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Original Article

Correlation between birth weight and placental weight in healthy and diabetic puerperae

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ABSTRACT

Objective: The birth weight/placental weight ratio has an important predictive value for perinatal mortality and morbidity and for cardiovascular diseases in adult life. In this study, we compared the birth weight/placental weight (BW/PW) ratio and the correlation between the two parameters in diabetic women with that observed in healthy women.
Materials and Methods: A total of 347 consecutive newborn infants from healthy puerperae, 164 newborns from puerperae with gestational diabetes, 148 newborns from puerperae with preexisting type 1 diabetes, and 40 newborns from puerperae with preexisting type 2 diabetes have been studied from the White population of Rome. The research project was approved by the Institutional Review Board and informed written consent was obtained from the participating mothers.
Results: The BW/PW ratio is higher, and the correlation between the two parameters is lower in all classes of diabetes as compared to healthy puerperae. A remarkably low correlation is observed in preexisting diabetes pointing to a dissociation of fetal growth from placental growth.
Discussion: In diabetic pregnancy the BW/PW ratio is higher, and the correlation between birth weight and placental weight is lower in all classes of diabetic as compared to healthy puerperae pointing to a relative dissociation between the two parameters. It has been suggested that the increase of glycemic levels in diabetic pregnancy predisposes to important diseases in adult life. The dissociation of BW from PW in infants of diabetic pregnancy could be a predictor of the risk for such diseases of adult life.

Introduction

A balanced growth of fetus and placenta is important for fetal development; perturbation of the maternal environment may alter this balance, increasing the risk of cardiovascular diseases, immunological diseases, and metabolic syndrome during adult life [1,2]. Indeed, the birth weight (BW)/placental weight (PW) ratio has been associated with perinatal mortality and morbidity and with mortality for cardiovascular disease in adult life [3,4].

Alterations in the PW/BW ratio have been reported in diabetic pregnancy [5–7], and it has been also observed that neonatal and parental factors influence PW and BW [8–12].

In previous papers, we have proposed the correlation between BW and PW as an index of a balanced fetoplacental development, and observed that such correlation is influenced by genetic factors [13,14]. In a recent study [15] on the role of adenylate kinase locus 1 genetic polymorphism (Ak_1) in diabetic pregnancy, we have observed that BW–PW correlation is influenced by Ak_1 genotype and that there are differences between normal and diabetic pregnancy. In the present study, we carried out an analysis of BW and PW in different classes of gestational age in healthy and diabetic puerperae. Large samples of gestational and type 1 diabetes (T1D) were examined, and a sample of women with type 2 diabetes (T2D) was also included. BW–PW correlation and BW/PW ratio were considered.

Material and methods

Our sample study consists of four groups of participants: 347 consecutive newborn infants from healthy puerperae, 164 newborns from puerperae with gestational diabetes, 148 newborns from puerperae with preexisting T1D, and 40 newborns from puerperae with preexisting T2D. All infants were from the White population of Rome. Birth weight and placental weight

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(untrimmed) of newborns were registered in the delivery room. Gestational length was estimated from the date of the last menstrual period and checked with Dubowitz score as an additional index of neonatal maturity. All women with T1D and 83% of those with T2D had been treated with insulin.

The research project was approved by the Institutional Review Board (Department of Biomedicine and Prevention, University of Tor Vergata, Rome) and informed written consent was obtained from the mothers.

Correlation describes the degree of the relationship between two variables. The square of the correlation represents the fraction of the variation in one variable that may be explained by the other variable. Correlation analysis was performed using SPSS programs (SPSS Inc., Chicago, IL, USA, Version 23). Differences between correlation coefficients were evaluated according to Snedecor and Cochran [16], whereas cumulative probability was calculated according to Sokal and Rohlf [17].

The standardization (standard deviation score) consists in the transformation of a variable in a standard score. The standard score indicates for each observation how many standard deviations are above or below the mean. The comparison of standard BW (BWst) with standard PW (PWst) reveals the degree of concordance in the growth of the two parameters.

Results

Table 1 shows the maternal age and mean glycemic values of diabetic patients.

