Obesity or diabetes: what is worse for the mother and for the baby?

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SUMMARY

Objectives: The aim of the present study is to evaluate pregnancy outcomes in a cohort of Caucasian pregnant women in relation to their body mass index and glucose tolerance status; the role of central fat distribution, as indicated by waist-to-hip circumference ratio, was also considered.

Methods: Seven hundred women were studied; they had gestational diabetes or impaired glucose tolerance (250) or normoglycaemia (450). Among them 117 had pre-pregnancy overweight/obesity (44 were obese), 133 hyperglycaemia, but normal weight, and 117 hyperglycaemia and overweight/obesity (42 were obese).

Results: Hypertension, cesarean delivery and prevalence of large-for-gestational age babies were higher in obese (both with normoglycaemia and hyperglycaemia), mainly in those with greater gestational weight gain and central fat distribution (waist-to-hip ratio > 0.90). Normal weight hyperglycaemic women showed better outcomes than obese normoglycaemic women did. In a multiple logistic regression model, obesity (OR = 10.6; 95% CI 5.00-22.54) was directly related to hypertension, and independent predictors of cesarean section were: gestational hyperglycaemia (OR = 1.78; 95% CI 1.21-2.62), gestational weight gain (OR = 1.06; 95% CI 1.02-1.10), and central obesity (OR = 1.51; 95% CI 1.02-2.24), while obesity (OR = 4.48; 95% CI 2.30-8.71) gestational weight gain (OR = 1.08; 95% CI 1.03-1.12) and central fat distribution (OR = 1.81; 95% CI 1.12-2.93) were directly related to delivering larger babies, after multiple adjustments.

Conclusion: These results suggest that pre-pregnancy obesity and gestational hyperglycaemia were independent risk factors for different adverse pregnancy and neonatal outcomes, while central distribution of fat, and gestational weight gain play an additive adverse role on these outcomes.

Key-words: Gestational Hyperglycaemia - Obesity - Waist-to-hip Ratio - Large-for-gestational Age Babies (LGA) - Cesarean Section.

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RÉSUMÉ

Obésité ou diabète : quel est le pire pour la mère ou pour le bébé ?

Objectif : Le but de cette étude était d’évaluer l’issue de la grossesse dans une cohorte de femmes caucasiennes en fonction de leur index de masse corporelle et de leur tolérance au glucose ; le rôle de la distribution de la graisse centrale, indiquée par le rapport taille sur hanche, a également été abordé.

Méthodes : Sept cent femmes ont été étudiées, présentant un diabète gestationnel ou une intolérance au glucose (250) ou une normoglycémie (450). Parmi elles, 117 présentaient avant la grossesse un surpoids ou une obésité (44 étaient obèses), 133 étaient hyperglycémiques mais normoglycémiques, et 117 avaient à la fois une hyperglycémie et un surpoids ou une obésité (42 étaient obèses).

Résultats : L’hypertension, la délivrance par césarienne et la prévalence de bébés macrosomes pour l’âge gestationnel étaient plus fréquentes chez les obèses (normo- et hyperglycémiques), principalement chez celles avec la prise de poids au cours de la grossesse la plus forte et avec une distribution centrale des graisses marquée (rapport taille/hanches > 0.90). Les femmes normoglycémiques hyperglycémiques ont présenté un meilleur résultat que les femmes obèses normoglycémiques. En régression logistique multiple, l’obésité (OR = 10.6 ; 95 % CI 5,00-22,54) était directement liée à l’hypertension, et les prédicteurs indépendants de césarienne étaient : l’hyperglycémie gestationnelle (OR = 1,78 ; 95 % CI 1,21-2,62), la prise de poids gravidique (OR = 1,06 ; 95 % CI 1,02-1,10), et l’obésité centrale (OR = 1,51 ; 95 % CI 1,02-2,24), tandis que l’obésité (OR = 4,48 ; 95 % CI 2,30-8,71), la prise de poids gravidique (OR = 1,08 ; 95 % CI 1,03-1,12) et la distribution centrale des graisses (OR = 1,81 ; 95 % CI 1,2-2,93) étaient directement corrélées à la macrosomie, après ajustements multiples.

Conclusion : Ces résultats suggèrent que l’obésité préexistante à la grossesse et l’hyperglycémie gestationnelle sont des facteurs de risque indépendants pour plusieurs issues indésirables de la grossesse, tandis que la distribution centrale des graisses et la prise de poids gravidique jouent un rôle adverse additionnel sur ces résultats.


