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Pathologic ventricular hypertrophy in the offspring of diabetic mothers: a retrospective study

THESE

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Sandra ULLMO

Médecin diplômée de la Confédération Suisse
Originaire de Gossens (VD)

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L'hypertrophie ventriculaire pathologique chez les nouveau-nés des mères diabétiques : une étude rétrospective

RESUME

Objectif :

L'incidence du diabète chez les femmes enceintes ne cesse de croître, de même que les complications chez leurs nouveau-nés. C'est pourquoi, nous avons étudié la population de mères diabétiques suivies dans notre établissement entre les années 2003-2005 dans le but d'analyser spécifiquement le problème d'hypertrophie ventriculaire pathologique (HVP) chez les nouveau-nés de cette population.

Méthode et résultats :

Dans notre étude rétrospective comprenant 87 grossesses de femmes diabétiques (92 nouveau-nés), 16 présentaient un diabète de type 1, 17 de type 2 et 54 ont développé un diabète gestationnel (DG). Le médian des hémoglobines glycquées (HbA1c) pour cette population est de 5.8% (5.3-6.5) : 17 avaient une HbA1c au-dessus de la norme, dont 2 souffrant d'une cardiomyopathie congénitale (CMC) et six d'une HVP. Un total de 75 nouveaux-nés étaient normaux, cinq avaient une CMC et 12 une HVP (1/12 décédé post-natalement, 1/12 mort-né, 2/12 nécessitant un accouchement prématuré, 8/12 normaux). Les 16 mères avec un diabète de type 1 accouchèrent de trois nouveau-nés avec une CMC et de 50% avec une HVP, comprenant un enfant décédé et un prématuré né par césarienne à cause d'une HVP. Dans le groupe des 17 nouveau-nés issus d'une mère connue pour un diabète de type 2, un cas présentait une CMC et 25% des cas une HVP. Parmi les 54 grossesses avec un DG, on dénombre un cas de CMC et un cas de HVP.

Conclusion :

Les grossesses de mères souffrant d'un diabète de type 1 et de type 2 comportent toutes deux un risque augmenté de développement d'une HVP comparées à celles de mères ayant développé un diabète gestationnel. Les contrôles glycémiques sont insuffisants pour éviter la survenue d'une HVP. Comme aucun autre paramètre prédictif n'a pu été défini jusqu'alors, nous concluons qu'un suivi échographique rapproché de ces grossesses peut prévenir des complications périnatales sévères.

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Clinical research

Pathologic ventricular hypertrophy in the offspring of diabetic mothers: a retrospective study

Sandra Ullmo[1], Yvan Vial[2], Stefano Di Bernardo[1], Matthias Roth-Kleiner[3], Yvan Mivelaz[1], Nicole Sekarski[1], Juan Ruiz[4], and Erik J Meijboom[1]*

[1]*Department of Paediatric Cardiology, Centre Hospitalier Universitaire Vaudois, BH 11-626, Rue du Bugnon 46, 1011 Lausanne, Switzerland;* [2]*Department of Gynaecology and Obstetrics, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland;* [3]*Department of Neonatology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; and* [4]*Department of Endocrinology, Diabetology, and Metabolism, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland*

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KEYWORDS
Maternal diabetes;
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Aims Diabetes in pregnant women is increasing and with that the complications in their offspring. We studied our population of diabetic mothers (2003–2005) for pathologic ventricular hypertrophy (PVH).
Methods and results In our retrospective study of all 87 diabetic pregnancies (92 neonates), 16 were type 1, 17 were type 2, and 54 were gestational diabetes (GD). Haemoglobin glycated (HbA1c) median was 5.8% (5.3–6.5): 17 with HbA1c above normal 2 with congenital heart disease (CHD) and six with PVH. A total of 75 neonates were normal, five had CHD, and 12 had PVH (1/12 died post-natally, 1/12 stillborn, 2/12 required premature delivery, 8/12 normal). The 16 type 1 pregnancies resulted in three neonates with CHD and in 50% PVH, including one death, one premature Cesarean section because of PVH. The 17 neonates of type 2 pregnancies showed in one CHD and in 25% PVH. Of the 54 GD pregnancies, one had CHD and one had PVH.
Conclusion Pregnancies of both type 1 and 2 diabetes carry an increased risk for foetal development of PVH compared with those with GD. The insufficient effect of preventive glycaemia controls leads to conclude that although no definite predictive parameters for malignant outcome can be presented, close monitoring of these pregnancies may prevent perinatal catastrophes.

