Gestational Diabetes

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Gestational diabetes mellitus (GDM) is a common medical complication of pregnancy, defined as "any degree of glucose intolerance with onset or first recognition during pregnancy." The initial criteria for its diagnosis were established over 40 years ago and, with modifications, remain in use today. The criteria were chosen to identify women who were at high risk for development of diabetes after pregnancy or were derived from criteria that were used for nonpregnant individuals and not necessarily to identify pregnancies with increased risk for adverse perinatal outcome [International Association of Diabetes and Pregnancy Study Groups Consensus Panel. *Diabetes Care* 2010].

The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study was conducted to clarify the risks of adverse outcomes that were associated with various degrees of maternal glucose intolerance that were less severe than that in overt diabetes mellitus. Participants in the HAPO Study included 25,505 pregnant women at 15 centers in nine countries who underwent 75-g oral glucose tolerance (OGTT) testing at 24 to 32 weeks of gestation. Subjects whose fasting plasma glucose results were >105 mg/dL (5.8 mmol/L) or whose 2-hour plasma glucose level >200 mg/dL (11.1 mmol/L) were unblinded. Results for all other subjects remained blinded. The primary study outcomes were birth weight above the 90th percentile for gestational age, primary cesarean delivery, clinically diagnosed neonatal hypoglycemia, and cord blood serum C-peptide level above the 90th percentile. Of the 25,505 women who completed an OGTT, data for 23,316 were available for analyses (746 [2.9%] subjects were excluded because their data were unblinded, 1412 [5.5%] for missing or unusable data). Adjusted odds ratios were calculated for adverse pregnancy outcomes that were associated with an increase of 1 standard deviation (SD) in the fasting plasma glucose level and the 1- and 2-hour glucose levels (Table 1).

The results of the HAPO study indicated strong, continuous associations of maternal glucose levels below those that are normally noted for a diagnosis of diabetes with increased birth weight and increased cord blood serum C-peptide levels [HAPO Study Cooperative Research Group. *Intl J Gynaecol Obstet* 2002; *N Engl J Med* 2008; *Diabetes* 2009].

Table 1. Odds Ratios (95% CI) for Adverse Pregnancy Outcomes for 1 SD Change In Glucose Level.

	Fasting Glucose OR (95% CI)	1-Hour Glucose OR (95% CI)	2-Hour Glucose OR (95% CI)
Birth weight above the 90th percentile	1.38 (1.32, 1.44)	1.46 (1.39, 1.53)	1.38 (1.32, 1.44)
Cord-blood serum C-peptide level above the 90th percentile	1.55 (1.47, 1.64)	1.46 (1.38 to 1.54)	1.37 (1.30, 1.44)
Primary cesarean delivery	1.11 (1.06, 1.15)	1.10 (1.06 to 1.15)	1.08 (1.03, 1.12)
Neonatal hypoglycemia	1.08 (0.98, 1.19)	1.13 (1.03, 1.26)	1.10 (1.00, 1.12)

Recently, the International Association of Diabetes in Pregnancy Study Groups (IADPSG) Consensus Panel suggested new diagnostic criteria for the diagnosis and classification of GDM (Table 2) [International Association of Diabetes and Pregnancy Study Groups Consensus Panel. *Diabetes Care* 2010]. Because of the extensive efforts that were used to standardize procedures for participant enrollment, laboratory analyses, data collection, and the methods that were used to analyze the results, HAPO data were used as the basis for the new GDM diagnostic thresholds. The following is a summary of two presentations that examined the effects of those changes on the diagnosis of GDM.

David R. Hadden, MD, Royal Victoria Hospital, Belfast, United Kingdom, presented the results of a study that showed that when the new IADPSG diagnostic criteria are used, there is substantial variability between and within regions (Table 3). There was also considerable center-to-center variation of study participants in maternal age, body mass index, frequencies of family history of diabetes, and hypertension. Adjusting for these variables and for field center reduced but did not eliminate center-to-center differences, which, in all likelihood, reflect racial/ethnic group differences in the potential risk of disorders of glucose metabolism in these populations.

The substantial variations may influence future efforts to develop optimal, cost-effective strategies for the detection and treatment of GDM, noted Prof. Hadden.

Table 2. Screening and Diagnosis of Hyperglycemia in Pregnancy.

