Diabetes and pregnancy: analysis of pregnant women submitted to fetal echocardiography during a ten-year period

Diabetes e gestação: análise das gestantes submetidas à ecocardiografia fetal em um período de dez anos

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ABSTRACT

Objectives: To analyze diabetic pregnant women who underwent fetal echocardiography, from April 1993 to December 2003, and to identify the fetal echocardiographic abnormalities and postnatal outcome. Methods: A retrospective cross-sectional study of 178 diabetic pregnant women who underwent fetal echocardiography. Clinical and laboratory maternal, fetal echocardiographic, delivery and newborn variables were studied. Means were calculated for quantitative variables and percentages for qualitative variables. Analysis of variance, Student’s t test and the Dunnet’s test were used. The adopted level of significance was \( p < 0.05 \). Results: There were 20,493 deliveries in the period considered, of which 380 were of diabetic mothers and 178 of them were studied. Mean age was 33.7 years (± 5.0). The mean body mass index (BMI) at the first prenatal appointment was 28.0 kg/m². The majority (84.8%) underwent fetal echocardiography at ≥ 28 weeks of gestation. Nine cases of interventricular septum hypertrophy were found (5.1%), three cases (1.7%) of cardiac malformation were identified, one of which was a false-positive and, among the normal cases, one false-negative was identified. Six stillbirths occurred, three from women with gestational diabetes (2.4%) and three from type 2 diabetes (6.3%, \( p = 0.305 \)). The rates of major congenital malformations among gestational and type 2 diabetes were 5.6 and 10.4%, respectively (\( p = 0.322 \)). Conclusions: The sample studied showed older women, of higher than normal BMI. Only few type-1 diabetes patients were observed. The frequency of malformation and perinatal mortality rate were similar to those reported in the literature. Perinatal outcomes in this population were also similar to those referred in the literature.

Keywords: Pregnancy in diabetics; Diabetes, gestational; Heart defects, congenital; Echocardiography; Fetal heart; Cardiomyopathy, hypertrophic; Pregnancy outcome

RESUMO

Objetivo: Analisar gestantes diabéticas submetidas à ecocardiografia fetal de abril de 1993 a dezembro de 2003, quanto às alterações ecocardiográficas nos fetos e evolução pós-natal. Métodos: Estudo retrospectivo transversal de 178 diabéticas, encaminhadas para ecocardiografia fetal. Foram estudadas variáveis clínicas e laboratoriais maternas, ecocardiográficas fetais, do parto e do recém-nascido. Foram calculadas as médias das variáveis quantitativas e os percentuais para as variáveis qualitativas. Foram usadas a análise de variância, o teste \( t \) de Student e o teste de Dunnet. Foi considerado significativo \( p < 0.05 \). Resultados: Ocorreram 20.493 partos no período, sendo 380 diabéticas, das quais, após critérios de exclusão, 178 foram estudadas. A média de idade foi de 33,7 anos (± 5,0). A média do índice de massa corpórea (IMC) foi de 28,0 kg/m². A maioria (84,8%) fez a ecocardiografia fetal com ≥ 28 semanas de gravidez. Foram identificados nove casos de hipertrofia do septo interventricular (5,1%) e três casos de malformações cardíacas (1,7%), dos quais um mostrou-se falso-positivo. Houve um caso falso-negativo entre os normais. Ocorreram três óbitos fetais entre as diabéticas gestacionais (2,4%) e outros três (6,3%) entre as diabéticas tipo 2 (\( p = 0.305 \)). Observaram-se sete malformações maiores entre as diabéticas gestacionais (5,6%) e cinco entre as do tipo 2 (10,4%, \( p = 0.322 \)). Conclusões: A população estudada se caracterizou por apresentar faixa etária elevada, IMC acima da normalidade, havendo pequeno número de diabéticas tipo 1. Os recém-nascidos mostraram frequência de anomalias congênitas maiores e mortalidade perinatal semelhante à literatura.

Descritores: Gravidez em diabéticas; Diabetes gestacional; Cardiopatias congênitas; Ecocardiografia; Coração fetal; Cardiomiopatia hipertrófica; Resultado da gravidez

INTRODUCTION

Fetuses of pregnant women display higher risk of malformations, with increased perinatal morbidity and mortality¹⁰. This association is more evident in women with type 1 diabetes (DM1) and is related to the severity

Study carried out at Service of Gynecology and Obstetrics at Hospital do Servidor Público Estadual “Francisco Morato de Oliveira” – HSPE-FMO, São Paulo (SP), Brazil.