Introduction

Diabetes mellitus constitutes a significant risk for the foetus if present in pregnant women. Reports so far have focused predominantly on the population of mothers wioth type 1 diabetes.[1–9] There is increasing evidence that foetuses of mothers with type 2 diabetes may be prone to a similar pathology inducing complications on a multitude of organ systems of the foetus and the placenta.[10–19] If proven true, this would constitute an important problem and might change the current prenatal diagnostic approach. Our study will focus on the consequences of all types of maternal diabetes on the foetal cardiac development.

The foetal heart is threatened in a double fashion. First, at the beginning of gestation, the disease has a teratogenic effect, cardiogenesis is impaired in the correct expression of genes coding for the cardiac development.[20,21] Early prenatal cardiac screening between 12 and 16 weeks gestation is generally advised to detect these pathologies. The incidence of cardiac malformations is 3–6% of the offspring,[22] five times higher than in normal pregnancies and frequently includes complex lesions.[1,4–5] Second, starting at the end of the second or beginning of the third trimester, the foetus may be affected by pathologic ventricular hypertrophy (PVH), commonly referred as hypertrophy cardiomyopathy.[3,4] Additional echographic investigation is required at the third trimester of gestation. PVH is characterized by an enlargement of heart; more precisely, a disproportionate hypertrophy of septum and/or ventricular free walls. Microscopic examination shows hypertrophic fibres and areas of cellular disarray. The aetiology of this cardiac anomaly is not really clear, but it is suggested that foetal hyperinsulinism may trigger hyperplasia and hypertrophy of myocardial cells by increasing fat and protein synthesis.[23,24] This condition may or may not be symptomatic. Most of cases of hypertrophic hearts return gradually to a normal size in the first months after birth. However, some patients develop severe perinatal cardiac dysfunction and may go on to die.[25–27]

Several studies presumed diminishing the incidence of complications by a stringent control of glycaemia of future mothers. This resulted in better glycaemic values and a positive effect on the incidence of congenital cardiac malformations,[28,29] but not necessary on the late development of hypertrophic cardiomyopathy. This leads us to hypothesize

* Corresponding author. Tel: +41 21 314 3553; fax: +41 21 314 3665.
E-mail address: Erik.Meijboom@chuv.ch.

that, although no definite predictive parameters[25–27,30–37] for foetal demise or malignant outcome can be presented, close cardiac foetal monitoring in these pregnancies may be helpful to prevent perinatal catastrophes. In order to assess the risk of the foetus for congenital heart disease (CHD) and/or PVH, we studied a population of mothers with all types of diabetes, well controlled regarding their glycaemia passing through our perinatal unit between 2003 and 2005.

Methods

Subjects and protocol

This retrospective study includes all offspring of diabetic mothers passing through our perinatal unit of the Centre Hospitalier Universitaire Vaudois in Lausanne, Switzerland. Criterion for inclusion was known diagnosis of maternal type 1 or type 2 diabetes or gestational diabetes (GD), treated with diet alone or associated with transient insulin therapy. All infants of mothers with those criteria admitted to our neonatal unit between 1 January 2003 and 31 December 2005 were also included.

The population consisted of 87 pregnancies, with twins in five pregnancies. The data included in the study consisted of prenatal echocardiographies, types of insulin therapy, glycaemia controls [haemoglobin glycated (HbA1c)], delivery details, postnatal conditions, and sequential echocardiographic follow-up until discharge. Criteria for the echographic diagnosis of a PVH are based to the wall thickness normalized to the body size.

Statistical analysis

Descriptive statistics were performed using the computer program StatView 5.0.1 (SAS Institute, USA). Continous variables were expressed in medians and interquartile ranges and were compared using the unpair comparison *t*-test (for normally distributed variables), Mann–Whitney *U* test (for non-normally distributed variables), and Fisher's exact test (for categorical values). Categorical variables were expressed in percentages. A *P*-value <0.05 was considered statistically significant.

