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In women with gestational diabetes mellitus factors influencing growth have a larger effect on placental weight than on birth weight

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ABSTRACT

Background and aims: Excessive fetal and placental growth are very common in diabetic pregnancy. We aimed to analyze in women with gestational diabetes mellitus (GDM) the association with birth weight (BW), placental weight (PW) and placental-to-birth weight (PWBW) ratio of acknowledged BW predictors.

Material and methods: We performed a retrospective analysis of a prospective cohort database from a tertiary hospital. Inclusion criteria were singleton pregnancy, diagnosis of GDM, delivery between 1982 and 2011 and gestational age at birth ≥23 weeks. Multiple regression analysis was performed using as dependent variables BW, PW and PWBW ratio and as independent ones maternal characteristics at baseline, metabolic characteristics (GDM diagnosis, treatment, control), pregnancy-induced hypertension, gestational age at delivery and fetal sex. Two sensitivity analyses were performed.

Results: We evaluated 2547 women, PW being available in 85.3%. BW was 3260 g (2976, 3575), PW 620 g (540, 720) and PWBW ratio 19.27 (17.20, 21.47). Among the 24 analyzed variables, there was an important overlap among those associated with BW, PW and PWBW ratio. For most characteristics associated with both BW and PW, the magnitude of the association was greater for the latter, both when promoting growth (i.e. prepregnancy body mass index, 3 h plasma glucose at diagnosis) and when restricting it (insulin treatment).

Conclusion: We conclude that in women with GDM and singleton pregnancies, variables associated with BW, PW and PWBW ratio overlap. The latter is the result of disproportionate associations with BW and PW, usually larger with PW.

Introduction

Numerous factors influence fetal growth, including maternal prepregnancy weight, weight gain, fetal sex, and maternal smoking among others [1]. Adequate fetal growth and normal birth weight (BW) are rough but long-term acknowledged parameters of a healthy pregnancy. First, maternal pathological conditions influence fetal growth and BW (i.e. maternal diabetes mellitus (DM) promotes higher fetal growth and BW while the contrary is true for preeclampsia). Second, higher morbidity and mortality are observed when BW is lower or higher than expected: perinatal mortality, polycythemia, hyperbilirubinemia and hypoglycemia are more frequent in small for gestational age infants [2] whereas a high BW is associated with a higher rate of birth injury for both mother and newborn [3], and with a higher rate of obesity in adulthood [4,5].

Placental weight (PW) is accepted as a rough surrogate of placental function, since both large and small placentas may be dysfunctional [6–8]. Both PW and placental-to-birth weight

Abbreviations: BW, birth weight; PW, placental weight; PWBW, placental weight and placental-to-birth weight ratio; BMI, body mass index; LGA, large-for-gestational age; GDM, gestational diabetes mellitus; DM, diabetes mellitus; PG, plasma glucose; CBG, capillary blood glucose; PIH, pregnancy-induced hypertension; OGTT, oral glucose tolerance test; GA, gestational age; IGT, impaired glucose tolerance.

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(PWBW) ratio are significantly associated with maternal physiologic and pathologic conditions. Examples of physiologic conditions influencing PW would be prepregnancy body mass index (BMI), ethnicity or prior pregnancies [9–11], whereas DM and hypertension would be examples of pathologic ones [12,13]. In turn, PW and PWBW ratio are associated with adverse pregnancy outcomes and childhood growth and development [14,15]: placentas that are underweight for BW have been associated with high hemoglobin values in neonates and lower-than-expected body size in later childhood whereas overweight placentas have been associated with indicators of antenatal hypoxia [14].

In diabetic pregnancy, excessive fetal growth is the most common complication [3]. The rate of large-for-gestational age newborns (>P90, LGA) that is expected to be ≈10% in the general population, is ≈18% in women with gestational diabetes mellitus (GDM) [16] and 40–50% in women with Type 1 DM [17]. Characteristics associated with BW in diabetic pregnancies are those in the general population together with parameters of glycemic control [18]. In diabetic pregnancies fetal overgrowth is associated with increased PW [19–21] and PWBW [21,22] but specific variables associated with PW and PWBW have not been addressed. As mentioned above, PW and PWBW ratio are associated with adverse outcomes at short and long-term. Thus, the gap of knowledge of specific characteristics of diabetic pregnancy associated with PW and PWBW ratio deserves to be investigated.