Table 2 shows the distribution of BW and PW of healthy and diabetic women in different classes of gestational ages. In general, the BW and PW values of infants from diabetic mothers are higher than those of infants from healthy puerperae. Figure 1 shows the mean BW/mean PW ratio in relation to gestational age in healthy puerperae and in puerperae with preexisting diabetes. In normal pregnancy, the BW/PW ratio is increasing from 37 weeks to 39 weeks, pointing to a relative retardation of placental growth with respect to fetal growth. In puerperae with preexisting diabetes at 37 weeks, there is a strong retardation of placental growth versus fetal growth compared to healthy puerperae. Such retardation continues during the following weeks of pregnancy.

To further evaluate the difference in the growth of fetus and placenta, in the following tables we have considered the BWst and PWst.

Table 3 shows the BWst and PWst of healthy and diabetic mothers considering all gestational ages. For each class of gestational age, we standardized the BW and PW of infants from diabetic mothers considering as reference the mean values and the standard deviations of BW and PW of infants from healthy puerperae. In healthy puerperae, PWst exceeds BWst by only a small degree, whereas in diabetic women PWst exceeds BWst. In particular, the comparison of the difference between BWst and PWst in puerperae with preexisting diabetes versus the difference between BWst and PWst of healthy puerperae is highly significant.

Table 1
Demographic clinical parameters of the sample study.

	Maternal age (y)		Glycemic level (mg/dL)	
	Mean	SE	Mean	SE
Healthy puerperae	28.50	0.31		
Type 1 diabetes	28.55	9.47	137.61	1.75
Gestational diabetes	32.68	0.62	121.69	1.20
Type 2 diabetes	31.57	9.64	126.29	3.03

SE = standard error.

Table 2
Birth weight and placental weight distributions in healthy and in diabetic puerperae in relation to gestational age.

Gestational age (wk)	Birth weight (g)			Placental weight (g)		
	Mean	SE	*n*	Mean	SE	*n*
Healthy puerperae ($N = 347$)						
≤37	2567	157	34	532	34	34
>37–≤38	3101	67	52	574	19	52
>38–≤39	3261	62	97	586	15	97
>39	3367	32	164	574	11	164
Puerperae with gestational diabetes ($N = 164$)						
≤37	3142	133	45	583	26	45
>37–≤38	3412	100	36	682	32	36
>38–≤39	3543	102	49	584	19	49
>39	3518	79	34	603	22	34
Puerperae with preexisting type 1 diabetes ($N = 148$)						
≤37	3099	102	81	566	18	81
>37–≤38	3545	116	38	598	23	38
>38–≤39	3646	77	27	619	23	27
>39	3100	—	2	650	—	2
Puerperae with preexisting type 2 Diabetes ($N = 40$)						
≤37	3602	237	13	645	70	13
>37–≤38	3461	146	16	643	44	16
>38–≤39	3516	232	7	576	46	7
>39	3777	243	4	567	117	4

SE = standard error.

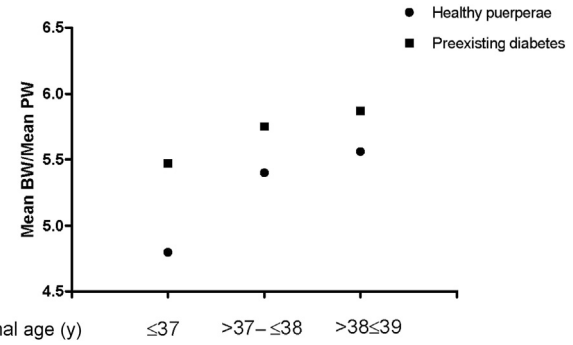

Figure 1. Mean birth weight/mean placental weight ratio in relation to gestational age in healthy puerperae and in puerperae with preexisting diabetes.

Table 3
Standardized birth weight (BWst) and placental weight (PWst) distribution in healthy and diabetic puerperae.

Standardized birth weight (BWst)		Standardized placental weight (PWst)		Difference between BWst and PWst	
Mean	SE	Mean	SE	Mean	SE
Healthy puerperae (a) ($N = 347$)					
0.0005	0.06	0.001	0.06	−0.009	0.06
Puerperae with gestational diabetes (b)* ($N = 164$)					
0.637	0.09	0.931	0.13	−0.294	0.13
Puerperae with preexisting type 1 diabetes (c)** ($N = 148$)					
0.718	0.08	1.109	0.13	−0.395	0.14
Puerperae with preexisting type 2 diabetes (d)*** ($N = 40$)					
0.783	0.19	1.331	0.27	−0.548	0.32

Comparison of difference BWst-PWst in the classes of diabetic pregnancy with the difference observed in healthy puerperae.
* b versus a, p¼ 0.048.
** c versus a, p¼ 0.014.
*** d versus a, p ¼ 0.150.