Results

Baseline data of all pregnancies included in the study are shown in *Table 1*. Of the 87 pregnancies, median age

Table 1 Baseline data for diabetic mothers and perinatal outcome

	Type 1 diabetes	Type 2 diabetes	GD	*P*-value
N	16	17	54	
Age	32 (26–36)	34 (33–39)	33.5 (30–38)	0.173* 0.432**
BMI	24 (22–32)	33.4 (29–35)	27.1 (23–31)	0.449* 0.007**
Origin				
Caucasian	16 (100)	10(59)	36 (67)[a]	>0.05
African	0	4 (24)	6 (11)[a]	>0.05
Asian	0	2 (12)	4 (7)[a]	>0.05
Hispanic	0	1 (6)	5 (9)[a]	>0.05
Parity				
Nullipara	8 (50)	4 (24)	25 (46)	>0.05
Primipara	5 (31)	5 (29)	14 (26)	>0.05
Multipara	3 (19)	8 (47)	15 (28)	>0.05
HbA1c	6.6 (6.1–7.9)	6.28 (5.8–7.3)	5.4 (5.0–5.8)	<0.001* 0.02**
Type of treatment				
Insulin pump	9 (56)	1 (6)	1 (2)	0.022
Insulin subcutaneous	7 (44)	16 (94)	37 (69)	0.035
Diet	0	0	16 (29)	0.022
Complications in pregnancy:				
Preeclampsia	2 (13)	0	3 (5)	0.303
C-section	13 (81)	7 (47)	33 (59)	0.121
Perinatal outcome[b]				
Prematurity	8 (47)	7 (39)	19 (33)	0.788
Macrosomia[c]	6 (35)	5 (28)	13 (23)	0.37
CHD	3 (18)	1 (6)	1 (2)	0.04
CHD mortality 1	2 (13)	0	0	>0.05
PVH	7 (41)	4 (22)	1 (2)	<0.001
PVH mortality 2	1 (6)	1 (6)	0	0.189
Hypoglycaemia	10 (59)	9 (50)	29 (51)	0.83
Respiratory distress	7 (41)	8 (47)	21 (37)	0.241

Data are medians (interquartile range) or *N* (%).
[a]Three origins are not known.
[b]Data included five twins.
[c]Macrosomia is defined as birth weight equal or above the 90th percentile.
*Comparison of the group with type 1 and GD.
**Comparison of the group with type 2 and GD.

was 34 years old,[29–38] median body mass index (BMI) 28 kg/m^2,[23–34] 62 (71%) mothers were Caucasians, 10 (11%) Africans, six (7%) Asians, six (7%) Hispanics, 37 (43%) were nullipara, 19 (22%) primipara, and 26 (30%) multipara. Type 1 diabetes was the diagnosis in 16, type 2 diabetes in 17, and GD in 54 future mothers, of which 38 were treated by insulin. Insulin treatment was performed in 11 women by an insulin pump and in 60 by insulin subcutaneous injection. In 16 cases, treatment consisted on dietary measures only. Median HbA1c was 5.8% (5.3–6.5). Of the 17 patients with HbA1c above normal (range 6.5–10.5%), two had CHD: one Atrial Septal Defect II (ASD II) and one Hypoplasic Left Heart Syndrome (HLHS), and six PVH.

Premature delivery occurred in 34 of 87 pregnancies, of whom two because of severe PVH. Cesarean section (C-section) was performed in 53 (61%) cases, nine (10%) because of diabetic complications (suspicion of macrosomia, diabetic decompensation, and premature labour), and five (6%) because of pre-eclampsia. One pregnancy was terminated because of cardiac and renal malformations (HLHS and renal dysplasia) and one macrosomic stillborn with a cardiac hypertrophy diagnosed at autopsy. Macrosomia, defined as birth weight above percentile 90, occurred in 24 neonates. Treatment for hypoglycaemia was required in 48 neonates and 36 patients manifested respiratory distress. Postnatal echocardiography was normal in 75 (82%) neonates. Five (5%) neonates had CHD, one had Double Outlet Right Ventricle (DORV), one Ventricular Septal Defect (VSD), one Tetralogy of Fallot (TOF), one HLHS, all four diagnosed prenatally, and one ASD of the secundum type (ASD II). The TOF died shortly after birth, because of severe prematurity in association with the cardiac malformation. One termination was performed because of the antenatal diagnosis of a combination of HLHS and a renal dysplasia.

Outcome of the 12 neonates (13%) born with a PVH is given in *Table 2*.