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Obese women are at increased risk of adverse pregnancy outcomes including hypertensive gestational disorders and diabetes, cesarean section and macrosomia [1-3]; central fat distribution, furthermore is an independent predictor of macrosomia [4]. Women with gestational diabetes (or milder gestational hyperglycaemia) show an increased risk of hypertensive disorders, cesarean delivery, fetal macrosomia and neonatal morbidity, too [5-6]. Indeed, some Authors suggested that some of the complications attributed to gestational diabetes mellitus are likely to be related to maternal weight excess/obesity [7], while others found a synergistic action of both obesity and diabetes in pregnancy on neonatal outcomes [8].

The aims of the present study are:
- to evaluate in a cohort of Caucasian pregnant women clinical and delivery characteristics and neonatal morbidity, according to their body mass index (BMI) and gestational hyperglycaemia;
- to verify whether central fat distribution in these subjects could play an additional role on pregnancy outcomes.

**Patients and methods**

All pregnant women attending the Gynaecological and Obstetrical Department of the University of Torino are routinely screened with a 50-g oral glucose test at 24-28 weeks of gestational age. Gestational age was calculated by ultrasound examination performed during the first trimester of gestation. A positive screening result (1-h serum glucose concentration ≥ 27.8 mmol/l) was followed after 1-2 weeks by a 3-h oral glucose tolerance test (OGTT) with 100 g glucose. The test was performed in the morning after an overnight fast of at least 8 h but not more than 14 h and after at least 3 days of unrestricted diet (≤150 g carbohydrates/day) and exercise. The cut-off values were those proposed by Carpenter and Coustan [9]: gestational diabetes mellitus (GDM) was diagnosed in women displaying 2 serum glucose concentrations exceeding the following criteria: 5.3 mmol/l (fasting), 10.0 mmol/l (1 h), 8.6 mmol/l (2 h), 7.8 mmol/l (3 h). Impaired glucose tolerance (IGT) was diagnosed if only one glucose value was higher than these cut-off levels.

Subjects selection was based on a sequential screening from April 1999 to February 2001; pregnant women known to have preexistent diabetes mellitus, a disease affecting glucose metabolism, or hypertension were excluded. A total of 150 women with GDM and 100 with IGT were identified. All consecutive subjects (450) with normal OGTT’s during the first three months of this period were enrolled. All women gave their informed consent to participate in the study and all the followed procedures were in accordance with the Helsinki Declaration of 1975.

Height, weight and blood pressure were measured at the time of the screening; pre-pregnancy weight was recorded from patients recall. The BMI was calculated as pregnancy weight in kilograms divided by the square of the height in meters. Waist circumference (at the point of minimal abdominal girth) was measured in all women, since it is minimally influenced by uterine growth between 24 and 28 weeks of gestational age [10]; hip circumference was measured at maximal gluteal protrusion, viewed laterally, and waist-to-hip ratio (WHR) was calculated.

Obesity and overweight were defined if pre-pregnancy BMI was, respectively ≥ 30 kg/m² and between 25-29 kg/m². According to BMI and glucose tolerance, subjects were thus divided into four classes: class 1 = normal weight, normal OGTT (number = 333); class 2 = overweight/obese, normal OGTT (number = 117); class 3 = normal weight, IGT/ GDM (number = 133); class 4 = overweight/obese, IGT/ GDM (number = 117). Hypertension was considered if systolic and/or diastolic blood pressure were ≥ 140/90 mmHg.

Information concerning diabetes diagnosed by a physician in parents (living or dead) was collected.

Plasma triglycerides and HDL-cholesterol were measured after an overnight fast at the time of the screening test.

Serum glucose was measured by the glucose oxidase method (Glucose-Analyzer II Beckman, Fullerton, CA, USA). Plasma triglycerides were measured by enzymatic colorimetric assay (Poli, Clinical Chemistry CL7000, Shimadzu, Kyoto, Japan); HDL-cholesterol by enzymatic colorimetric assay after precipitation of LDL and VLDL fractions using heparin-MnCl₂ solution and centrifugation at 4°C.

Data about children’s birth weight and health status were obtained from the clinical records. Data were available for each classes in 90% of women (all carrying singleton pregnancies): respectively 305/333, 92% (class 1), 105/117, 90% (class 2), 120/133, 90% (class 3) and 106/117, 91% (class 4). Babies were classified as large-for-gestational age (LGA) and small-for-gestational age (SGA) if their birth weight was higher than the 90th and lower than the 10th percentile respectively, according to sex- and gestational age- neonatal anthropometric standards for a population of Northern Italy [11]. Premature births were defined if maternal gestational age at delivery was < 37 weeks. Neonatal morbidity was defined in the presence of any pathological conditions described on the clinical records, which required a specific treatment or a prolonged in-hospital stay (i.e. malformations, respiratory diseases, infections, icterus, neurological, gastrointestinal or hematological diseases, etc).

