# IADPSG and WHO 2013 Gestational Diabetes Mellitus Criteria Identify Obese Women With Marked Insulin Resistance in Early Pregnancy

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Implementation of the International Association of Diabetes and Pregnancy Study Groups (IADPSG) and the World Health Organization 2013 (WHO 2013) recommendations leads to an increased prevalence of gestational diabetes mellitus (GDM) due to more stringent criteria and early screening of women at high risk for diabetes in pregnancy (DIP) (1,2). IADPSG members now recommend that their GDM criteria should not be used in early pregnancy but have not provided alternative criteria (3). We have compared the characteristics of overweight/obese women early in pregnancy, with and without GDM using the new criteria, to assess whether those testing positive are metabolically distinct.

Pregnant women with a BMI $\geq$29.0 kg/m$^2$ underwent a 75-g oral glucose tolerance test in early pregnancy as part of enrollment into the DALI (Vitamin D And Lifestyle Intervention for GDM prevention) pilot and lifestyle Pan-European multicenter trials (4). GDM and DIP were diagnosed using WHO 2013 criteria.

A high rate of GDM (237/1,035 or 22.9%: DIP 0.5%; total hyperglycemia in early pregnancy 23.4%) was found at a mean of 15.2 $\pm$ 3.0 gestational weeks (interquartile range 13.4–16.8). A fasting glucose alone identified 190/242 (78.5%) women. The other 52 women (21.5%) were diagnosed with elevated

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**Table 1—Descriptive analysis, surrogate parameters of insulin sensitivity, insulin secretion, and metabolic parameters of DALI pilot and lifestyle study population in early pregnancy**