IADPSG Criteria: Threshold values for diagnosis of GDM	
OGTT: 75 g	
Plasma glucose: one or more value equaled or exceeded	
Fasting:	5.1 mmol/L (92 mg/dL)
1-h	10.0 mmol/L (180 mg/dL)
2-h	8.5 mmol/L (153 mg/dL)
To diagnose overt diabetes in pregnancy	
FPG	≥7.0 mmol/L (126 mg/dL) or
HbA1C	≥6.5% (DCCT/UKPDS standardized) or
Random PG	≥11.1 mmol/L (200 mg/dL)
Strategy for detection and diagnosis of hyperglycemic disorders in pregnancy (for women without known diabetes antedating pregnancy)	
1st prenatal visit	
Measure FGP, HbA1C or random PG on all women (or only high-risk women)	
If results indicate overt diabetes, treat and follow-up as for pre-existing diabetes	
If not diagnostic of overt diabetes and FPG ≥5.1 mmol/L (92 mg/dL), but <7.0 mmol/L (126 mg/dL), diagnose as GDM or	
FGP< 5.1 mmol/L (92 mg/dL), to have 75 g OGTT for GDM at 24 to 28 weeks gestation	
At 24 to 28 weeks gestation	
2h 75 g OGTT after overnight fast on all women not previously found to have overt diabetes or GDM	
Diagnose overt diabetes if FPG ≥7.0 mmol/L (126 mg/dL)	
Diagnose GDM if one or more values equals or exceeds thresholds	
Diagnose normal if all values on OGTT less than thresholds	

Table 3. Unadjusted Frequency of GDM at HAPO Field Centers.

Field Center	Frequency (%)*	Field Center	Frequency (%)
Cleveland, USA	23.7	Providence, USA	14.2
Bellflower, USA	22.9	Newcastle, Australia	13.6
Singapore, Singapore	22.4	Hong Kong, China	13.4
Bangkok, Thailand	21.2	Brisbane, Australia	12.1
Manchester, UK	21.0	Barbados, West Indies	9.9
Chicago, USA	16.5	Petah Tiqva, Israel	9.2
Belfast, UK	15.5	Beersheba, Israel	8.7
Toronto, Canada	14.6	**HAPO Overall**	**16.1**

* Unadjusted; HAPO=Hyperglycemia and Adverse Pregnancy Outcome

Annunziata Lapolla, MD, University of Padova, Padova, Italy, presented the results of a study that evaluated the clinical and metabolic characteristics, and pregnancy outcome in women previously classified as normal by Carpenter and Coustan criteria [Carpenter MW & Coustan DR. *Am J Obstet Gynecol* 1982] and now classified as having GDM utilizing the new IADPSG criteria.

Results of this retrospective analysis of 3953 pregnancies indicated an increase in the diagnosis of GDM of approximately 20% (n=112) with the new criteria (Table 4). Women who were diagnosed only under the new criteria were younger (32.4 ± 4.5 years vs 33.4 ± 4.4 years; p<0.005) and had a lower prepregnancy body mass index (23.7 ± 4.3 kg/m^2 vs 24.7 ± 5.1 kg/m^2; p<0.005) than women who were diagnosed only under the older criteria. HbA1C levels at diagnosis and at the 3rd trimester were not different. Glucose levels on the OGTT were significantly higher in newly diagnosed women compared with those women with normal glucose tolerance on fasting (90.5 ± 7.8 mg/dL vs 79.2 ± 6.8 mg/dL; p<0.0001) and at 1 (153.7 ± 18.8 mg/dL vs 140.6 ± 23.7; p<0.0001) and 2 hours (129.3 ± 20.6 vs 116.3 mg/dL ± 20; p<0.0001).

Table 4. Impact of the New Diagnostic Criteria.

	Carpenter and Coustan Criteria	New IADPSG Criteria	Difference
GDM	34.5%	54.1%	+19.7%
One abnormal value	15.9%	-------	-15.9%
Normal glucose tolerance	48.7%	45.9%	-2.8%

Cesarean section was significantly (p<0.005) more common among women who were newly diagnosed (43.6%) and previously diagnosed (41%) with T2DM compared with women with normal glucose tolerance (31.1%). Gestational age at delivery and birth weight were not different. Ponderal index (g/cm^3) was significantly higher in previously diagnosed and newly diagnosed women versus those with normal glucose tolerance (2.95 ± 0.61 mg/dL vs 2.8 ± 0.41 mg/dL and vs 2.77 ± 0.34 mg/dL; p<0.0001, respectively). A correlation analysis showed that prepregnancy BMI and basal glucose level were significantly related with newborn ponderal index (p<0.0001 and p<0.05, respectively).

The new GDM diagnostic criteria that have been recommended by IADPSG identified a new group of women who were previously classified as normal with Carpenter and Coustan criteria. These women have metabolic characteristics and pregnancy outcomes that are similar to those of women who are diagnosed under the older criteria.