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of the metabolic disorder present at the beginning of pregnancy\(^{(1-2)}\). Clinical trial data suggest that the disturbed glucose metabolism occurring during embryogenesis is the main determining factor for risk of fetal anomalies in pregnancies complicated by *diabetes mellitus*\(^{(2-3)}\).

Malformations may affect different organs, and the absolute risk of major malformations in children of diabetic mothers is 18.4% in general, 5.3% in the central nervous system, and 8.5% in the cardiovascular system\(^{(3)}\).

In addition to structural cardiac malformations, due to metabolic disturbances during embryogenesis, other disorders may occur, such as cardiac hypertrophy, as well as changes in fetal growth\(^{(4)}\).

Considering the prognostic importance of intrauterine diagnosis of congenital heart diseases and severe arrhythmias, the assessment of fetal heart should be done, depending on the human and material resources available. In this context, fetal echocardiography (ECO) is the test of choice\(^{(5)}\).

ECO, therefore, has become a fundamental tool for intrauterine cardiologic diagnosis\(^{(5)}\). The immediate implication is that many heart diseases and arrhythmias might be treated intrauterus and, in severe cases needing immediate post-partum emergency clinical-surgical management, early diagnosis allows anticipated planning\(^{(4)}\).

The test may be performed in the first trimester, transvaginally and transabdominally\(^{(5)}\). However, the structural anomalies of the fetal heart can only be identified after the 16\(^{th}\) week of gestation\(^{(6)}\).

Based on these facts, a study was carried out to characterize the pregnant diabetic women undergoing ECO at the Hospital do Servidor Público Estadual “Francisco Morato de Oliveira” (HSPE-FMO) in the city of São Paulo, Brazil.

**OBJECTIVE**

To assess the characteristics of pregnant diabetic women, the ECO results, the fetal cardiac disorders, and the post-natal outcome of newborns (NB).

**METHODS**

**Type of study**

Cross-sectional, retrospective study.

**Setting – Hospital do Servidor Público Estadual “Francisco Morato de Oliveira” (HSPE-FMO), São Paulo (Brazil).**

This hospital cares for a population composed by civil servants of the State of São Paulo, of favorable socio-economic and cultural levels\(^{(7)}\). All pregnant women are eligible to prenatal care and care by specialists, when pertinent, according to clinical obstetric evaluation.

**Sample**

Pregnant diabetic women seen at the hospital with gestational age (GA) from the 17\(^{th}\) week until term, referred for testing at the ECO division of the institution, from April, 1993 until December, 2003.

The NB clinical data were obtained from their charts. When such information was not available, phone or mail contact was done. Some of these NB also underwent echocardiography testing.

**Inclusion criteria**

- Pregnant women who underwent ECO because of diabetes, for the identification of presence of fetal cardiac disorders.

**Exclusion criteria**

- Pregnant women not meeting diagnostic criteria of gestational diabetes (GD), after the oral 100 g glucose load, with prior 12 hour fast, according to the National Diabetes Data Group (NDDG) 1979 criteria\(^{(8)}\);
- When the ECO was inconclusive;
- When the pregnant woman's chart was not found;
- When the NB’s chart was not found and/or delivery did not occur at the hospital and there was no confirmation of the NB cardiologic follow-up.

The final sample was constituted by 178 pregnant women (85.6% of the total number of women undergoing ECO). Of these, 177 delivered at the maternity ward of the hospital in the period from April, 1993 to December, 2003. One had the baby delivered not at the hospital but was eligible for medical care at the hospital and was included in the study, since her chart contained the necessary data for it. Pregnant women who had more than one pregnancy were considered as independent cases for each gestation.

GA at ECO performance was determined by the first ultra-sound (US) exam.

Data from the charts of all patients and their NB were obtained from the Medical File and Statistics Service of the hospital. The charts were fully revised and the data plotted in Excel\(^{®}\), 2000 9.0 (Microsoft Corporation), for further statistical analysis.

