Screening and Diagnosis of Gestational Diabetes Mellitus

Critical appraisal of the new International Association of Diabetes in Pregnancy Study Group recommendations on a national level

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OBJECTIVE—To study the implications of implementing the International Association of Diabetes in Pregnancy Study Group (IADPSG) recommendations for screening and diagnosis of gestational diabetes mellitus (GDM) in Israel and explore alternative methods for identifying women at risk for adverse pregnancy outcomes.

RESEARCH DESIGN AND METHODS—We analyzed data of the Israeli Hyperglycemia and Adverse Pregnancy Outcomes study participants (N = 3,345). Adverse outcome rates were calculated and compared for women who were positive according to *1*) IADPSG criteria, *2*) IADPSG criteria with risk stratification, or *3*) screening with BMI or fasting plasma glucose (FPG).

RESULTS—Adopting IADPSG recommendations would increase GDM diagnosis by ~50%. One-third of IADPSG-positive women were at low risk for adverse outcomes and could be managed less intensively. FPG ≥89 mg/dL or BMI ≥33.5 kg/m^2 at 28–32 weeks of gestation detected proportions of adverse outcomes similar to IADPSG criteria.

CONCLUSIONS—Implementing IADPSG recommendations will substantially increase GDM diagnosis. Risk stratification in IADPSG-positive women may reduce over-treatment. Screening with FPG or BMI may be a practical alternative.

Diabetes Care 35:1894–1896, 2012

Gestational diabetes mellitus (GDM) is associated with a high risk of immediate and late adverse outcomes for mothers and their offspring (1–4). This risk correlates with the level of maternal hyperglycemia (5), and glucose-lowering interventions were reported to decrease the risk of some of these adverse outcomes (6).

In many countries, including Israel, a two-step approach for GDM screening is used: pregnant women undergo a 50-g oral glucose challenge test, followed by a 100-g oral glucose tolerance test (OGTT) for women who test positive on the first test (7). This practice is based on little evidence. Furthermore, the glucose thresholds used for GDM diagnosis have been set according to maternal risk of later developing type 2 diabetes rather than the immediate risk of adverse pregnancy outcomes (8).

The Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) prospective study addressed the debate about the best screening practice and diagnostic criteria for GDM. Of 25,505 pregnant women recruited, 3,345 were from Israel. The results showed an association between fasting and postload plasma glucose levels and adverse pregnancy outcomes, even in the range previously considered normal (9). These results motivated the International Association of Diabetes in Pregnancy Study Group (IADPSG) to recommend a new screening practice and diagnostic criteria for GDM (10).

The yield and practicality of screening methods may differ according to prevalence of risk factors and availability of health care resources. The current analysis was conducted to evaluate the effect of endorsing the IADPSG recommendations in Israel and to explore alternative methods for detecting women at risk for adverse pregnancy outcomes.

RESEARCH DESIGN AND METHODS

The data of the Israeli HAPO participants were analyzed and compared with the rest of the study participants. In further analyses of the Israeli HAPO participants, we focused on two adverse pregnancy outcomes: fetal macrosomia (FM) and pre-eclampsia/eclampsia.

Several alternatives to the IADPSG recommendations were explored. First, among IADPSG-positive women, we aimed to identify a subgroup at lower risk for FM, using a FM management risk score based on the maternal characteristics of BMI, height, and parity (see Supplementary Data online). Second, we explored two alternative screening methods, based on fasting plasma glucose (FPG) or BMI at 28–32 weeks of gestation, with cutoffs for positivity that yielded the same proportion of positive cases as the IADPSG criteria. Third, we explored a two-step screening approach, using FPG for screening all women and further OGTT for those at higher risk for FM. An FM diagnosis risk score, based on maternal characteristics and FPG level, was used to identify higher

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Received 8 January 2012 and accepted 16 April 2012.
DOI: 10.2337/dc12-0041
This article contains Supplementary Data online at http://care.diabetesjournals.org/lookup/suppl/doi:10.2337/dc12-0041/-/DC1.
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risk for FM (see Supplementary Data online).

