI ≥30)	0.0	21.2	27.7	11.6	<0.001
Excessive gestational weight gain	12.5	23.4	28.9	13.0	0.001
Postpartum BMI (kg/m²)	24.7 ± 4.8	28.9 ± 5.8	28.9 ± 5.7	25.5 ± 4.6	<0.001
Post-partum overweight (BMI ≥25)	50.0	75.9	84.6	47.7	<0.001
Post-partum obesity (BMI ≥30)	12.5	44.8	30.8	15.3	<0.001

GDM: gestational diabetes; OGTT: oral glucose tolerance test; BMI: body mass index.

incomplete data. Ethical approval to conduct this study was provided by the Hospital Ethics Committee.

A first postpartum visit was systematically scheduled for all women with GDM. The visit took place at the end of breastfeeding or three months after delivery otherwise. A total of 2,076 eligible women attended this visit at the percentage of 66.5% of initial GDM women.

Diagnosis of GDM was made after a universal screening of the population and in accordance with the *National Diabetes Data Group* (NDDG) criteria by a 100-g oral glucose tolerance test (OGTT). GDM was diagnosed whenever two points were above the following glucose values: 5.8mmol/l fasting glycemia, 10.6mmol/l 1h, 9.2mmol/l 2h, 8.1mmol/l 3h. Women received medical nutrition and physical activity education during pregnancy and at the postpartum visit by expert nurses. A standard GDM diet of 25-40kcal/kg/d, depending on body mass index and physical activity habit, was complied from GDM diagnosis to delivery. In absence of contraindications, women were recommended to walk at a moderate intensity for one hour daily. Women were counselled to preserve this diet quality and to stay physically active after delivery.

Glucose tolerance was evaluated postpartum by a standard 75g OGTT (fasting glycemia, 30', 1h and 2h timepoints). Serum fasting insulin levels were obtained at the first postpartum visit in 1,208 (8 Asian, 55 Latinas, 27 African and 1,118 European) women.

GDM severity was measured as the fasting venous glycemia and the area under the 100g-OGTT curve performed at GDM diagnosis. Trapezoidal method [(fasting glycemia + 2 · 1h glycemia + 2 · 2h glycemia + 3h glycemia) / 2] was used to calculate the area. Pre-pregnancy body mass index was calculated on the basis of self-reported pre-pregnancy weight and measured height. Prepregnancy BMI groups of overweight or obese (≥ 25.0kg/m²) and obese (≥ 30kg/m²) were considered. The gestational weight gain was the difference between last weights measured before delivery and self-reported pre-pregnancy weight. Excess gestational weight gain was defined as suggested by the *Institute of Medicine* guidelines [7] for each pre-pregnancy BMI category. Postpartum body mass index at the first postpartum visit was calculated on the basis of measured body weight by a calibrated scale and the prenatal measured height that was obtained by the same Seca® stadiometer.

Serum glucose (pre and postpartum) was measured by the glucose oxidase method (Hitachi 717, Boehringer, Mannheim, Germany). Serum insulin was measured by a two-sided immunoenzimometric assay (*ST AIA-pack IRI*, Tosoh Bioscience, San Francisco, California, USA). Measurements were performed after an overnight fast.

Data were entered into Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) Windows 20.0 software. Differences between baseline GDM population and the sample collected in the first postpartum visit were examined for potential

Table 2: Abnormal glucose tolerance at the early postpartum of mothers with gestational diabetes by ethnicity and categories of prepregnancy body mass index.

	Asia/Pacific Islands (N=14)	Latin America (N=71)	Africa (N=43)	Europe (N=1,948)	P value
Postpartum abnormal glucose tolerance (%)	64.3	50.7	62.8	35.5	<0.001
Normoweight prepregnancy (BMI <25kg/m²)	55.6	35.5	58.3	29.7	<0.001
Overweight or obese prepregnancy (BMI ≥ 25)	66.7	62.5*	63.7	44.5*	0.013
Obese prepregnancy (BMI ≥30)	0.0	73.3*	91.7*	55.1*	0.025

*P value<0.050 obtained by comparison to prepregnancy BMI <25 or <30 kg/m² in the respective ethnic group.

selection bias. For this purpose, unpaired t tests, median test and Pearson or X^2 tests were performed under valid conditions. A two-sided P value < 0.05 was considered significant. Differences among ethnic groups in prepregnancy BMI, severity of GDM, postpartum BMI and abnormal glucose tolerance after delivery were evaluated by one-way ANOVA with Bonferroni post-hoc test, Fisher or X^2 tests. The effect of ethnicity, BMI and GDM severity on glucose tolerance was adjusted by multiple logistic regression analyses. Two multivariate models were constructed that included prepregnancy and postpartum categories of BMI, respectively. Associations that remained predictive of postpartum abnormal glucose metabolism were expressed as adjusted odds ratios (AOR), 95% CI.