Two showed a catastrophic evolution following a severe PVH:

(1) One type 1 diabetic patient under subcutaneous insulin pump had a diabetic decompensation at 35 weeks [hydramnios (amniotic fluid index 25), pathologic cardiotocogram (CTG) (hyporeactivity), and high glucose level (8.52–10 mmol/L)]. The mother developed oedema and gained weight at 36 weeks. Repeated CTG worsened (micro-oscillations) and hydramnios aggravated (AFI 30–32). After C-section at 37 weeks, the neonate was hypotonic, areactive, and cyanotic (Apgar 0/0/1, 4.68 kg >95th percentile), requiring a resuscitation and a transfer to the neonatal unit. An echocardiography revealed a PVH with a severe hypertrophic interventricular septum and left ventricular posterior wall (IVS: 11.9, LVPW: 12.1), tricuspid insufficiency revealing supra-systemic pulmonary hypertension with right-to-left shunting through a Patent Ductus Arteriosus (PDA). Cardiac failure leads to neonatal demise a few hours after arrival. Post-mortem findings include cardiomegaly (64.2 g, normal: 23 ± 8 g), biventricular hypertrophy, right atrial dilatation, and fibroelastosis.

(2) One patient with a BMI at 30 kg/m^2, referred for a gestational pruritus, was diagnosed during the hospitalization for a GD (HbA1c mean: 4,9%), which proved later to be a type 2 diabetes and a suspicion of a macrosomic foetus. Insulin therapy was proposed but cancelled owing to premature membrane rupture and the foetal death at 35th week of gestation. Autopsy revealed a macrosomic stillborn with an enlarged heart (31.7 g, normal: 13.4 ± 3.9 g) including a dilated left ventricle with fibroelastosis and a biventricular hypertrophy.

The three following patients showed a favourable development, but required close monitoring:

(1) One type 1 diabetic patient (BMI at 25 kg/m^2) under insulin pump (HbA1c mean: 6.9%) showed echographically a macrosomic foetus, a mild hydramnios (AFI 24), a constrictive septal hypertrophy of 8 mm, and a small pericardial effusion at the 36th week (*Figure 1*). Therefore, a vaginal delivery was induced prematurely. The newborn showed a good adaptation (Apgar 7/9/10, 3.2 kg = 90th percentile), but was transferred to the intensive care unit because of PVH. The first ultrasound confirmed a right ventricular and septal moderate hypertrophy (4.6 and 5 mm, respectively) and a PDA. Cardiac function improved in 2 days. Echocardiographic follow-up showed the normalization of the IVS size

Table 2 Outcome of the 12 neonates born with a PVH

Patient	Origin	Birth	Type of diabetes	HcA1c mean (range)	Weight (g)	Apgar	Evolution
1	African	Premature	Type 1	6.9	3200 (P90)	Apgar 7/9/10	Alive
2	Caucasian	At term	Type 1		4680 (>P90)	Apgar 0/0/1	Dead
3	Caucasian	Premature	Type 1		3230 (P90)	Apgar 5/8/9	Alive
4	Caucasian	Premature	Type 1	9.5	2500 (>P90)	Apgar 5/9/10	Alive
5	Caucasian	Premature	Type 1	7.8	3710 (>P90)	Apgar 4/5/8	Alive
6	Caucasian	At term	Type 1		3480 (P50–90)	Apgar 5/7/8	Alive
7	Caucasian	Premature	Type 1	7 (6–8)	1990 (P50–90)	Apgar 2/7/8	Alive
8	Caucasian	Premature	Type 2	7.8	3370 (>P90)	Apgar 7/8/9	Alive
9	Caucasian	At term	Type 2	6	4400 (>P90)	Apgar 9/9/9	Alive
10	African	At term	Type 2	8.56 (6.4–10.5)	4750 (>P90)	Apgar 9/10/10	Alive
11	Caucasian	Stillborn at 35 weeks	Type 2	4.9	3810 (>P90)	Apgar 0/0/0	Dead
12	South American	At term	GD	5.6	2510 (<P10)	Apgar 7/9/9	Alive

