Postpartum glucose tolerance status 6 to 12 weeks after gestational diabetes mellitus: a Brazilian cohort

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ABSTRACT

Objectives: The aims of this study were to estimate the local rate of postpartum diabetes screening after gestational diabetes mellitus (GDM) pregnancies, and to identify clinical variables associated with retesting rates and with the persistence of decreased glucose tolerance. Subjects and methods: Prospective cohort of GDM women with prenatal delivery at a specialized center, from November 2009 to May 2012. All women were advised to schedule a 6 weeks postpartum 75-g oral glucose tolerance test (OGTT). Results: Of the 209 women included, 108 (51.7%) returned to be tested with fasting plasma glucose (n = 14), OGTT (n = 93) or random glucose (n = 1). Return was associated with lower parity rate (2 vs. 3, p < 0.001) and higher pregnancy 2-h OGTT (165 vs. 155 mg/dL, p = 0.034), but not with socio-demographic characteristics. Four women (3.7%) had diabetes, 22 (20.4%) had impaired fasting glucose or impaired glucose tolerance. Persistent hyperglycemia was associated with a positive family history of diabetes (relative risk - RR 2.41, p = 0.050), diagnostic 2-h OGTT in pregnancy (RR 1.01, p = 0.045), insulin use during pregnancy (RR 2.37 , p = 0.014), and cesarean section (RR 2.61, p = 0.015). Conclusions: Even though postpartum abnormalities were frequent in GDM, rates of postpartum diabetes screening were undesirably low. As no specific clinical profile defines who will adhere to postpartum testing, it is essential to encourage all women to reevaluate their glucose status, particularly those with a family history of diabetes and more severe hyperglycemia.

Keywords
Gestational diabetes; postpartum testing; GDM; type 2 diabetes; oral glucose tolerance test

RESUMO

Objetivos: Os objetivos foram estimar a taxa de reavaliação de diabetes pós-parto em mulheres com diabetes melito gestacional (DMG) e identificar fatores associados ao retorno e à persistência das alterações glicêmicas. Sujeitos e métodos: Coorte prospectiva de mulheres com DMG atendidas em ambulatório de pré-natal especializado, de novembro de 2009 a maio de 2012. Todas foram orientadas a agendar o teste oral de tolerância à glicose (TOTG) a partir da sexta semana pós-parto. Resultados: Das 209 mulheres arroladas na gestação, 108 (51,7%) foram avaliadas após o parto: 14 com glicemia de jejum, 93 com o TOTG e uma com glicemia ao acaso. O retorno para reavaliação foi associado com menor paridade (2 vs. 3, p < 0.001) e com glicemia de 2-h mais elevada no TOTG diagnóstico (165 vs. 155 mg/dL, p = 0,034). Diabetes foi diagnosticado em quatro mulheres (3,7%) e pré-diabetes em 22 (20,4%). Análise multivariada evidenciou que a história familiar de diabetes (risco relativo – RR 2,41, p = 0,050), a glicemia de 2 horas no TOTG da gestação (RR 1,01, p = 0,045), o uso de insulina na gestação (RR 2,37, p = 0,014) e a taxa de cesariana (RR 2,61, p = 0,015) foram os fatores associados à persistência da hiperglycemia. Conclusões: O retorno para reavaliação foi baixo, embora as alterações glicêmicas tenham sido frequentes. Como não houve fatores que indiquem quais mulheres retornarão, estratégias para aumentar a adesão são necessárias, especialmente quando há história familiar ou o DMG foi mais grave. Arq Bras Endocrinol Metab. 2014;58(2):197-204

Descritores
Diabetes gestacional; reavaliação pós-parto; DMG; diabetes tipo 2; teste oral de tolerância à glicose

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Received on Oct/16/2013
Accepted on Nov/7/2013
INTRODUCTION

The prevalence of gestational diabetes mellitus (GDM) is increasing in parallel with higher rates of obesity and type 2 diabetes, as well as with more inclusive diagnostic criteria intended to be used worldwide; rates of almost 20% are described in some peculiar settings (1-3). Women with GDM are at increased risk of developing type 2 diabetes (4) or pre-diabetes in the follow-up, and should have a postpartum evaluation in order to disclose persistent alterations of glucose metabolism, either by performing an oral glucose tolerance test (OGTT) or fasting plasma glucose (5,6).