Results

Characteristics of the ethnic groups are described in Table 1. Non-European and European women differed significantly by frequency of family history of diabetes: 46.0 vs. 59.0%, P=0.002; GDM severity: fasting glucose at GDM diagnosis 97.1 ± 18.7 vs. 89.1 ± 13.6, P<0.001; area under the curve 526.2 ± 67.7 vs. 511.2 ± 50.4mg/dl·min⁻¹, P=0.011, prepregnancy BMI: 26.5 ± 4.8 vs. 24.6 ± 4.6kg/m², P<0.001, excess gestational weight gain: 23.9 vs. 13.0%, P<0.001, and postpartum BMI 28.4 ± 5.7 vs. 25.5 ± 4.6kg/m², P<0.001. The groups were similar by age, previous gestational diabetes, gestational age at GDM diagnosis and breastfeeding.

Abnormal glucose tolerance appeared in 37.3% of all women at 3-9 months postpartum. Abnormal glucose tolerance was more frequent in non-European than in European women (56.2 vs 35.5%, P<0.001). Type 2 diabetes was diagnosed in 12.5 of Asian, Latinas or African women and in 3.5% of European women at the first postpartum evaluation (P<0.001). Comparisons of dysglycemia by ethnicity and prepregnancy BMI categories are described in Table 2. Mean (95% CI) fasting insulin

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levels were 9.8 (5.4-14.1) in Asian-Pacific Islanders, 15.8 (10.1-21.6) in Latinas, 10.1 (7.6-12.6) in African and 9.2 (8.8-9.7)μU/mL (P<0.001). Insulin levels were increased in Latinas as compared to African (P=0.029) and European (P<0.001) women.

There was an effect of being overweight (AOR 1.38, 95% CI 1.12-1.71, P<0.001), obese (2.10, 1.56-2.83, P<0.001) pre-pregnancy and of non-European ethnicity (1.80, 1.2-2.7, P=0.004) on postpartum abnormal glucose in the multivariate analysis. At prenatal time, the main predictors of postpartum dysglycemia were prepregnancy obesity and GDM fasting glycemia. The effect of ethnicity disappeared when the effect of postpartum BMI (2.14, 1.61-2.84, P<0.001 of overweight, and 2.31, 1.60-3.32, P<0.001 of obesity) was added to the regression analysis. The analyses were adjusted for age, family history of diabetes, previous gestational diabetes, gestational age at GDM diagnosis and excess gestational weight gain.

Discussion

Ethnicity had an effect on abnormal glucose tolerance at the early postpartum of this cohort of women with gestational diabetes. Nevertheless, the effect of ethnicity was over passed by that of being overweight or obese at the postpartum.

An ethnic proclivity to type 2 diabetes has been documented in populations from Central and South America, North of Africa, Middle East, South Asia and Pacific Islands [8]. Within Europe, the T2DM proclivity seems to be higher in South-Mediterranean than in Central countries. In this study, prediabetes or diabetes was more frequently found in Asian-Pacific Islanders and African, followed by Latinas and European women. Of note, Asian-Pacific Islanders were a normoweight group overall, whereas the risk of abnormal glucose was high in obese rather than in overweight African women. We suggest that standard WHO definitions of overweight /obesity may underestimate risk in Asian and overestimate risk in African GDM women.

The risk of T2DM was described to be exacerbated by ethnicity in women with history of GDM in previous studies [5,6]. GDM ranges from 10% in Asian and Pacific Islanders, followed by Latinas, to 4% among Caucasian and African American pregnant women [6], and is diagnosed in 8.8% of Spanish women [9]. It is logical that such proclivity to abnormal glucose tolerance persists after delivery. Illustratively, impaired glucose tolerance or diabetes was found in 28% of European and in 44% of Asian-Indian post-GDM women in a previous study [10].