The variables recorded were:

- maternal variables: age; weight prior to pregnancy; height; body mass index in kilograms per square meter of body surface (BMI/kg/m\(^2\)) based on pre-
pregnancy weight; diabetes classification (DM1, DM2, GD); diabetes control during pregnancy (diet, insulin, date insulin treatment was introduced when the post-prandial glucose level > 120 mg/dl); GA determined at the first US performed when insulin was started;

- delivery and NB variables: type of delivery; GA at delivery according to the first US; NB weight; NB classification according to birth weight and GA (pre-term or term), and according to the appropriateness of birth weight/GA (appropriate for GA, small for GA or large for GA), according to the intrauterine growth chart by Lubchenco et al.(9); the occurrence of fetal death (FD); interventricular septum hypertrophy (ISH); malformations with their description and/or diagnosis; presence of cardiopathy; heart rhythm changes;

- ECO: GA from the first US; anatomical findings; measures of ascending aorta maximum velocity (AAMV) and of pulmonary artery maximum velocity (PAMV); measures of diastolic diameters of the interventricular septum (IVS); cardiac rhythm; presence of ISH.

For performing ECO, the US equipment HP® Sonos 2000 with 2.5 MHz-7.5 MHz high resolution sectorial transducer, bi-dimensional, with pulse and continuous Doppler and color flow mapping was used.

The structural assessment of the fetal heart was done by one of the authors, according to the segmental sequential approach(10), determining the atrial situs, the heart positioning in the chest, the systemic and pulmonary venous drainage, the type of atrioventricular and ventriculoarterial connections, and assessing the aortic arch and the presence of malformations.

The thickness of the left and right ventricles posterior walls, and of the IVS were measured with the M-mode ECO. For these measures, the projection of the ventricles minor axis was obtained and the cursor was made perpendicular to the IVS, when a frozen graphic image in bi-dimensional in M-modes were obtained. The measure of diastolic thickness was obtained by positioning the cursor transverse to the ventricles’ walls and to the IVS at the limit of the diastolic thickness of these structures. The flows were analyzed with pulse Doppler and color flow mapping, when curves of ascending aorta and of pulmonary artery flows were obtained.

The flow velocity curves through the pulmonary and aortic valves were obtained from the image of the oblique projection of the right and left chambers, long axis of the left ventricle and of the four chambers, and the volume sample assessed with immediately distal positioning to the coaptation point of the leaflets. The Doppler tracing was considered appropriate when the angle between the US flow and the flow direction was not larger than 30º. The maximum velocities at the pulmonary and aortic valves were recorded in three consecutive heart beats and at the absence of fetal respiratory movements. For each patient, the measures were obtained by the same observer and all tests were recorded in video tapes.

The inter and intraobserver variabilities were not calculated because reproducibility of the method had been previously established(10).

The cut-off point adopted for considering it hypertrophic was an interventricular septum thickness ≥ 5mm(4).

Statistical analysis
The means of the quantitative variables and the proportions of the qualitative variables were calculated.

The analysis of variance (comparing more than two groups) and the Student’s *t* test (comparing two groups) were used to detect differences between means. The Dunnet *post hoc* test was used to detect differences in multiple comparisons after the analysis of variance. The level of significance adopted in all tests was *p* < 0.05.

The Statistical Package for Social Sciences (SPSS) version 10.0 was used.

Ethical considerations
The study was approved by the Research Ethics Committee of the Instituto de Assistência Médica ao Servidor Público Estadual, under number 029/03, abiding to resolution 196/96 of the National Health Council [Conselho Nacional de Saúde], which regulates ethics in research in humans.

RESULTS
The number of deliveries of pregnant diabetic women at the hospital was 380, corresponding to 1.8% of 20,493 deliveries at this hospital during the study period. A total of 178 of these patients was studied, corresponding to 46.8% of 380 pregnant diabetic women and 85.6% of the total of pregnant diabetic women who underwent ECO.

Table 1 depicts the characteristics of the patients. Most pregnant women studied had GD (n = 125 or 70.2%), followed by those who had DM2 (n = 48 or 27.0%) and DM1 patients (n = 5 or 2.8%).

As to the use of insulin for metabolic control, Table 1 shows that 26 (20.8%) of the pregnant women with GD needed it as compared to 41 (85.4%) of DM2
subjects. Patients with DM1 already used insulin prior to the pregnancy.

The total number of vaginal deliveries was 57 (32%), while C-sections were performed in 68% (n = 121/178). The type of delivery was not associated to the type of diabetes, when considering only GD and DM2 (p = 0.393).

The mean age was 33.7 years ± 5.0 (95%CI = 32.9-34.4). The proportion of patients with age equal to or greater than 35 years was 46.4%.

Mean BMI at the beginning of pre-natal care was 28 kg/m² (95%CI = 27.6-29.3).

Table 2 shows the mean GA when insulin was introduced and the relation to the type of diabetes. Treatment was associated to the type of diabetes, considering GD and DM2 patients ($\chi^2 = 61.05$, p < 0.0001).