Rates of return after postpartum vary across studies, ranging from as low as 3.4% after routine care advice in the three month postpartum period, to a rate as high as 92.6% with active reminder strategies, as described in a recent systematic review including 54 studies (7).

A number of clinical characteristics are related both to the return for reevaluation and to postpartum glucose alterations, such as age, race, social parameters, and labelling patients as GDM carriers at postpartum discharge from hospital in a large series (8). The use of medication, either insulin (8-11) or oral agents (8) for glycemic control during pregnancy, is associated with persistent hyperglycemia, whereas body mass index (BMI) (10), race (9,11) and other risk factors (1-h blood glucose in diagnostic OGTT (11), previous GDM (9), parity rates (10)) are described in other studies.

Rates of pre-diabetes or diabetes after GDM may vary according to different methods and criteria used to define glucose alteration, to the postpartum time elapsed since pregnancy, and to clinical characteristics of the study population. A wide range of postpartum glycemic alterations are described: from 1.1% to 25.3% for diabetes, and from 2.2% to 42.3% for both impaired glycemic alterations are described: from 1.1% to 25.3% of the study population. A wide range of postpartum elapsed since pregnancy, and to clinical characteristics to define glucose alteration, to the postpartum time

SUBJECTS AND METHODS

All women with GDM whose pregnancy prenatal care was carried out at a specialized outpatient clinic from November 2009 to May 2012 were included. The university hospital delivers tertiary care to Brazilian public health system patients. The outpatient clinic includes a multidisciplinary prenatal care with regular appointments with an obstetrician, an endocrinologist, a nutritionist and a nurse.

All subjects were interviewed by one of the authors (LSW). They answered a structured questionnaire that included socio-demographic characteristics, past and present medical history, and current pregnancy information. Physical examination was performed to evaluate height, weight, blood pressure and obstetric parameters. All women were followed up until delivery. At the discharge from the hospital they were instructed to schedule a 75-g OGTT 6 and 12 weeks after delivery, according to official recommendations (5,6). Medical data on delivery and the newborn(s) were retrieved from hospital records. All participants signed an informed written consent, and the hospital ethical committee approved the study protocol.

Until the end of 2010, diagnosis of GDM followed the recommendations of the 2a Reunião do Grupo de Trabalho em Diabetes e Gestação (2th Meeting of The Diabetes and Pregnancy Task Force) (12): after a positive screening (fasting plasma glucose – FPG – ≥ 85 mg/dL), a 75-g OGTT was performed and GDM was diagnosed if fasting plasma glucose ≥ 110 mg/dL, or 2-h plasma glucose ≥ 140 mg/dL. After the release of the International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommendation (13) and its adoption by the American Diabetes Association (6), women with fasting plasma glucose ≥ 92 mg/dL or 1-h plasma glucose ≥ 180 mg/dL, or 2-h plasma glucose ≥ 153 mg/dL in the 75-g OGTT were included.

The following information was collected: maternal age, self-reported skin color (white or dark skin tone), marital status, work outside home, socioeconomic status (14), years of study, parity, self-reported pre-pregnancy weight, active smoking at registration, chronic diseases, regular use of medicines and supplements, previous GDM, gestational hypertension, preeclampsia or eclampsia, or a macrosomic newborn. Height was measured at the first prenatal visit and blood pressure was recorded at all prenatal visits. Data on maternal weight gain, delivery route and medical emergencies were extracted from medical records. The A1c test, lipid profile, fasting insulin and C-peptide were measured at the third trimester in addition to routine prenatal evaluation. Insulin and C-peptide were measured only in non-insulin users at the time of blood sampling. BMI was calculated using the informed pre-gestational
weight, with the equation weight (kg)/height (m²).

Preeclampsia was defined as blood pressure ≥ 140/90 mmHg detected after the 20th gestational week with significant proteinuria and gestational hypertension in the absence of significant proteinuria (15). Insulin resistance was evaluated by the homeostasis model assessment (HOMA-IR), and was calculated as: glucose in mg/dL x 0.0555 x insulin/22.5 (16); a value > 4.31 (the population specific 75th percentile) was defined as insulin resistance.