Analysis of variance (ANOVA) and the chi-square test were used to compare means for continuous variables or frequencies for discrete variables. Multiple logistic regression analyses were performed to evaluate the independent association of obesity, WHR and gestational hyperglycaemia with hypertension, cesarean deliveries and neonatal macrosomia after adjustment for multiple variables.
Since triglyceride values were not normally distributed, they were log-transformed. Data were presented as mean ± standard deviation or percentages, with p < 0.05 as the significance cut-off.

Results and discussion

Clinical characteristics of the subjects studied according to classes of glucose tolerance and BMI. (Tab I). Women with IGT/GDM were a few older, had lower HDL-cholesterol values, and higher level of triglycerides and WHR. Systolic, diastolic blood pressure and percentage of hypertension were significantly higher in overweight/obese women both with and without hyperglycaemia (Tab I). Pregnancy weight gain was lower in obese/overweight women, while neonatal birth weight and percentage of LGA babies were higher in these latter categories (Tab I). No difference in neonatal pathologies (overall and singularly considered) was evident between the four classes. After excluding overweight subjects from class 2 and 4, we found 44 obese only women (class 2) and 42 obese/hyperglycaemic patients (class 4). In these two classes prevalence of hypertension, cesarean delivery and of LGA babies raised respectively to 20%, 50% and 29.5% in class 2, and to 25%, 43% and 36% in class 4. These percentages were significantly higher than in the hyperglycaemic normal weight women (for hypertension: p < 0.01 class 2 and 4 vs class 3; for LGA babies: p < 0.05 class 2 vs class 3, p < 0.01 class 4 vs class 3). The highest prevalence of cesarean sections and LGA babies were found in obese normoglycaemic women who gained more than 8 kg during pregnancy (respectively 80% of cesarean sections and 40% of LGA babies).

In a multiple logistic regression model obesity was directly related to hypertension in pregnancy (OR = 10.6; 95% CI 5.00-22.54; p < 0.0001), after adjustment for age, gestational age and weight gain, and gestational hyperglycaemia, while this latter was not. Gestational hyperglycaemia was, indeed, an independent predictor of cesarean sections (OR = 1.78; 95% CI 1.21-2.62; p = 0.004), together with gestational weight gain (OR = 1.06; 95% CI 1.02-1.10; p = 0.003 for each kg-weight increase), while age and obesity were not, in a multiple logistic regression model. Furthermore, obesity (OR = 4.48; 95% CI 2.30-8.71; p = 0.0001) and gestational weight gain (OR = 1.08; 95% CI 1.03-1.12; p = 0.001 for each kg-weight increase) were directly related to LGA babies.

Table I
Clinical characteristics of the subjects studied according to classes of glucose tolerance and BMI.

<table>
<thead>
<tr>
<th></th>
<th>1*</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>P</th>
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<tr>
<td>Number</td>
<td>333</td>
<td>117</td>
<td>133</td>
<td>117</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>31.7±4.2</td>
<td>31.1±4.9</td>
<td>32.9±4.8</td>
<td>32.6±4.8</td>
<td>0.006</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.63±0.06</td>
<td>1.63±0.07</td>
<td>1.62±0.06e</td>
<td>1.62±0.07e</td>
<td>Ns</td>
</tr>
<tr>
<td>Pre-pregnancy BMI (kg/m²)</td>
<td>21.2±1.9b</td>
<td>29.9±4.6b</td>
<td>21.5±2.0b</td>
<td>29.9±4.5f</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Nulliparous (%)</td>
<td>63.7ae</td>
<td>53.0</td>
<td>62.4</td>
<td>51.3</td>
<td>0.042</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>11.4e</td>
<td>15.4</td>
<td>15.0</td>
<td>18.8</td>
<td>Ns</td>
</tr>
<tr>
<td>Parental diabetes (%)</td>
<td>25.2e</td>
<td>37.6</td>
<td>33.8</td>
<td>40.2f</td>
<td>0.0057</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>89.7±9.4b</td>
<td>102.9±9.3h</td>
<td>94.3±10.9m</td>
<td>105.0±10.9l</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.86±0.07</td>
<td>0.87±0.067</td>
<td>0.89±0.09d</td>
<td>0.90±0.09n</td>
<td>Ns</td>
</tr>
<tr>
<td>Systolic pressure (mmHg)</td>
<td>107.4±12.3b</td>
<td>118.9±15.9g</td>
<td>112.7±13.4m</td>
<td>121.9±16.7l</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic pressure (mmHg)</td>
<td>68.2±10.6b</td>
<td>76.1±10.7h</td>
<td>71.6±10.5m</td>
<td>79.0±10.1l</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>1.2b</td>
<td>10.3</td>
<td>4.5cm</td>
<td>11.1f</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.77±0.67a</td>
<td>1.93±0.68</td>
<td>2.08±0.74d</td>
<td>2.06±0.79l</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HDL-cholesterol (mmol/l)</td>
<td>1.99±0.39</td>
<td>1.93±0.36</td>
<td>1.93±0.39m</td>
<td>1.83±0.39h</td>
<td>0.0021</td>
</tr>
<tr>
<td>Pregnancy kg-increase</td>
<td>13.2±4.1b</td>
<td>10.5±6.1</td>
<td>11.8±5.7cm</td>
<td>9.5±6.8f</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Weeks of delivery</td>
<td>39.0±1.7</td>
<td>38.9±2.5</td>
<td>38.7±2.1</td>
<td>39.0±1.7</td>
<td>Ns</td>
</tr>
<tr>
<td>Cesarean sections (%)</td>
<td>30.5</td>
<td>38.1</td>
<td>39.2</td>
<td>44.3f</td>
<td>0.044</td>
</tr>
<tr>
<td>Pre-term delivery (%)</td>
<td>6.9</td>
<td>6.7</td>
<td>9.2</td>
<td>8.5</td>
<td>Ns</td>
</tr>
<tr>
<td>Offspring birthweight (g)</td>
<td>3271±446a</td>
<td>3413±589h</td>
<td>3186±578h</td>
<td>3389±447e</td>
<td>0.001</td>
</tr>
<tr>
<td>LGA babies (%)**</td>
<td>13.1f</td>
<td>27.6n</td>
<td>13.3o</td>
<td>27.4j</td>
<td>0.00024</td>
</tr>
<tr>
<td>SGA babies (%)**</td>
<td>3.6</td>
<td>5.7</td>
<td>5.0</td>
<td>6.6</td>
<td>Ns</td>
</tr>
<tr>
<td>Neonatal pathologies (%)</td>
<td>22.6</td>
<td>23.8</td>
<td>25.8</td>
<td>29.2</td>
<td>Ns</td>
</tr>
</tbody>
</table>