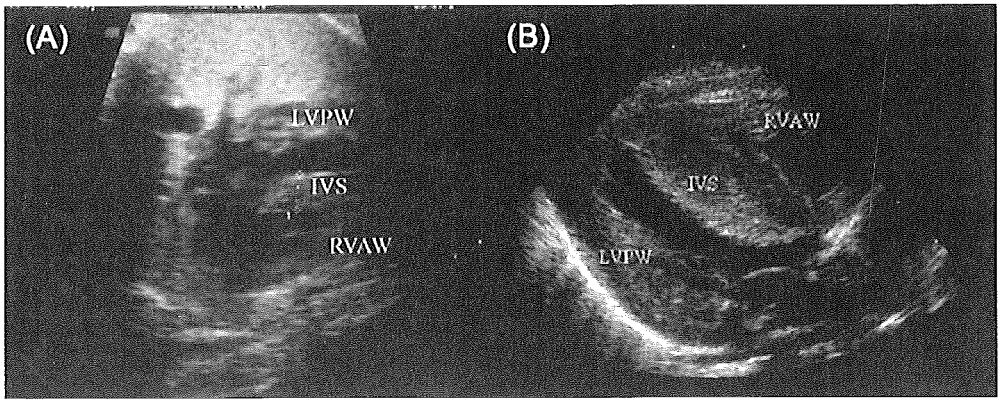

Figure 1 (*A*) Prenatal bidimensional echocardiographic image showing the thickening of the cardiac septum (8 mm) and a small pericardial effusion; (*B*) Postnatal bidimensional echocardiographic image of a severe interventricular hypertrophy (RVAW, right ventricular anterior wall).

(5 mm, still marginally elevated) and the decrease of the LVPW diameter (3.3 mm) a month later, which allowed the discharge from further cardiac follow-up.

(2) One obese type 2 diabetic patient (BMI: 49 kg/m^2), treated by insulin (HbA1c mean: 7.8%), had ultrasound controls that showed a macrosomic foetus with a progressive severe septal cardiac hypertrophy at 36th week, necessitating a premature induced delivery. At birth, the newborn was hyporeactive, but improved on oxygen (Apgar 7/8/9, 3.4 kg >90th percentile). A non-obstructive septal hypertrophy of 11 mm was confirmed by ultrasound. The newborn remained in a stable circulatory condition and follow-up controls showed a slow reduction of the septal diameter at 4 (8.6 mm) and 15 months (6.7 mm).

(3) One woman, suffering of a type 2 diabetes since 3 years, showed good glycaemic controls (HbA1c mean: 6) before requiring subcutaneous insulin therapy from the 31st week. Echocardiographic control detected a macrosomic foetus with a septal hypertrophy of 5 mm at 34 weeks. A C-section was performed at 39 weeks. The neonate (Apgar 9/9/9, 4.4 kg >90th percentile) presented a respiratory distress syndrome and a 2/6 cardiac murmur. A moderate LV hypertrophy without sub-aortic obstruction was noted echocardiographically and normalized at 3 months (4.2 mm).

Seven neonates with PVH followed a relative unremarkable course:

(1) The mother with a HELLP syndrome at 34 weeks had premature, macrosomic, plethoric, and erythrodermic neonate (Apgar 5/8/9, 3.25 kg >90th percentile) and suffered of hypoglycaemias before being stabilized. The echocardiographic diagnosis showed septal hypertrophic cardiomyopathy (4.4 mm).

(2) Two patients had diabetic decompensation [HbA1c mean: 9.5% (first), 7% (second)] and threatening premature delivery. One was delivered at 32 weeks (Apgar 5/9/10, 2.5 kg >90th percentile) and the other at 31 weeks (Apgar 2/7/8, 1.99 kg 50–90th percentile). Both developed wet lung syndrome and hypoglycaemia and showed echocardiographically cardiac septal hypertrophy (4.2 and 2.3 mm, respectively).

(3) Four neonates showed only mild cardiomyopathic features:
- One presented at birth an Apgar of 7/9/9, with a weight of 2.53 kg (<10 percentile). However, saturations remained below 75%. A cardiomegaly was noted on the chest X-ray, septal cardiac hypertrophy was confirmed using echocardiography.
- The second had a bad neonatal adaptation with a respiratory distress syndrome (Apgar 5/7/8, 3.48 kg 50–90th percentile). Echocardiography showed a non-obstructive biventricular hypertrophy (IVS: 7.5 mm, LVPW: 3.9 mm) with mitral- (2/4), aortic- (1/4), and tricuspid-insufficiency (2/4). Ascites and a pleural effusion were present. After the institution of NO therapy, a favourable evolution occurred in 4 days.
- The third had asphyxia accompanied by a central cyanosis (Apgar 4/5/8, 3.7 kg >90th percentile). Echocardiography showed an important unobstructive biventricular hypertrophy predominant at the interventricular septum (IVS: 6.6 mm, LVPW: 3.9 mm) with cardiac hyperkinesias.
- A last patient presented good condition at birth (Apgar 9/10/10, 4.75 kg >90th percentile), but with a cardiac murmur. Echocardiography confirmed septal hypertrophy (10 mm).