Outcomes

The primary outcome was the diagnosis of postpartum pre-diabetes (impaired fasting glucose (IFG): FPG 100-125 mg/dL; impaired glucose tolerance (IGT) 2-h plasma glucose in the 75-g OGTT 140-199 mg/dL) or diabetes (FPG ≥ 126 mg/dL or 2-h plasma glucose ≥ 200 mg/dL in the OGTT, or random plasma glucose ≥ 200 mg/dL) (6). Additionally, we evaluated the rate of return after the postpartum, and the time elapsed since parturition, as well as clinical characteristics related to return and maintenance of hyperglycemia.

Laboratory tests

Glucose was measured by enzymatic colorimetric assays, HbA1c by high performance liquid chromatography (Variant II, BioRad Laboratories, Hercules, CA), and fasting insulin and C-peptide by chemiluminescence (Advia Centaur XP, Siemens Healthcare, Erlangen, Germany).

Statistical analysis

Descriptive statistics were used to present clinical and demographic variables of returning and non-returning women, and for those who remained hyperglycemic or not. Absolute and relative frequencies, means and standard deviation, and median and inter-quartile intervals were used as appropriate.

Differences in the distribution of categorical variables were analyzed with the chi-square test. The Shapiro-Wilk test was used to verify if continuous variables were normally distributed. Parametric continuous variables were evaluated with the T-test, and non-parametric ones with the Mann-Whitney test.

Mean and median time to the return for reevaluation was calculated with the Kaplan Meier analysis. Glycemias on diagnostic OGTT were correlated to postpartum OGTT using the Spearman correlation test.

Univariate Poisson regression analysis was used to calculate the risk ratio of factors associated to persistent postpartum glucose impaired tolerance. All significant variables in the univariate analyses were included in a robust multivariate Poisson regression.

Statistical analyses were performed with the SPSS software version 18.0 (IBM Company). The significance level used was 0.05.

RESULTS

Gestational diabetes was diagnosed by the Brazilian criterion in 183 women; 26 had GDM according to the IADPSG criteria. Of the 209 women, 111 did at least one of the following postpartum tests: only fasting plasma glucose (n = 14, 12.6%), OGTT (n = 93, 83.8%), random blood glucose (n = 2, 1.8%) or A1c test (n = 1, 0.9%). A subject with a random glucose of 150 mg/dL, one with only the A1c test, and one with an undated FPG were excluded. Another woman included in the analysis had random blood glucose of 350 mg/dL and was treated at emergency room for symptomatic hyperglycemic decompensation. The return rate for reevaluation was, therefore, of 108 among 209 women (51.7%; 95% CI: .45 – 59).

Clinical characteristics of women who returned and who did not return are shown in table 1. Reevaluation occurred 4 to 734 days postpartum. Median time was 63 days (95% CI: 60.8-65.2): 10 women (9.3%) returned before 6 weeks, 77 (72%) between 6 and 12 weeks, and 9 (8.4%) until 6 months postpartum. The remaining 11 women (10.3%) returned more than 180 days after delivery, and, in general, the glucose test was carried out due to a routine evaluation, either by a clinician, a gynecologist, or a surgeon. Return was only associated with lower parity rate (2 vs. 3, p < 0.001), and higher pregnancy 2-h OGTT (165 vs. 155 mg/dL, p = 0.034).

A significant correlation was found between the OGTT FPG during pregnancy with postpartum FPG (r = 0.394, p < 0.001) and postpartum 2-h glucose (r = 0.215, p = 0.038). There was also a positive correlation between the postpartum FPG and the 2-h postpartum glucose (r = 0.353, p < 0.001).