Table 4 shows the correlations between standardized and non standardized values of BW and PW in healthy and in diabetic puerperae. In all classes of diabetes, the correlation is lower as compared to healthy puerperae. In preexisting T1D, but not in gestational diabetes, the difference is statistically significant. In all

classes of diabetes, the value of r^2 is lower than that in healthy puerperae. Compared to gestational diabetes, a remarkably lower value is observed in preexisting diabetes pointing to a consistent dissociation of birth weight from placental weight.

Table 5 shows the distribution of the BWst/PWst ratio in healthy and diabetic puerperae. The ratio is higher in all classes of diabetes as compared to healthy puerperae.

We considered the effects of the following variables: gestational age, maternal age, smoking, and sex. In healthy puerperae a lower correlation is observed in gestational age $\leq$ 37 weeks and in smoking mothers, whereas in preexisting diabetes a lower correlation is observed in gestational age > 37 weeks and in females.

Discussion

The correlation between BWst and PWst and the value of r^2 are particularly lower in puerperae with preexisting diabetes as compared to healthy puerperae, pointing to a dissociation between the two parameters. A lower correlation is also observed in gestational diabetes, but this is not statistically significant.

During pregnancy, the fetal development of the fetus is influenced by many maternal factors (e.g., genetic, uterine, hormonal) and by nutrients. The placenta is a transient organ that provides nutrients, endocrine signals, cytokines, and growth factors that regulate embryo development. Placenta is an active organ that is able to adapt itself to metabolic perturbations in the mother with changes of its structure and function [1].

Alteration of glycemic level in the maternal environment could be responsible for the dissociation between placental and fetal growth. It has been suggested that an increase of the glycemic level in diabetic pregnancy induces the fetus to introduce a "metabolic memory" — as a consequence, at birth the offspring can experience several disturbances including macrosomia, hyperinsulinemia, hypoxia, polycythemia, cardiomegaly, outflow tract obstruction, metabolic syndrome, and iron abnormalities, and as an adult he/she can experience hypertension, obesity, diabetes, neurologic abnormalities, cardiovascular diseases, and behavioral effects because of early iron deficiency [18–21].

Today, a small percentage of pregnant women have gestational diabetes, whereas a greater number of mothers have preexisting T1D and T2D. Our data show that, compared with healthy puerperae, the discordance between placental and fetal growth is much more marked in preexisting diabetes than in gestational diabetes, pointing to an important role of the alteration of maternal biochemical environment that is more intense in preexisting as compared to gestational diabetes. At present, however, it cannot be ruled out that genetic factors underlying T1D and T2D have a direct influence on the degree of dissociation between placenta and fetal growth.

Table 4
Correlation between birth weight and placental weight in healthy and diabetic puerperae.

	r	r^2
Healthy puerperae (a) ($N = 347$)		
Nonstandardized values	0.473	0.22
Standardized values	0.500	0.25
Puerperae with gestational diabetes (b)* ($N = 164$)		
Nonstandardized values	0.315	0.10
Standardized values	0.326	0.11
Puerperae with preexisting type 1 diabetes (c)** ($N = 148$)		
Nonstandardized values	0.214	0.05
Standardized values	0.183	0.03
Puerperae with preexisting type 2 diabetes (d)*** ($N = 40$)		
Nonstandardized values	0.081	0.007
Standardized values	0.078	0.006

Significance of difference between diabetic and healthy puerperae (nonstandardized values).
* b versus a, $p = 0.065$.
** c versus a, $p = 0.002$.
*** d versus a, $p = 0.027$.

Table 5
Distribution of birth weight (BW)/placental weight (PW) ratio in infants from healthy and diabetic puerperae (nonstandardized values).

Healthy puerperae		Puerperae with gestational diabetes		Puerperae with preexisting type 1 diabetes		Puerperae with preexisting type 2 diabetes	
Mean	SE	Mean	SE	Mean	SE	Mean	SE
5.835	0.116	5.297	0.109	4.998	0.121	4.997	0.206
Significance of ratio BW/PW difference between diabetic and healthy puerperae							
p		0.0006		0.0001		0.0002	

SE = standard error.

Conflicts of interest

All authors have no potential conflicts of interest.

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