All of them showed a slow regression of the myocardial hypertrophy during follow-up.

Distribution of all patients following the type of maternal diabetes

Baseline data for diabetic mothers and perinatal outcome are given in *Table 1*. Mean HbA1c in each group of mothers with different types of diabetes are shown in *Figure 2*.

Type 1 Diabetic pregnancies

Sixteen pregnancies resulted in three neonates with CHD (HLHS, VSD, and TOF), one PVH mortality, one PVH delivered prematurely, and six PVH with spontaneous regression. The remaining six patients were normal.

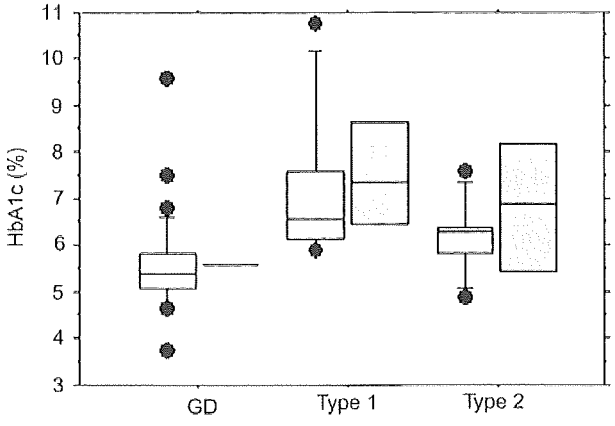

Figure 2 Mean HbA1c in each group of mothers with different types of diabetes represented with medians and interquartile range. Cross-hatched, patient without PVH. Grey, patient with PVH.

Type 2 Diabetic pregnancies

Seventeen pregnancies resulted in one neonate with CHD (ASD II), four with PVH, of whom one delivered prematurely, one was stillborn, and 12 were normal.

GD pregnancies

Fifty-four GD pregnancies resulted in one CHD (DORV) and one with PVH and spontaneous postnatal regression. The patient with DORV and hypoplastic arch had a planned delivery, was started on prostaglandin, and subsequently underwent successful surgical correction.

Discussion

Insulin-treated or type 1 diabetes was generally thought to be prevalent in 0.5% of pregnancies,[38] but recent publications indicate that this percentage is increasing during the last two decades, mainly because of an expanding number of young patients developing a type 2 diabetes.[12,39-42] This increase might even prove to be more pronounced when one considers that there is possibly a grey area of patients diagnosed with GD, who in fact might have previously not noted type 2 diabetes.[14,43,44] Cardiac complications consisting of an increased risk of neonatal CHD and PVH is a major cause of diabetes-induced morbidity and mortality of foetus and newborn.[4-5,10,45]

PVH can be seen in hypertrophy cardiomyopathy (HCM), an autosomal dominant genetic heart disease that probably is the most frequently occuring cardiomyopathy. However, none of the diabetic mothers studied had HCM or a family history of this disease. A genetic cause for the ventricular hypertrophy in our foetal patients seems even more unlikely in view of regression of this pathology during follow-up. Therefore, we have not used the terminology HCM of the foetus of a diabetic mother, but rather used the term PVH, to prevent a misleading use and underscoring the difference from classical HCM.