Among the 108 women that were reevaluated, 82 (76%) had normal postpartum glucose tolerance, while 26 (24%) remained with dysglycemia: 22 (20%) had IFG or IGT and 4 (4 %) had diabetes. The main characteristics of the women, according to postpartum reclassification, are displayed in table 2. Previous GDM, a positive
Table 1. Clinical profile of postpartum returning and non-returning GDM women

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Postpartum reevaluation</th>
<th>No postpartum reevaluation</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 108</td>
<td>N = 101</td>
<td></td>
</tr>
<tr>
<td>Age¹ (y)</td>
<td>32 (6)</td>
<td>32 (6)</td>
<td>0.565</td>
</tr>
<tr>
<td>Pre-pregnancy BMI² (kg/m²)</td>
<td>28.5 [24.1 – 34.4]</td>
<td>27.9 [24.4 – 33.5]</td>
<td>0.712</td>
</tr>
<tr>
<td>Unemployed³</td>
<td>31 (29)</td>
<td>36 (35)</td>
<td>0.406</td>
</tr>
<tr>
<td>Years in school⁰ (&lt; 8)</td>
<td>31 (27)</td>
<td>38 (37)</td>
<td>0.168</td>
</tr>
<tr>
<td>Socioeconomic level Brazil⁰ (A or B)</td>
<td>29 (37)</td>
<td>18 (23)</td>
<td>0.082</td>
</tr>
<tr>
<td>Living with a partner³</td>
<td>79 (74)</td>
<td>75 (74)</td>
<td>&gt; 0.999</td>
</tr>
<tr>
<td>White skin color³</td>
<td>82 (77)</td>
<td>71 (70)</td>
<td>0.322</td>
</tr>
<tr>
<td>Parity rate³ (n)</td>
<td>2 (1-3)</td>
<td>3 (2-4)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Family history of DMP³</td>
<td>62 (59)</td>
<td>58 (60)</td>
<td>&gt; 0.999</td>
</tr>
<tr>
<td>Previous GDM³</td>
<td>13 (12)</td>
<td>16 (16)</td>
<td>0.590</td>
</tr>
<tr>
<td><strong>GDM diagnostic OGTT glucose² (mg/dL)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting</td>
<td>93 [86 – 103]</td>
<td>96 [86 – 110]</td>
<td>0.143</td>
</tr>
<tr>
<td>1-h*</td>
<td>195 [165 – 207.5]</td>
<td>170 [155.5 – 199]</td>
<td>0.107</td>
</tr>
<tr>
<td>2-h</td>
<td>165 [147 – 187]</td>
<td>155 [146 – 168]</td>
<td>0.034</td>
</tr>
<tr>
<td>Diagnostic A1c test⁰ (%)</td>
<td>5.5 [5.2 – 6.0]</td>
<td>5.7 [5.3 – 6.3]</td>
<td>0.122</td>
</tr>
<tr>
<td>Pregnancy weight gain² (kg)</td>
<td>9.2 [4.4 – 13.1]</td>
<td>9.1 [5.4 – 14.4]</td>
<td>0.400</td>
</tr>
<tr>
<td>Drug-treated GDM³</td>
<td>64 (60)</td>
<td>57 (60)</td>
<td>0.663</td>
</tr>
<tr>
<td>Complications in index pregnancy³ **</td>
<td>49 (45.8)</td>
<td>49 (49)</td>
<td>0.747</td>
</tr>
</tbody>
</table>

GDM: gestational diabetes mellitus; BMI: body mass index; DM: diabetes mellitus; OGTT: oral glucose tolerance test.
* n = 26; ** fetal macrosomia, neonatal hypoglycemia or intensive care unit admission, maternal hypertensive disorders.
Results are expressed as: ¹ mean (DP); ² median [inter-quartile interval]; ³ n (%).

Table 2. Clinical and laboratory characteristics of GDM patients according to postpartum glucose test results