* class 1= normal weight, normal OGTT; class 2= overweight/obese, normal OGTT; class 3= normal weight, IGT/GDM; class 4= overweight/obese, IGT/GDM; ** LGA = large-for-gestational age babies; SGA = small-for-gestational age babies. * p < 0.05 1 vs 2; ** p < 0.01 1 vs 2; † p < 0.05 1 vs 3; ‡ p < 0.01 1 vs 3; § p < 0.05 1 vs 4; ¶ p < 0.01 1 vs 4; # p < 0.05 2 vs 3; ¥ p < 0.01 2 vs 3; µ p < 0.05 2 vs 4; ¶ p < 0.01 2 vs 4; | p < 0.05 3 vs 4; © p < 0.01 3 vs 4.
while age, gestational hyperglycaemia and smoking habits were not in a multiple regression analysis. Pre-pregnancy overweight, indeed, was not significantly associated with adverse outcomes.

WHR significantly increased with the worsening of the glucose tolerance (Tab I). A WHR > 0.90, expression of central fat distribution was independently associated with delivering a LGA baby (OR = 1.81; 95% CI 1.12-2.93; p = 0.015) and cesarean-sections (OR = 1.51; 95% CI 1.02-2.24; p = 0.04), after adjustments for age, gestational age and weight gain, presence of gestational hyperglycaemia and obesity, smoking habits.

Height and parity did not result significantly associated with any pregnancy outcomes, after multiple adjustments, nor their introduction in the model modified the above reported results.

These data suggest that pre-pregnancy obesity and gestational hyperglycaemia play a significant, but different role on pregnancy outcomes. Pre-pregnancy obesity significantly predicted gestational hypertension and the delivering of a LGA baby. Gestational hyperglycaemia seems, on the other hand, to be the most important predictor of cesarean sections in our women; however, as the obstetricians were not blinded about the results of the OGTT, we cannot exclude this knowledge might have influenced their decision about the method of delivery. Gestational weight gain and central fat distribution have an additive role on pregnancy outcomes (independent predictor of larger newborn babies and cesarean sections) according to the possible influence on fetal growth of the metabolic alterations associated with maternal central body fat stores [4]. Height and parity do not affect pregnancy outcomes, contrary to another study, performed in a US low-risk cohort, thus not comparable to ours [5].

In conclusion, maternal pre-pregnancy obesity and gestational diabetes carry significant, but different risks for the mother and the foetus; gestational weight gain and central body fat disposition play a synergistic role on adverse neonatal outcomes, the latter being a risk factor worth to be considered in the follow-up of the pregnancy. For primary prevention, adverse pregnancy outcomes related to maternal fat might, at least theoretically, be preventable, by preconceptional counselling regarding dietary and life-style modifications.

References