Our retrospective study shows an important number of cases of cardiomyopathies, 5% neonates developed CHD and 13% had PVH. The number of patients with CHD coincides with previously published studies concerning the potential teratogenic effect of diabetes[20,21] and the increased incidence of CHD[22] among the offspring of diabetic mothers. Less detailed information exists on the incidence of PVH. Pildes[46] gives a percentage of 30% of HCM in offspring of type 1 diabetic mothers, but prevalence in type 2 and GD pregnancies is much less known. Our study differs and we found relatively high number of cases with PVH: in type 1 diabetes mothers almost half of the newborns suffered from PVH and a quarter of pregnancies with a type 2 diabetes. In total, we found that the percentage of neonates suffering of PVH upon the pregnancies of women with the type 1 and 2 diabetes amounts to 33%, which is much higher than the rate of CHD among the same group of diabetic women (12%). Moreover, the mortality due to PVH in the population studied is relatively high (1/6 patients with PHV). The lowest risk for PVH was present for newborns of mothers with GD, this shows that the offspring of mothers with a type 1 and 2 diabetes are at a significantly increased risk to develop PVH, although we realize that we have not been able to compare this to the normal population.

In our study, the group of mothers with a GD showed not only to have the lowest percentage of neonates with PVH, but also to have significantly lower values of HbA1c than the one with a pre-existing diabetes. The emphasis in the literature on the tight control of glucose levels is generally accepted.[28] In analysing the group of patients with and without PVH, we mark that the first group has a significant higher HbA1c median [6.9% (interquartile range: 5.9–8.0)] than the second one [5.7% (interquartile range: 5.2–6.3)]. Despite a serious effort in a well organized and readily available healthcare system, 21% of our patients had an HbA1c above the normal limit (>6.4%), which emphasizes the difficulty of realizing good glycaemic control—a fact that may be explained by technical difficulties to control diabetes, bad attendance in the follow-up during pregnancy, late discovery of GD, non-compliance with diet and insulin treatment, and the late referral by gynaecologist or endocrinologist for a specific high-risk multidisciplinary consultation, but also the different social-economical status and ethnicity may play a role. A disturbing factor is, however, that if we look at the 12 patients with PVH, half of them had an HbA1c below and the other half above 7%, implying that PVH can develop in well and less good controlled patients. We must be so aware that the rigorous glycaemic control of those pregnancies is not sufficient to prevent the occurrence of PVH.

Another problem concerns the cardiac implications of the GD diagnosis for the foetus or neonate. Even though we found only one patient in the offspring of mothers with a GD who presented a PVH and that this one does not represent any significance, we can ask ourself whether these women had really GD or was it not yet diagnosed type 2 diabetes, as retrospectively observed in some of our cases. The question whether GD may trigger cardiac complications, however, is nowadays not resolved and further screening of GDM may help solve this question.[14]

A serious point, however, becomes the fact that if PVH develops just as well in the offspring of type 2 diabetic women, the currently observed increase of this disease may cause an increased amount of foetuses in danger of developing PVH. Moreover, our study includes an important number of women, with a BMI well above the normal (44%). This phenomenon reflects the worldwide problem of the obesity, also present in our country, and underlines the problem of the increasing incidence of new women

diagnosed with type 2 diabetes. This worry is underscored by the embryologic research in diabetic rats that shows a similar outcome in their foetuses.[20,21]

The occurrence of neonatal PVH complications has been described in several case reports,[25–27] but there is little information in the literature on series. In comparing the first five case reports described earlier, the combination at the end of gestation of hydramnios, severe ventricular hypertrophy, and pericardial effusion, proved to be an ominous sign. According to our data, we think that these signs are indications for either close observation by more frequent echographic controls or immediate intervention (induction or C-section), suggesting that a timely diagnosis is very important to avoid complications and allows the escape of a premature delivery.

The inherent limitations of this study include its retrospective aspect and the limited number of pregnancies included. Especially, the numbers and outcome of mothers with GD are too small to draw conclusions. This study suggests the need of a prospective study on these high-risk women and their offspring.

To conclude, the presence of an important number of cases of PVH in the offspring of mothers with type 1 and 2 diabetes, despite an effort to achieve good glycaemic controls, suggest that PVH remains an unpreventable complication in these patients. This supports Hawthornes[18] statement that 'Diabetic pregnancy remains a high risk state with perinatal mortality and foetal malformations rates much higher than the back population' and that the goal of the St. Vincent declaration[47] of 1989, saying that the outcome of pregnancies, complicated by a diabetes should be the same of a non-diabetic pregnancy in 5 years, is not reached yet. We admit that we cannot provide definitive predictive parameters for foetal demise or malignant outcome but conclude that, according to the results of our study, close monitoring of these pregnancies may prevent perinatal catastrophes.

Conflict of interest: none declared.

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