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Normal postpartum glucose</th>
<th>Abnormal postpartum glucose</th>
<th>P</th>
<th>Relative risk²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 82)</td>
<td>(n = 26)</td>
<td></td>
<td>RR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Age² (y)*</td>
<td>31.2 [27 – 35]</td>
<td>25 [29 – 39]</td>
<td>0.144</td>
<td>1.04 (0.97 – 1.12)</td>
<td>0.227</td>
</tr>
<tr>
<td>Pre-gestational BMI² (kg/m²)</td>
<td>28.2 [23.3 – 34.5]</td>
<td>28.5 [26.3 – 33.8]</td>
<td>0.448</td>
<td>1.01 (0.97 – 1.1)</td>
<td>0.56</td>
</tr>
<tr>
<td>Previous GDM³</td>
<td>5 (6)</td>
<td>8 (31)</td>
<td>0.002</td>
<td>3.25 (1.78 – 5.90)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Family history of DMP³</td>
<td>42 (52)</td>
<td>21 (81)</td>
<td>0.017</td>
<td>2.94 (1.20 – 7.19)</td>
<td>0.019</td>
</tr>
<tr>
<td>Fasting glucose – GDM diagnosis OGTT² (mg/dL)*</td>
<td>91 [84 – 102]</td>
<td>102.5 [94 – 112]</td>
<td>&lt; 0.001</td>
<td>1.012 (1.009 – 1.015)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>2-h glucose – GDM diagnosis OGTT² (mg/dL)*</td>
<td>158 [145 – 179]</td>
<td>184.5 [161 – 195]</td>
<td>0.004</td>
<td>1.015 (1.008 – 1.022)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>A1c – GDM diagnosis² (%)</td>
<td>5.5 [5.1 – 5.9]</td>
<td>6.0 [5.2 – 6.6]</td>
<td>0.045</td>
<td>1.49 (1.22 – 1.82)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HOMA² *</td>
<td>2.7 [1.9 – 4.1]</td>
<td>4.3 [3.1 – 5.4]</td>
<td>0.017</td>
<td>1.16 (1.02 – 1.32)</td>
<td>0.023</td>
</tr>
<tr>
<td>Drug treated GDM³</td>
<td>44 (64)</td>
<td>21 (81)</td>
<td>0.026</td>
<td>2.78 (1.13 – 6.8)</td>
<td>0.025</td>
</tr>
<tr>
<td>Insulin treated GDM³</td>
<td>9 (11)</td>
<td>12 (46)</td>
<td>&lt; 0.001</td>
<td>3.55 (1.94 – 6.51)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Weight gain in pregnancy²</td>
<td>7.2 [3.9 – 10.9]</td>
<td>5.0 [2.8 – 8.5]</td>
<td>0.149</td>
<td>0.96 (0.91 – 1.02)</td>
<td>0.232</td>
</tr>
<tr>
<td>Complications in index pregnancy² §</td>
<td>32 (39)</td>
<td>18 (69)</td>
<td>0.014</td>
<td>2.61 (1.24 – 5.48)</td>
<td>0.011</td>
</tr>
<tr>
<td>Cesarean section³</td>
<td>39 (47.6)</td>
<td>19 (73.1)</td>
<td>0.041</td>
<td>2.34 (1.07 – 5.10)</td>
<td>0.033</td>
</tr>
<tr>
<td>Fasting glucose – postpartum OGTT² (mg/dL)</td>
<td>87 [84 – 92]</td>
<td>105 [99 – 117]</td>
<td>&lt; 0.001</td>
<td>1.008 (1.006 – 1.01)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>2-h glucose – postpartum OGTT² (mg/dL)</td>
<td>93 [84 – 108]</td>
<td>151 [124 – 191]</td>
<td>&lt; 0.001</td>
<td>1.006 (1.004 – 1.009)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

GDM: gestational diabetes mellitus; BMI: body mass index; DM: diabetes mellitus; OGTT: oral glucose tolerance test; HOMA-IR: homeostasis model assessment – insulin resistance.
Results are expressed as: ¹ mean (DP); ² median [inter-quartile interval]; ³ n (%).
* at GDM diagnosis in index pregnancy.
§ fetal macrosomia, neonatal hypoglycemia or intensive care unit admission, hypertensive disorders.
* “no presence” is the reference category.
family history of diabetes, higher glucose levels on the diagnostic OGTT, higher A1c test, higher plasma insulin and HOMA, as well as the need of medication to control GDM, and higher rate of pregnancy complications and cesarean section were found in the group with persistent hyperglycemia. Other possible risk factors, such as triglycerides and height < 151 cm were analyzed, but were not different between the two groups.

The final multivariate model showed sustained significance for a positive family history of diabetes (relative risk – RR 2.41, p = 0.050), the 2-h glucose value on the diagnostic OGTT (RR 1.01, p = 0.045), the need of insulin in pregnancy (RR 2.37, p = 0.014), and cesarean section (RR 2.61, p = 0.015) as predictors of persistent postpartum hyperglycemia (Table 3).