The ethnicity-associated risk of postpartum dysglycemia was not explained by a higher severity of GDM or by a higher prepregnancy body mass index. Steinhart et al found that a more severe GDM (fasting glucose at diagnosis ≥106 mg/dl) was followed by an incidence of postpartum T2DM multiplied per eleven in Navajo Indian population [11]. In contrast, this excess risk was ameliorated, being multiplied per 2.4 for fasting glucose ≥105 mg/dl, in a European (German) cohort studied by Schaefer et al. [12].

Fasting glucose and prepregnancy BMI were independent predictors of T2DM at the early postpartum period of GDM women previously studied by our group [13]. The multicentric French study DIAGEST found similar risk factors at a prolonged follow-up period [14]. These predictors were in agreement with the initially suggested by Coustan [15]. However, only glucose centred predictors were obtained in a multiethnic cohort at Malmö, Sweden [16]. Adjusted for ethnicity, a pronounced effect of fasting glucose, and not of third trimester BMI, was documented at different periods after delivery. Postpartum BMI was higher among glucose intolerant compared to normotolerant mothers in that study.

Weight retention and waist circumference are other weight related parameters that may influence the development of T2DM after GDM. Timing seems to be crucial in this sense. In a previous study, an effect of weight gain from the postpartum and of waist circumference were observed, but only after a prolonged (≥ 2 years) monitoring [17]. In the current analysis, postpartum overweight was more sensitive than gestational weight gain or waist circumference in order to detect glucose abnormalities at an early postpartum period.

The probability of abnormal glucose intolerance increased with postpartum overweight or obesity, regardless ethnicity, in GDM women. A remainder is that gestational weight gain is the main determinant of postpartum weight retention [18]. Counselling against excessive gestational weight gain may decrease postpartum overweight in all ethnic groups as a consequence. Likewise, the correction of postpartum weight retention may restore the glucose metabolism impairment. A healthy diet and regular physical activity with an objective of 3-5% weight loss after delivery was accompanied by a 58% reduction of T2DM incidence in high risk women [19]. Similar lifestyle changes may have a positive effect on glucose tolerance among different ethnic groups [19,20].

This study had limitations. First, overweight and obesity definitions (WHO) may not be applicable in all ethnic groups. Asian women may have a risk of glucose impaired metabolism at a BMI below 25 kg/m^2 [21]. Second and main limitation is the frequent lost to follow-up of GDM women after delivery. It is estimated that only one third of GDM women receive a postpartum evaluation of glucose tolerance in developed countries [1]. In our cohort, a 33.5% of women did not attend a postpartum visit to clinics. Severe GDM (20.9 vs. 10.7%) and prepregnancy overweight or obesity (42.5 vs. 37.9%) were more frequent characteristics of non-attendant women (P value <0.050 for all comparisons). Gestational weight gain was similar between groups. Prepregnancy and postpartum BMI were highly correlated in attendant women (data not shown). If we assume that this correlation was maintained in non-attendant women, the prevalence of postpartum abnormalities is probably underestimated in these results. If we add that obese women more probably quit any physical activity or nutritional therapy program [22,23], the diabetes incidence over time may be further increased in women unaware of being at risk.

In conclusion, ethnicity, prepregnancy overweight/ obesity and severe gestational diabetes are predictors of abnormal glucose tolerance at the early postpartum of women with gestational diabetes. An effect of postpartum BMI is invariable in all ethnic groups. Nonetheless, women being overweight prepregnancy are more frequently lost to follow-up. The opportunity for health providers to adequately inform these at-risk women is unique during pregnancy. Changing these women perception of self-risk and planning an early postpartum glucose tolerance test are crucial to promote a healthy life in overweight mothers with gestational diabetes.

Ethical Statement

Principles of good clinical practice were complied to conduct this study.

References

1. Kim C, Newton KM, Knopp RH (2002) Gestational diabetes and the incidence of type 2 diabetes: a systematic review. Diabetes Care 25: 1862-1868.

2. Bellamy L, Casas JP, Hingorani AD, Williams D (2009) Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet 373: 1773-1779.

3. O'Sullivan JB (1982) Body weight and subsequent diabetes mellitus. JAMA 248: 949-952.

4. Catalano PM, Hauguel-De Mouzon S (2011) Is it time to revisit the Pedersen hypothesis in the face of the obesity epidemic? Am J Obstet Gynecol 204: 479-487.