Mean GA at the start of insulin treatment was 23 weeks (considering GD and DM2). The patients with DM2 started therapy approximately at 21 weeks and those with GD, in the last trimester of pregnancy, with statistically significant difference (p < 0.001).

Of the total number of deliveries, 27 (15.7%) were pre-term and 145 (84.3%), term. The cases of FD (n = 6) were excluded from the calculation. Among the patients with DM1 (n = 5), three had pre-term and two term deliveries.

Babies of DM1 mothers were born at lower GA than those of GD patients and this difference between GA means at delivery was statistically significant (according to the analysis of variance and the Dunnet test for multiple comparisons at 5% significance levels). Although NB of DM2 mothers were delivered earlier than those of GD mothers, this difference was not statistically significant.

**General echocardiographic findings**

The mean GA at the last ECO was of 32.3 weeks (95%CI = 17.6-40.3 weeks). Most patients (n = 151/178 or 84.8%) underwent ECO after 28 weeks of gestation.

Table 3 shows ECO findings according to the type of maternal diabetes.

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### Table 1. General characteristics of 178 diabetic pregnant women

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DM1 (%)</th>
<th>DM2 (%)</th>
<th>GD (%)</th>
<th>Mean (%)</th>
<th>Total (%)</th>
<th>CI95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>5 (2.8)</td>
<td>48 (27.0)</td>
<td>125 (70.2)</td>
<td>178 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>27.4</td>
<td>34.3</td>
<td>33.7</td>
<td>33.7</td>
<td>32.9-34.4</td>
<td></td>
</tr>
<tr>
<td>Mean BMI (kg/m²)</td>
<td>24.0</td>
<td>29.6</td>
<td>27.6</td>
<td>28.0</td>
<td>27.6-29.3</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>5 (100)</td>
<td>41 (85.4)</td>
<td>26 (20.8)</td>
<td>72 (40.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet</td>
<td>0.0</td>
<td>7 (14.6)</td>
<td>99 (79.2)</td>
<td>106 (59.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mode of delivery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cesarean section</td>
<td>5 (100)</td>
<td>36 (75.0)</td>
<td>80 (64.0)</td>
<td>121 (68.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal</td>
<td>0.0</td>
<td>11 (22.9)</td>
<td>34 (27.2)</td>
<td>45 (25.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forceps</td>
<td>0.0</td>
<td>1 (2.1)</td>
<td>11 (8.8)</td>
<td>12 (6.7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DM1 = diabetes mellitus type 1; DM2 = diabetes mellitus type 2; GD = gestational diabetes; BMI = body mass index; CI = confidence interval

### Table 2. Treatment in relation to type of diabetes and mean gestational age at initiation of insulin

<table>
<thead>
<tr>
<th>Type of diabetes</th>
<th>Insulin</th>
<th>Diet</th>
<th>Total</th>
<th>Mean GA at initiation of insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM1</td>
<td>5 (100)</td>
<td>5 (100)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>DM2</td>
<td>41 (85.4)</td>
<td>7 (14.6)</td>
<td>48 (100)</td>
<td>21*</td>
</tr>
<tr>
<td>GD</td>
<td>26 (20.8)</td>
<td>99 (79.2)</td>
<td>125 (100)</td>
<td>29.9</td>
</tr>
</tbody>
</table>

GA = gestational age; DM1 = diabetes mellitus type 1; DM2 = diabetes mellitus type 2; GD = gestational diabetes; *mean in 38 patients (in 3 cases there was no information available)

### Table 3. Fetal echocardiography results in relation to type of diabetes

<table>
<thead>
<tr>
<th>Findings</th>
<th>Type of diabetes</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>5</td>
<td>45</td>
</tr>
<tr>
<td>ISH</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Change in cardiac rhythm</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HMF</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
<td>48</td>
</tr>
</tbody>
</table>

DM1 = diabetes mellitus type 1; DM2 = diabetes mellitus type 2; GD = gestational diabetes; ISH = interventricular septal hypertrophy; HMF = heart malformation

* 1 false-negative case; ** 1 false-positive case

ECHO was normal in 164 cases (92.1%). However, in one case, patent ductus arteriosus and interventricular shunt were found in one NB, which was a false-negative case. In two cases (1.1%), single interventricular chamber and atrioventricular septal defect were detected, one in a fetus of a DG mother and another in a DM2 patient, respectively. ECHO identified coarctation of the aorta in one case, which was not confirmed in the NB, constituting a false-positive case.