Table 3. Risks factors for persistent postpartum hyperglycemia – multivariate analysis

<table>
<thead>
<tr>
<th>Characteristic (independent variable)</th>
<th>RR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of diabetes</td>
<td>2.41 (1.00 – 5.80)</td>
<td>0.050</td>
</tr>
<tr>
<td>2-h glucose – GDM diagnostic OGTT</td>
<td>1.01 (1.00 – 1.02)</td>
<td>0.045</td>
</tr>
<tr>
<td>Insulin use</td>
<td>2.37 (1.19 – 4.70)</td>
<td>0.014</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>2.61 (1.21 – 5.66)</td>
<td>0.015</td>
</tr>
</tbody>
</table>

**DISCUSSION**

In this prospective cohort of 209 GDM women, the rate of return for postpartum reevaluation was 51.7%; women who returned had lower parity rate and higher 2-h value on diagnostic 75-g OGTT, and were retested as recommended by official positions. Characteristics associated to the persistence of dysglycemia after pregnancy were family history of diabetes, some metabolic alterations in the third trimester of pregnancy, and the need for cesarean section in the index pregnancy.

Since the first studies by O’Sullivan describing estimated incidence of type 2 diabetes of up to 52% in a period of 6 to 7 years after a GDM pregnancy (17), special concerns on follow-up strategies of these women were raised. The concept that GDM represents previously undiagnosed impaired glucose tolerance that is uncovered by active search during pregnancy, and the presence of risk factors associated with type 2 diabetes (18) corroborate the need of postpartum reevaluation. In a systematic review including 20 cohort studies, a seven-fold risk of presenting type 2 diabetes in the future was found in the presence of previous GDM pregnancy (19). In a reevaluation after 4 to 8 years of the index pregnancy in a Brazilian cohort, the risk of developing any glucose alteration was 1.9 higher in women with GDM pregnancy compared with normal glucose tolerant pregnant women (20). Irrespective of gestational diabetes being a risk factor, a stage of the natural history of type 2 diabetes, or a pre-existing alteration disclosed during pregnancy, postpartum reevaluation is mandatory and is advocated by endocrine and obstetric organizations, due to the possibility of early diagnosis and treatment of the metabolic alteration (21,22).

Nevertheless, despite traditional recommendation for postpartum testing, the rates of return are still low and vary across different studies, depending on population characteristics. Spontaneous return may be of 64.2% in the first three months postpartum (raw average 35%), whereas active search (reminder calls and other tools) is associated with a 92.6% rate (raw average 64.8%) (7). Our study disclosed a little more than half percent of spontaneous return, with more than 70% of women being tested in the recommended 6 to 12 week postpartum period. However, this may be considered a low rate of retesting, since these women were participating in a cohort study and had received prenatal care in a University hospital. Surprisingly, our rate is only slightly higher than the one found in a Brazilian cohort of women in the same region (42%) more than 10 years ago (23); and very similar to the one described in a large retrospective American cohort (50.2%) (8). Reevaluation in 4 to 8 years after a GDM pregnancy in Brazilian women disclosed rates of return of 74% for those with glucose alterations in pregnancy, and of 50% for those with normal glucose tolerance (20). In the present study, almost 20% of those returning did it after the recommended period. Rates of return after the 3 first months postpartum in other studies are similar to 30%, rising to around 60% with active search (7). In one of the largest studies, only 46% of the women were retested in the recommended period (8).

Return rate was associated with race, older age, null parity rate, and higher income or education in a recent systematic review (24), contrasting with our results: we did not find any social or economical variable associated with reevaluation. In our study, return was associated with lower parity rate, suggesting that planning a future pregnancy may be an important stimulus for reevaluation. Higher parity rate was also associated to lack of adherence in a Canadian study with a similar return rate (48%)(9). As expected, having a higher 2-h value in pregnancy OGTT...
was associated with higher rates of return, as found in the present cohort, since women are generally aware of the risk of developing type 2 diabetes after having a GDM diagnosis (25). Surprisingly, complications in index pregnancy, such as fetal macrosomia, neonatal hypoglycemia, or ICU admission, and maternal hypertensive disorders were not related with a higher rate of returning, meaning that even complicated pregnancies were not enough to alarm these women about future risks.