| | NGT (total $N = 793$) | | Early GDM (total $N = 237$) | | DIP (total $N = 5$) | | |
|---|---|---|---|---|---|---|---|
| | *n* | Mean ± SD or % | *n* | Mean ± SD or % | *n* | Mean ± SD or % | *P* (NGT vs. GDM) |
| Age (years) | 780 | 31.9 ± 5.3 | 230 | 32.8 ± 5.1 | 5 | 31.7 ± 3.7 | **0.04** |
| Height (cm) | 778 | 165.5 ± 6.8 | 227 | 165.7 ± 6.2 | 5 | 163.1 ± 1.2 | 0.75 |
| Prepregnancy weight (kg) | 780 | 92.4 ± 13.8 | 228 | 96.9 ± 16.1 | 5 | 93.3 ± 15.4 | **<0.001** |
| Prepregnancy BMI (kg/m$^2$) | 777 | 33.7 ± 4.3 | 222 | 35.2 ± 5.3 | 5 | 35.0 ± 5.3 | **<0.001** |
| BMI at screening (kg/m$^2$) | 778 | 34.4 ± 4.3 | 226 | 36.1 ± 5.6 | 5 | 35.6 ± 4.9 | **<0.001** |
| Weight gain until first visit (kg)* | 778 | 2.0 ± 4.4 | 221 | 2.5 ± 7.8 | 5 | 1.7 ± 4.1 | 0.25 |
| Gestational age (weeks) | 779 | 15.2 ± 3.1 | 228 | 15.0 ± 2.4 | 5 | 13.4 ± 4.3 | 0.36 |
| Waist circumference (cm) | 764 | 107.2 ± 10.4 | 219 | 110.3 ± 11.6 | 5 | 109.4 ± 9.7 | **<0.001** |
| Sum of skinfolds (mm) | 763 | 107.6 ± 28.1 | 217 | 114.8 ± 30.7 | 5 | 104.6 ± 11.9 | **0.001** |
| European descent | 674/778 | 86.6% | 195/225 | 86.7% | 1/5 | 20.0% | 1.00 |
| Higher education | 431/777 | 55.5% | 121/223 | 54.3% | 3/5 | 60.0% | 0.81 |
| Lives with partner | 730/777 | 94.0% | 203/221 | 91.9% | 4/5 | 80.0% | 0.28 |
| Smoking | 132/781 | 16.9% | 34/237 | 14.3% | 0/5 | 0% | 0.37 |
| Alcohol consumption | 46/781 | 5.9% | 7/237 | 3.0% | 0/5 | 0% | 0.09 |
| Multiparity | 389/777 | 50.1% | 110/224 | 49.1% | 1/5 | 20% | 0.82 |
| Diabetes in family | 185/781 | 23.7% | 64/237 | 27.0% | 3/5 | 60.0% | 0.30 |
| History of GDM | 38/483 | 7.9% | 22/137 | 16.1% | 1/2 | 50.0% | **0.01** |
| Previous stillbirth | 49/480 | 10.2% | 19/140 | 13.6% | 1/2 | 50.0% | 0.28 |
| Previous macrosomia | 86/480 | 17.9% | 44/138 | 31.9% | 0/2 | 0% | **0.001** |
| Previous congenital malformation | 16/482 | 3.3% | 9/139 | 6.5% | 0/2 | 0% | 0.14 |
| Previous chronic hypertension | 99/772 | 12.8% | 31/222 | 14.0% | 0/5 | 0% | 0.74 |
| Systolic blood pressure (mmHg) | 778 | 116.4 ± 11.1 | 225 | 118.3 ± 10.1 | 5 | 123.6 ± 7.0 | **0.02** |
| Diastolic blood pressure (mmHg) | 778 | 72.8 ± 9.2 | 225 | 75.1 ± 8.4 | 5 | 78.2 ± 6.8 | **0.001** |
| Heart rate (bpm) | 738 | 79.4 ± 10.0 | 206 | 82.0 ± 10.6 | 5 | 79.2 ± 9.4 | **0.001** |
| FPG (mmol/L) | 713 | 4.6 ± 0.4 | 215 | 5.1 ± 0.6 | 5 | 6.2 ± 1.1 | **<0.001** |
| 1-h plasma glucose (mmol/L) | 669 | 6.7 ± 1.4 | 201 | 8.5 ± 2.0 | 4 | 12.4 ± 1.7 | **<0.001** |
| 2-h plasma glucose (mmol/L) | 670 | 5.8 ± 1.1 | 200 | 7.0 ± 1.6 | 5 | 9.0 ± 3.3 | **<0.001** |
| Fasting insulin (mU/L) | 706 | 14.9 ± 11.6 | 209 | 18.8 ± 9.0 | 5 | 32.1 ± 26.5 | **<0.001** |
| 1-h insulin (mU/L) | 656 | 107.7 ± 73.4 | 194 | 148.2 ± 90.5 | 5 | 149.6 ± 107.9 | **<0.001** |
| 2-h insulin (mU/L) | 656 | 76.2 ± 59.1 | 196 | 121.9 ± 97.5 | 5 | 187.3 ± 195.7 | **<0.001** |
| AUC glucose (mmol/L) | 665 | 12.3 ± 1.9 | 200 | 14.9 ± 2.7 | 4 | 20.5 ± 2.8 | **<0.001** |
| AUC insulin (mU/L) | 647 | 164.8 ± 94.6 | 193 | 226.1 ± 129.9 | 3 | 347.6 ± 231.1 | **<0.001** |
| HOMA IR** | 702 | 3.1 ± 2.9 | 208 | 4.3 ± 2.2 | 5 | 9.3 ± 8.9 | <0.001 |
| QUICKI | 702 | 0.33 ± 0.03 | 208 | 0.31 ± 0.02 | 5 | 0.29 ± 0.03 | **<0.001** |
| OGIS (mL/min/m$^2$) | 358 | 424.8 ± 69.0 | 72 | 338.9 ± 65.7 | 0 | N/A† | **<0.001** |
| Matsuda index** | 644 | 4.8 ± 3.5 | 192 | 2.9 ± 2.1 | 5 | 1.8 ± 1.0 | **<0.001** |
| IGI** | 339 | 2.5 ± 3.2 | 73 | 2.1 ± 3.3 | 0 | N/A† | 0.32 |
| DI** | 328 | 8.0 ± 8.6 | 69 | 3.6 ± 3.8 | 0 | N/A† | **<0.001** |
| Stumvoll first phase** | 647 | 794.4 ± 802.8 | 192 | 1151.6 ± 1063.4 | 4 | 901.6 ± 1,804.4 | **<0.001** |
| Stumvoll second phase** | 647 | 505.8 ± 196.4 | 192 | 597.9 ± 260.9 | 4 | 547.2 ± 437.2 | **<0.001** |
| Plasma leptin (ng/mL) | 687 | 36.8 ± 18.5 | 206 | 38.7 ± 19.5 | 5 | 52.8 ± 16.2 | 0.22 |
| Triglycerides (mmol/L) | 257 | 1.32 ± 0.44 | 99 | 1.52 ± 0.58 | 4 | 1.39 ± 0.58 | **0.002** |
| FFA (mmol/L) | 357 | 0.67 ± 0.24 | 99 | 0.74 ± 0.24 | 4 | 0.60 ± 0.29 | **0.01** |
| LDL (mmol/L) | 357 | 2.90 ± 0.75 | 99 | 2.99 ± 1.01 | 4 | 2.58 ± 0.51 | 0.80 |
| HDL (mmol/L) | 356 | 1.46 ± 0.28 | 99 | 1.45 ± 0.30 | 4 | 1.21 ± 0.07 | 0.30 |
| 3-β-Hydroxybutyrate (mmol/L) | 357 | 0.08 ± 0.08 | 99 | 0.11 ± 0.08 | 4 | 0.05 ± 0.06 | **0.01** |