Among the NB with normal ECO, four showed symptoms related to the cardiovascular system. Of these, one was the false-negative case described above who, in addition to heart malformations, had hypoplasia of the cerebellar vermis, pulmonary hypertension and normal karyotype. The three remaining cases were not interpreted as false-negative: one had ISH in the
postnatal echocardiography and a heart murmur at physical examination, and ECO had been performed at the 23rd week of gestation. The second NB had an atrial septal defect (ASD) of oval foramen type with mild repercussion at the postnatal echocardiography, which was indicated due to a murmur; later clinical outcome was not available. The third NB had multiple malformations at birth, possibly part of the Jarche-Levin syndrome, ASD in the echocardiography done at 48 hours after birth, but with a normal test at the sixth month of life.

Three cases of structural cardiac defects were detected at the ECO. In the first case, a mild narrowing of the aorta isthmus region was suspected. This NB showed no clinical intercurrences in the post-partum period and was discharged from hospital 72 hours after birth (false-positive case). The second case showed a single ventricle at the ECO and evolved to FD; the diagnosis was of Edwards syndrome with multiple malformations. The third fetus had an atrioventricular septal defect at the ECO, also evolved to FD and had the diagnosis of Down syndrome.

Nine fetuses (5.1%) had ISH (Figure 1) and, of these, eight had no cardiovascular clinical symptoms post-partum. One NB had cardiomegaly in the chest X-ray and a systolic murmur. When this child was examined again at ten months of age, the physical examination and the echocardiography were normal, and the child was discharged from the cardiology department.

The minimum thickness of the IVS was of 2.7 mm, the maximum, 8.0 mm and the mean, 4.3 mm (95% CI = 4.1-4.6). Considering only fetuses with GA ≥ 30 weeks, mean thickness was the same.

AAMV and PAMV at the ECO and their distribution according to time of pregnancy were obtained. The AAMV values ranged from 40 cm/sec to 140 cm/sec, with the mean of 77.2 cm/sec. PAMV ranged between 45 cm/sec and 127 cm/sec, with mean velocity of 75.3 cm/sec.

Heart rate was abnormal in two cases, prolonged sinus bradycardia in one, sinus tachycardia in the other. In both cases, cardiac rhythm became normal during the neo-natal period, without treatment.

**Fetal death**

Chart 1 shows the cases of FD and their respective causes.

<table>
<thead>
<tr>
<th>Case</th>
<th>Type of diabetes</th>
<th>GA (wks)</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>DM2</td>
<td>28.1</td>
<td>visceral malformation, webbed neck, genetic syndrome</td>
</tr>
<tr>
<td>12</td>
<td>DM2</td>
<td>37.6</td>
<td>not defined</td>
</tr>
<tr>
<td>22</td>
<td>GD</td>
<td>27.6</td>
<td>not defined</td>
</tr>
<tr>
<td>48</td>
<td>GD</td>
<td>36.4</td>
<td>not defined</td>
</tr>
<tr>
<td>125</td>
<td>DM2</td>
<td>31.6</td>
<td>Edwards syndrome, multiple malformations</td>
</tr>
<tr>
<td>176</td>
<td>GD</td>
<td>34.6</td>
<td>Down syndrome, multiple malformations</td>
</tr>
</tbody>
</table>

GA = gestational age; wks = weeks; DM2 = diabetes mellitus type 2; GD = gestational diabetes

There were six (3.4% of sample) cases of FD, and three of these NB (50%) had congenital anomalies. One of the NB had Down syndrome with multiple malformations; the second, Edwards syndrome, also with multiple malformations; and the third one had visceral malformation and webbed neck, with a non-confirmed syndromic diagnosis. ECO detected the two cases with heart malformations. Autopsy was performed only in two cases, confirming the malformations detected by ECO: in one case an atrioventricular septal defect and, in the other, a single ventricular chamber.

Among the 125 GD, there were three FD (2.4%), two with no apparent cause and one with malformation. Among the DM2, there were three FD (6.3%), two with malformations and one with no apparent cause, with no significant difference (p = 0.305).

**Congenital anomalies**

A total of 12/178 (6.7%) cases of congenital anomalies were found, including FD. The anomalies occurred among the DM2 (n = 5/48 or 10.4%) and GD (n = 7/125 or 5.6%), with no significant difference (p = 0.322).

None of the NB of the five DM1 mothers had congenital anomalies. Among the congenital anomalies, three cases (1.7%) were of cardiac malformation.

As to the age of the pregnant women whose fetuses presented congenital anomalies, nine of them had age equal to or greater than 35 years, and the two cases of Down syndrome were in this group, as seen in Chart 2.

