



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 ≥ 29.0 kg/m² 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 ± 3.0 gestational weeks (interquartile range 13.4–16.8).

Jürgen Harreiter,¹ David Simmons,² Gernot Desoye,³ Rosa Corcoy,^{4,5} Juan M. Adelantado,⁴ Roland Devlieger,^{6,7,8} Andre van Assche,⁶ Sander Galjaard,^{6,7,9} Peter Damm,¹⁰ Elisabeth R. Mathiesen,¹⁰ Dorte M. Jensen,^{11,12} Lise Lotte T. Andersen,¹² Fidelma Dunne,¹³ Annunziata Lapolla,¹⁴ Maria G. Dalfra,¹⁴ Alessandra Bertolotto,¹⁵ Urzula Mantaj,¹⁶ Ewa Wender-Ozegowska,¹⁶ Agnieszka Zawiejska,¹⁶ David Hill,¹⁷ Judith G.M. Jelsma,¹⁸ Frank J. Snoek,¹⁹ Christof Worda,²⁰ Dagmar Bancher-Todesca,²⁰ Mireille N.M. van Poppel,^{18,21} and Alexandra Kautzky-Willer,¹ on behalf of the DALI Core Investigator group

A fasting glucose alone identified 190/242 (78.5%) women. The other 52 women (21.5%) were diagnosed with elevated

¹Gender Medicine Unit, Division of Endocrinology and Metabolism, Department of Medicine III, Medical University of Vienna, Vienna, Austria

²Institute of Metabolic Science, Addenbrooke's Hospital, Cambridge, England and Macarthur Clinical School, Western Sydney University, Sydney, Australia

³Department of Obstetrics and Gynecology, Medizinische Universität Graz, Graz, Austria

⁴Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

⁵CIBER Bioengineering, Biomaterials and Nanomedicine, Instituto de Salud Carlos III, Zaragoza, Spain

⁶Department of Development and Regeneration, KU Leuven, Leuven, Belgium

⁷Department of Obstetrics and Gynecology, University Hospitals Leuven, Leuven, Belgium

⁸Department of Obstetrics, Gynecology and Fertility, GasthuisZusters Antwerpen Sint-Augustinus, Wilrijk, Belgium

⁹Department of Obstetrics and Gynaecology, Division of Obstetrics and Prenatal Medicine, Erasmus MC, University Medical Centre, Rotterdam, the Netherlands

¹⁰Center for Pregnant Women with Diabetes, Departments of Endocrinology and Obstetrics, Rigshospitalet and The Clinical Institute of Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

¹¹Department of Endocrinology, Odense University Hospital, Odense, Denmark

¹²Department of Gynaecology and Obstetrics, Odense University Hospital and Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark

¹³Galway Diabetes Research Centre (GDRC) and National University of Ireland, Galway, Ireland

¹⁴Università degli Studi di Padova, Padua, Italy

¹⁵Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy

¹⁶Medical Faculty I, Poznan University of Medical Sciences, Poznan, Poland

¹⁷Recherche en Santé Lawson SA, St. Gallen, Switzerland

¹⁸Department of Public and Occupational Health, EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, the Netherlands

¹⁹Department of Medical Psychology, EMGO Institute for Health and Care Research, VU University Medical Center, and Medical Psychology Academic Medical Center, Amsterdam, the Netherlands

²⁰Division of Obstetrics and Feto-Maternal Medicine, Department of Obstetrics and Gynecology, Medical University of Vienna, Vienna, Austria

²¹Institute of Sports Sciences, University of Graz, Graz, Austria

Corresponding author: Alexandra Kautzky-Willer, alexandra.kautzky-willer@meduniwien.ac.at.

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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)		P (NGT vs. GDM)
	n	Mean ± SD or %	n	Mean ± SD or %	n	Mean ± SD or %	
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 $\geq 29.0 \text{ kg}/\text{m}^2$. 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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