We aimed to analyze, in women with GDM and singleton pregnancies, the association with BW, PW and PWBW ratio of acknowledged BW predictors [7,21,23,24] and, specifically of diabetes-related factors.

Methods

We performed a retrospective analysis of the prospective cohort database of the Diabetes and Pregnancy clinic of the Hospital de la Santa Creu i Sant Pau, a tertiary hospital in Barcelona.

Inclusion criteria were singleton pregnancies, GDM diagnosis, delivery between 1982 and 2011 and gestational age at birth ≥23 weeks. The number of women fulfilling inclusion criteria was 2547 and PW was available for 2172 (85.3%) of them. The analysis was restricted to these 2172 women.

GDM diagnosis was performed with a universal screening strategy with a 50 g glucose oral load (1 h plasma glucose (PG) cut-off 7.8 mmol/l) and National Diabetes Data Group criteria [25].

GDM treatment at the center uses a normocaloric diet distributed in 4–6 meals. Patients are instructed in self-monitoring of blood glucose and measurements are recommended before and after all meals (4–6 measurements/day). Capillary blood glucose (CBG) goals are 60–90 mg/dl (3.3–5.0 mmol/l) fasting/preprandial and 100–120 mg/dl (5.6–6.7 mmol/l) 1 h postprandial. When insulin treatment is required, a basal-bolus schema is contemplated with women using the full schema or part of it as required.

BW was measured in grams, shortly after birth. PW was also measured in grams shortly after delivery with membranes and umbilical cord attached (untrimmed) [18].

The PWBW ratio was calculated as ratio of PW to neonatal weight multiplied by 100 [15].

The Ethics Committee of the Center approved the research protocol and all patients signed an informed consent.

Statistical analysis

We performed descriptive statistics using frequencies to summarize categorical variables and expressing quantitative variables as median (P25, P75).

Factors influencing BW, PW and PWBW ratio were addressed in multiple regression analysis (enter method). We considered as potential independent variables: maternal age, anthropometrics, maternal ethnicity, smoking habit, prior glucose intolerance, family history of DM, prior pregnancy, prior macrosomia, glucose

Table 1
Baseline, metabolic and perinatal characteristics of women with gestational diabetes mellitus ($N = 2172$).

	Characteristic	%	P50 (P25, P75)
Baseline	Age (years)		33 (29, 36)
	Height (cm)		1.60 (1.55, 1.63)
	BMI (kg/m^2)		23.34 (21.30, 26.24)
	Ethnicity (non-Caucasian)	5.1	
	Chronic hypertension	2.0	
	Smoking habit		
	• At the beginning of pregnancy	35.0	
	• Continued during pregnancy	23.6	
	Prior history of diabetes mellitus	14.3	
	Family history of diabetes mellitus	55.3	
	Prior pregnancy	63.2	
	Prior macrosomia	5.5	
Metabolic	Gestational age at diagnosis (weeks)		31 (27, 34)
	Fasting PG[a] at diagnosis (mmol/L)		4.7 (4.31, 5.10)
	1 h PG[a] at diagnosis (mmol/L)		11.6 (10.9, 12.5)
	2 h PG[a] at diagnosis (mmol/L)		10.2 (9.5, 11.1)
	3 h PG[a] at diagnosis (mmol/L)		7.8 (6.6, 8.8)
	Number abnormal glucose values		2 (2, 3)
	Delay between diagnosis and treatment (weeks)		2 (1, 3)
	Insulin treatment	46.5	
	Insulin dose in the 3rd trimester[b]		0.098 ± 0.215[b]
	Mean HbA1$_c$ in the 3rd trimester (%)		5.10 (4.80, 5.40)
	Gestational age at delivery (weeks)		39 (38, 40)
	Weight gain (kg)		10.1 (7.7, 13)
	Pregnancy-induced hypertension	3.7	
	Newborn sex (male)	50.8	
	Birth weight (g)		3260 (2976, 3575)
	Placental weight (g)		620 (540, 720)
	Placenta-to-birth weight ratio		19.27 (17.20, 21.47)

[a] PG: plasma glucose.
[b] Median being 0, mean and SD are used for descriptive purposes.