There were four cases of hip dysplasia, three of them occurring in NB of GD mothers and one, of a DM2 mother; two cases with minor malformations (pre-auricular appendix), one in a NB of a GD mother and the other, in one of a DM2 mother.
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### Chart 2. Characteristics of pregnant women, fetuses and newborns with major malformations

<table>
<thead>
<tr>
<th>Case</th>
<th>Diabetes classification</th>
<th>Age</th>
<th>Treatment</th>
<th>ECHO</th>
<th>Mode of delivery</th>
<th>Heart malformation</th>
<th>Perinatal result</th>
<th>MF identified in newborn</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>DM2</td>
<td>30</td>
<td>Insulin</td>
<td>Normal</td>
<td>Cesarean section</td>
<td>No</td>
<td>Discharge</td>
<td>Microcephaly</td>
</tr>
<tr>
<td>7</td>
<td>DM2</td>
<td>35</td>
<td>Insulin</td>
<td>Normal</td>
<td>Cesarean section</td>
<td>No</td>
<td>FD</td>
<td>Probable genetic syndrome, syndromic face, visceral MF, webbed neck, short upper limb</td>
</tr>
<tr>
<td>37</td>
<td>GD</td>
<td>35</td>
<td>Insulin</td>
<td>Normal</td>
<td>Cesarean section</td>
<td>No</td>
<td>Discharge</td>
<td>Down syndrome</td>
</tr>
<tr>
<td>58</td>
<td>GD</td>
<td>32</td>
<td>Diet</td>
<td>Normal</td>
<td>Vaginal</td>
<td>No</td>
<td>Discharge</td>
<td>SUA</td>
</tr>
<tr>
<td>72</td>
<td>GD</td>
<td>30</td>
<td>Diet</td>
<td>Normal</td>
<td>Vaginal</td>
<td>No</td>
<td>Discharge</td>
<td>Hip dysplasia</td>
</tr>
<tr>
<td>79</td>
<td>DM2</td>
<td>35</td>
<td>Insulin</td>
<td>Normal</td>
<td>Cesarean section</td>
<td>No</td>
<td>Discharge</td>
<td>Hip dysplasia</td>
</tr>
<tr>
<td>120</td>
<td>GD</td>
<td>35</td>
<td>Diet</td>
<td>Normal</td>
<td>Cesarean section</td>
<td>Yes</td>
<td>Death</td>
<td>Heart failure, cerebellar vermix hypoplasia, IVC, PDA, pulmonary hypertension, normal karyotype</td>
</tr>
<tr>
<td>125</td>
<td>DM2</td>
<td>37</td>
<td>Insulin</td>
<td>Single interventricular chamber</td>
<td>Vaginal</td>
<td>Yes</td>
<td>FD</td>
<td>Edwards syndrome, multiple MF</td>
</tr>
<tr>
<td>134</td>
<td>GD</td>
<td>38</td>
<td>Diet</td>
<td>Normal</td>
<td>Forceps</td>
<td>No</td>
<td>Discharge</td>
<td>Hip dysplasia</td>
</tr>
<tr>
<td>138</td>
<td>DM2</td>
<td>43</td>
<td>Insulin</td>
<td>Normal</td>
<td>Cesarean section</td>
<td>No</td>
<td>Discharge</td>
<td>Hip dysplasia</td>
</tr>
<tr>
<td>152</td>
<td>DM2</td>
<td>36</td>
<td>Insulin</td>
<td>Normal</td>
<td>Cesarean section</td>
<td>No</td>
<td>Discharge</td>
<td>Probable Jarcho-Levin syndrome</td>
</tr>
<tr>
<td>176</td>
<td>GD</td>
<td>45</td>
<td>Diet</td>
<td>Atroventricular septal defect</td>
<td>Cesarean section</td>
<td>Yes</td>
<td>FD</td>
<td>Down syndrome with multiple MF</td>
</tr>
</tbody>
</table>

GA = gestational age; ECHO = fetal echocardiography; PDA = patent ductus arteriosus; FD = fetal death; SUA = single umbilical artery; MF = malformation; GD = gestational diabetes; GD = gestational diabetes; NC = interventricular communication

As to diabetes control in these patients, seven of them were controlled with diet alone and the remaining, with insulin.

Figure 2 summarizes the distribution of the major malformations and fetal deaths in the studied population.

In 76.2% of NB, weight was appropriate for GA and, in 18.6%, large for gestational age. The cases of FD (n = 6) were not included in the calculation.