5. Shah A, Stotland NE, Cheng YW, Ramos GA, Caughey AB (2011) The association between body mass index and gestational diabetes mellitus varies by race/ethnicity. Am J Perinatol 28: 515-520.

6. Kim SY, England L, Wilson HG, Bish C, Satten GA, et al. (2010) Percentage of gestational diabetes mellitus attributable to overweight and obesity. Am J Public Health 100: 1047-1052.

7. Rasmussen KM, Catalano PM, Yaktine AL (2009) New guidelines for weight

gain during pregnancy: what obstetrician/gynecologists should know. Curr Opin Obstet Gynecol 21: 521-526.

8. Golden SH, Brown A, Cauley JA, Chin MH, Gary-Webb TL, et al. (2012) Health disparities in endocrine disorders: biological, clinical, and nonclinical factors-an Endocrine Society scientific statement. J Clin Endocrinol Metab 97: E1579-1639.

9. Ricart W, López J, Mozas J, Pericot A, Sancho MA, et al. (2005) Body mass index has a greater impact on pregnancy outcomes than gestational hyperglycaemia. Diabetologia 48: 1736-1742.

10. Kousta E, Efstathiadou Z, Lawrence NJ, Jeffs JA, Godsland IF, et al. (2006) The impact of ethnicity on glucose regulation and the metabolic syndrome following gestational diabetes. Diabetologia 49: 36-40.

11. Steinhart JR, Sugarman JR, Connell FA (1997) Gestational diabetes is a herald of NIDDM in Navajo women. High rate of abnormal glucose tolerance after GDM. Diabetes Care 20: 943-947.

12. Schaefer-Graf UM, Buchanan TA, Xiang AH, Peters RK, Kjos SL (2002) 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 186: 751-756.

13. Pallardo F, Herranz L, Garcia-Ingelmo T, Grande C, Martin-Vaquero P, et al. (1999) Early postpartum metabolic assessment in women with prior gestational diabetes. Diabetes Care 22: 1053-1058.

14. Vambergue A, Dognin C, Boulogne A, Réjou MC, Biausque S, et al. (2008) Increasing incidence of abnormal glucose tolerance in women with prior abnormal glucose tolerance during pregnancy: DIAGEST 2 study. Diabet Med 25: 58-64.

15. Coustan DR, Carpenter MW, O'Sullivan PS, Carr SR (1993) Gestational diabetes: predictors of subsequent disordered glucose metabolism. Am J Obstet Gynecol 168: 1139-1144.

16. Ekelund M, Shaat N, Almgren P, Groop L, Berntorp K (2010) Prediction of postpartum diabetes in women with gestational diabetes mellitus. Diabetologia 53: 452-457.

17. Pallardo LF, Herranz L, Martin-Vaquero P, Garcia-Ingelmo T, Grande C, et al. (2003) Impaired fasting glucose and impaired glucose tolerance in women with prior gestational diabetes are associated with a different cardiovascular profile. Diabetes Care 26: 2318-2322.

18. Yogev Y, Visser GH (2009) Obesity, gestational diabetes and pregnancy outcome. Semin Fetal Neonatal Med 14: 77-84.

19. Ratner RE, Christophi CA, Metzger BE, Dabelea D, Bennett PH, et al. (2008) Diabetes Prevention Program Research Group. Prevention of diabetes in women with a history of gestational diabetes: effects of metformin and lifestyle interventions. J Clin Endocrinol Metab 93: 4774-4779.

20. Tobias DK, Hu FB, Chavarro J, Rosner B, Mozaffarian D, et al. (2012) Healthful dietary patterns and type 2 diabetes mellitus risk among women with a history of gestational diabetes mellitus. Arch Intern Med 172: 1566-1572.

21. Zeng Q, He Y, Dong S, Zhao X, Chen Z, et al. (2014) Optimal cut-off values of BMI, waist circumference and waist:height ratio for defining obesity in Chinese adults. Br J Nutr 112: 1735-1744.

22. Mottola MF, Campbell MK (2003) Activity patterns during pregnancy. Can J Appl Physiol 28: 642-653.

23. Katon J, Maynard C, Reiber G (2012) Attempts at weight loss in U.S. women with and without a history of gestational diabetes mellitus. Womens Health Issues 22: e447-453.