AUC, area under the curve; DI, disposition index; FFA, free fatty acids; FPG, fasting plasma glucose; HOMA IR, HOMA of insulin resistance (product of fasting plasma insulin and FPG divided by the constant 22.5); IGI, insulinogenic index; NGT, normal glucose tolerant; OGIS, oral glucose insulin sensitivity index; PIH, pregnancy-induced hypertension; QUICKI, quantitative insulin sensitivity check index. Boldface type indicates statistical significance. *Weight gain prepregnancy to first study visit. **Analysis after logarithmic transformation. †Oral glucose tolerance test (30- or 90-min) values missing for calculation.

1-h and/or 2-h glucose levels. Obese women with DIP were less likely to be of European ancestry than women with early GDM (20.0% vs. 86.7%, $P = 0.002$).

Women with early GDM had significantly greater insulin resistance and higher BMI, waist circumference, systolic and diastolic blood pressures, triglycerides, free fatty acids, 3-β-hydroxybutyrate, and heart rate at screening (Table 1). Significant differences in insulin secretion and disposition index were also found. Differences persisted after adjustment for age, pregestational BMI, gestational week, and fetal sex.

In multivariate logistic regression analyses, which also included gestational week, educational level, and employment status, early GDM was significantly more common with higher prepregnancy BMI (kg/m$^2$; odds ratio [OR] 1.05, 95% CI 1.00–1.10, $P < 0.04$), sum of skinfolds in early pregnancy (mm; OR 1.01, 95% CI 1.00–1.02, $P < 0.01$), prior history of GDM (OR 2.74, 95% CI 1.66–4.50, $P < 0.001$), and previous macrosomia (OR 1.97, 95% CI 1.03–3.98, $P < 0.04$). Nulliparity was found to be protective (OR 0.51, 95% CI 0.30–0.86, $P < 0.01$). In a subanalysis of nulliparous women, multivariate logistic regression found that higher prepregnancy BMI was the only risk factor (OR 1.09, 95% CI 1.03–1.15, $P < 0.01$) for an early GDM diagnosis.

Although the new criteria have not been validated in early pregnancy, their use in our DALI cohort has identified a profile akin to the metabolic syndrome (5). Prepregnancy BMI was a significant predictor of early GDM and the only predictor among nulliparous women in spite of the cohort only including women with a BMI ≥29.0 kg/m$^2$. This supports the need for weight control before and after pregnancy. On the basis of these data, we suggest that dropping the IADPSG criteria for GDM diagnosis early in pregnancy may be premature. Continuing their use would provide criteria for GDM early in pregnancy and maintain common criteria throughout pregnancy. How such women are managed should be tested in a randomized controlled trial of immediate GDM treatment versus usual care and to explore the impact on perinatal outcome.

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