In three (1.7%) of the live born NB, neurological problems were identified (microcephaly, Down syndrome and Jarcho-Levin syndrome).

**DISCUSSION**

At hospital, the frequency of pregnant diabetic women was lower than that found in Brazilian statistics(11), with GD occurring in 7.6% and DM, in approximately 8% of population, yet closer to the figures of the international literature reporting 2 to 5% of all pregnancies(12). This might be due to the characteristics of the population studied, and one should regard the possibility that this difference might be the result of the use of different tests, diagnostic criteria and cut-off points for the diagnosis of diabetes and of glucose intolerance.

In the present study, the number of pregnant women who underwent ECO at the hospital because of diabetes was less than half of the total of patients with this diagnosis in a ten-year time. This may have occurred due to different reasons: missed information of diabetes when ECO was indicated, non-referral by the obstetrician because of delayed GD diagnosis, and delivery occurred in a different hospital. The small number of DM1 cases may have been, merely, casual.

The rate of older pregnant patients aged over of 35 years was higher than the rate of 22.5% found in the population seen at hospital(13) and even much higher than the Brazilian rate of 9% in the year 2003(13). It is well known that GD, corresponding to the largest number

**Characteristics of the newborns**

The mean weight of the NB of GD mothers was higher than that of NB of DM2 mothers, which was higher than that of NB of DM1 mothers. However, there was no statistically significant difference in the NB mean weight according to the type of maternal diabetes.

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In three (1.7%) of the live born NB, neurological problems were identified (microcephaly, Down syndrome and Jarcho-Levin syndrome).
of patients, has a higher incidence in women aged over 25 years\(^{(10)}\).

The mean BMI of patients categorized them as pre-obese, and more than half of them were overweight or obese, which agrees with the findings of Montenegro Jr et al., who found that in the population of Ribeirão Preto, State of São Paulo, 47.6% of GD pregnant women and 65.9% of DM2 pregnant women were obese\(^{(15)}\).

In the present study, the proportion of GD among pregnant women was lower than that in the USA\(^{(16)}\). Such difference might be due to different population characteristics, such as the pre-conception care delivered at hospital. In the present study, the proportion of pregnant diabetic women, whether type 1 (more remarkably), type 2 or GD, was much lower than that found in studies carried out at the Faculdade de Medicina de Ribeirão Preto (FMFRP)\(^{(15)}\), or at the Hospital Universitário Pedro Ernesto (HUPE) of the Universidade do Estado do Rio de Janeiro (UERJ)\(^{(17)}\). However, since these were university hospitals, high risk pregnancies may have been referred to them, increasing the number of DM1 and DM2. The small number of pregnant women with DM1 in this sample might be related to the type of population studied at hospital.

Regarding treatment, the DM1 patients already used insulin prior to their pregnancies. Most of the DM2 patients needed insulin for their metabolic control during pregnancy and few GD patients needed to use insulin, because it was controlled with diet alone as reported in the literature\(^{(2)}\).

The high rate of C-sections found in the present study is similar to that reported by Montenegro Jr et al., who attributed it to patients’ obesity, fetal macrosomy and presence of conditions often associated to diabetes, such as toxemia of pregnancy or, yet, because of the older age of the patients (as observed in the present study); moreover, the diagnosis of diabetes itself would influence the clinical decision of indicating C-section\(^{(15,18)}\).

Although the literature data are very different depending on where it refers to, the rate of macrosomy was similar to that reported in the literature\(^{(15)}\).

The frequency of premature deliveries was higher than that reported for the general population, yet, lower than the rate in pregnant diabetic women\(^{(15)}\). The small number of DM1 in the sample and the good metabolic control of the pregnant women, which might avoid complications triggering premature labor, are factors that could justify this difference. It is worth mentioning that, among DM1, mean GA at delivery was lower than that among GD, with statistically significant difference, likely due to the greater difficulty of blood glucose control in those pregnant women. For the DM2 patients, although GA at delivery was also lower than for those with GD, this was not a significantly different. This finding might have also occurred because, in the case of a pregnant diabetic woman, there is an unsafe feeling about fetal and maternal health, increasing the propensity for pregnancy interruption\(^{(18)}\) and iatrogenic prematurity.