Strategies to increase return for evaluation include, besides routine counseling during pregnancy and at delivery, making reminder calls to patients after the medical staff is informed by an electronic system that the scheduled return was not met (26). In our study, a remind call would benefit not only the 48.3% women who did not return to postpartum testing, but also the 20% that came after 6 months of the delivery. Central hospital reminder calls were associated with a 82.5% return rate in a Finnish study (27). Routine care after delivery provided by obstetricians and family physicians, although frequent, did not improve rates of testing and was considered a “missed opportunity” by some authors (28). Active and systematic actions to improve compliance and return must be optimized by the medical staff, since they can potentially double reevaluation rates (7).

A high rate of postpartum glucose alteration was found in our study (24.1%), mainly IGT and IFG (20.4%). In studies from 1990 to 2012 that described the initial 12 week postpartum return, reported rates ranged from 2.2% to 42.3% for either IGT or IGF, and from 1 to 16% for diabetes, depending on the population characteristics and the criteria that defined the metabolic alteration (7). In the large cohort by Lawrence and cols. (8), 16.3% had IFG or IGT and only 1.1% had diabetes, an incidence slightly lower than ours. Persistent glucose alteration was associated with maternal age, race, education, income, parity and pharmacological GDM treatment (8). As in our cohort, family history of diabetes, glucose values in the diagnostic test and insulin use in pregnancy were predictors of a nine-fold increase in type 2 diabetes rates 15 years after GDM in an Australian retrospective cohort (11). A “metabolic syndrome-like cluster in pregnancy” with specific thresholds for BMI, insulin triglycerides, HDL-cholesterol and systolic blood pressure measured in GDM women was reported as a good predictor of type 2 diabetes development 10 years after the index pregnancy (29).

Although A1c is not a recommended test for GDM diagnosis, it was routinely measured in our cohort and was a significant predictor of persistent glucose alteration. The association of metabolic derangement at diagnosis to glucose impairment after pregnancy, either considering the A1c test or the glucose diagnostic values, was described in other studies (9,11,30). Maternal and neonatal complications and delivery by cesarean section in the index pregnancy more than doubled the risk of postpartum glycemic alteration in univariate analysis, certainly due to their association with the presence of more severe hyperglycemia during pregnancy. The effect of maternal complications disappeared in multivariate analysis.

As expected, family history of diabetes and the severity of GDM, especially when insulin was used, were important predictors of future glucose alterations.

Another issue concerning postpartum reevaluation is which test should be performed. Official recommendations suggest either the FPG or OGTT. Fasting plasma glucose or even the A1c test would be more feasible and comfortable for the women, and could potentially increase return rates. In our cohort, although fasting glucose measured during the postpartum OGTT was significantly correlated with the 2-h glucose measurement, the correlation was weak and precludes its recommendation as the sole tool for reclassification. In a systematic review of 13 studies comparing the FPG to the OGTT performance for the postpartum reevaluation of GDM women, FPG lacked sensitivity as a screening test (31).

Our study has an important methodological strength over previous studies, since it is a prospective cohort. Our data about pregnancy variables and socioeconomic characteristics of participants were collected during the beginning of the third trimester. Moreover, our study results had a broad external validity because we evaluated all women who had been referred to our high-risk prenatal care. One possible limitation of the study is that we enrolled women labeled as gestational diabetes both by the Brazilian and the IADPSG/ADA criteria, since the discussion on GDM diagnostic procedures still remains a matter of great controversy (5,6,32,33). Another possible limitation is that the frequency of impaired glucose we found may be overestimated due to more frequent return of GDM women with higher 2-h glucose values on the diagnostic OGTT.

In conclusion, the return rate for postpartum reevaluation was low, but glucose alterations were frequently
found in retested women of this Brazilian GDM cohort. Reminder calls or other actions for postpartum glucose reassessment are highly recommended, particularly for women with a family history of GDM or who had a more severe GDM presentation, since these women are at increased risk of persistent hyperglycemia after pregnancy.

Acknowledgments: we would like to thank Renata Castro Rodrigues for her help in preparing the manuscript.

Funding: this study was funded by Fundo de Incentivo à Pesquisa e Eventos (FIPE), Hospital de Clínicas de Porto Alegre.

Disclosure: no potential conflict of interest relevant to this article was reported.

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