ECO, as it was performed in a population with the characteristics described above, identified disorders of the cardiac rhythm, cases of ISH, according to the cutoff point adopted (corresponding to most findings) and a smaller number of structural cardiac anomalies. Some disorders later found in the NB referred to findings considered normal in fetal life. Maternal obesity, fetal position and very small defects are limiting factors in ECO accuracy\(^{(19-20)}\). Obese patients show high rates of suboptimal ultrasound tests and, the greater the BMI, the greater the rate of suboptimal tests for detection of structural cardiac defects\(^{(19)}\).

As a result of the presence of patent oval foramen and ductus arteriosus in fetal life, the pressures in both right and left ventricles are similar, not causing shunts in prenatal life, and, besides this, small defects are beyond ultra-sonographic resolution\(^{(20)}\).

Patent oval foramen is a normal anatomical situation in intrauterine life, and its spontaneous closure may occur, in most cases, up to the age of five years\(^{(21)}\). Among the NB analyzed, one was described as having oval foramen, which is a normal post-partum situation; the other one had normal echocardiography at nine months of age; therefore, both cases may not be considered as a true ASD.

In the present study, the ECO detected a lower number of ISH than what is described in the literature (20 to 30%)\(^{(22)}\); this difference could be attributed to good metabolic control of the pregnant women or to the gestational age in which ECO was performed\(^{(19,23)}\). The ISH, most of the time, is observed after the 28th week of gestation when the fetal bone structure is already shaped. This factor, added to maternal obesity and depending of the position of the fetal back at the time of the test, as previously highlighted, might have caused problems for measuring IVS thickness\(^{(19)}\). On the other hand, in order to search for ISH, ECO must be performed in the third trimester of pregnancy. In this study, the ISH was diagnosed only at the post-partum echocardiography (no ECO diagnosis), and the test was carried out at non-appropriate time (GA of 23 weeks) to find the disorder.

The Doppler-assessed AAMV and PAMV increased linear and progressively with GA, with no hemodynamic repercussion. The difference between measured AAMV and PAMV values is due to the different GA in which the tests were done. These findings were similar to those observed both in normal pregnancies\(^{(23)}\) as well as pregnancies of diabetic mothers with no complications\(^{(10)}\).

The frequency of congenital anomalies found in NB of the present study was similar to that reported in
the design of further studies in this area. However, if the cases with recognized genetic syndromes are excluded, the frequency of anomalies is smaller than the quoted figures. When only DM2 pregnant women are considered, the frequency of anomalies was less than that described by Lazalde et al.\(^{(24)}\) and close to that reported by Nazer Herrera, Garcia Huidobro e Cifuentes Ovalle\(^{(25)}\), although in GD it was similar to that published by the same authors. The general frequency of structural cardiac malformations, including the cases diagnosed in the NB, is lower than what was found by Xavier et al.\(^{(26)}\). The fact that no malformations were found in fetuses and/or NB from DM1 mothers may be explained by the small number of such women in the sample. The non-uniform distribution of the types of diabetes, with a large number of GD, could also be a reason for the lower number of congenital malformations found in the present sample. In addition to these factors, we believe that the difference could be ascribed to the good pre-conception control of the pre-diabetes state attained by women seen at the hospital.

The rate of perinatal mortality found in the present study was similar to that in pregnant diabetics referred in recent publications\(^{(27)}\), which might also support the impression of the good care offered to these pregnant women.

ECO is considered the gold standard to detect cardiac malformations in the fetus, although it may give false-positive and false-negative results, as remarked by Buskens et al.\(^{(28)}\). In the present study, the results obtained may be attributed both to technical problems inherent to the method, already mentioned above, and to the fact that the tests were done with no specific criterion regarding the appropriate GA for a diagnostic investigation, based on the risk in each type of diabetes. However, this type of study may allow better use of a technology which paves the road for designing the best possible perinatal care.

Some limitations of the study are as follows: the tests were performed after 17 weeks of gestation, therefore, abortion and malformations occurring prior to that GA could not be detected; FD occurring before the referral for ECO could not be detected; finally, the initial sample did not include all pregnant diabetic women. The limitations found in the present study may serve for the design of further studies in this area.

CONCLUSIONS

The pregnant diabetic women who underwent ECO at the hospital were of older age, had BMI above the normal reference values and only a few were DM1, thus composing a group with specific characteristics.

Echocardiography identified fetuses with cardiac disorders including ISH, septal defects and arrhythmias. The incidence in the fetuses of diabetic mothers was lower than that reported in the literature, with no apparent definitive justification.

The frequency of major malformations was similar to that described in the literature for pregnant women with good metabolic control.

The perinatal outcomes were not different from those reported, also pointing to the good management of the pregnant diabetic women in this population.

REFERENCES