RESULTS—The Israeli HAPO participants were younger and weighed less than the rest of the study population. They were less likely to report cigarette smoking or alcohol consumption. Their fasting and postload plasma glucose levels were significantly lower compared with other participants (Supplementary Table 1). By use of the IADPSG diagnostic criteria, the estimated GDM prevalence among the Israeli participants was 9.0%, approximately half the rate found among the rest of HAPO participants (17.8%). Nevertheless, it was still 50% higher than the 6% of pregnancies currently diagnosed with GDM in Israel (11).

A total of 277 Israeli HAPO participants (8.3%) met the IADPSG criteria for GDM. The prevalence of FM among these women was 16.4% compared with 8.1% among IADPSG-negative women. By use of an FM management risk score, the prevalence of FM among the one-third of IADPSG-positive women who scored <166 was 9.8% compared with 19.7% in the two-thirds of IADPSG-positive women who scored ≥166.

We examined two alternative risk markers for adverse pregnancy outcomes: FPG and BMI. The threshold that 8.3% of Israeli HAPO participants exceeded (the same proportion as were IADPSG-positive) was 89 mg/dL for FPG and 33.5 kg/m^2 for BMI. By use of these thresholds, FPG, BMI, and the IADPSG criteria identified similar proportions of FM and pre-eclampsia/eclampsia (Table 1)

Finally, we focused on those women with an FPG value <89 mg/dL threshold and, using an FM Diagnosis Risk Score, determined a subgroup with greater risk for FM despite their lower FPG level. The 20% of the women with an FPG <89 mg/dL who had a risk score ≥200 had an FM rate of 17.5%, similar to that for women with an FPG ≥89 mg/dL. Accordingly, we defined a two-step screening approach as follows: all pregnant women would have an FPG test, with levels ≥89 mg/dL defining GDM. Among women with an FPG <89 mg/dL, those with a risk score ≥200 would undergo OGTT, with GDM determined according to postload IADPSG thresholds. By use of this approach, ~18.5% of women would undergo an OGTT, and the proportion diagnosed with GDM would increase to 9.5%.

CONCLUSIONS—Our results show that implementing the IADPSG recommendations in Israel will substantially increase the proportion of women diagnosed with GDM. According to HAPO data, the expected increase in the GDM diagnosis could be even higher in other countries. This is causing a worldwide debate over the adoption of the IADPSG recommendations (12).

Evidence from randomized trials showing benefit from interventions in mild GDM support the adoption of the IADPSG recommendations (13,14). However, 80–90% of the women included in these trials were managed with lifestyle modification only, which can be delivered effectively also in less care-intensive environments. We found that an identifiable one-third of the IADPSG-positive women had rates of FM only slightly greater than the rates among IADPSG-negative women. These women may benefit from less intensive management that focuses mainly on lifestyle modification. Using such risk stratification may promote efficient use of health care resources while avoiding over-treatment.

Universal use of OGTT for GDM screening may impose excessive burden, especially where resources are scarce. Two alternative screening methods, using BMI or FPG, identified subgroups of women with similar rates of FM and pre-eclampsia/eclampsia as in IADPSG-positive women.

The FM risk stratification models developed in this study were not validated in other populations. Thus, validation of these models is necessary before implementation elsewhere.

The objective of GDM screening is to identify women at risk for adverse pregnancy outcomes to improve prognosis through evidence-based interventions. This study provides pertinent information for making locally relevant and evidence-based decisions on screening and diagnosis policy in GDM.

Table 1—*Rate (95% CIs) of adverse outcomes detected using three alternative risk markers: IADPSG criteria for GDM diagnosis, FPG, and BMI**

	IADPSG negative	IADPSG positive	FPG ≥89 mg/dL	BMI ≥33.5 kg/m^2
n	2,930	277	277	278
FM†	7.6 (6.6–8.6)	16.4 (12.0–20.8)	18.8 (14.2–23.2)	17.3 (12.8–21.8)
Pre-eclampsia/ eclampsia§	1.2 (0.8–1.6)	1.8 (0.6–4.2)	2.2 (0.8–4.7)	4.3 (2.3–7.4)

*None of the differences in outcome rates between the IADPSG-positive, FPG ≥89 mg/dL, and BMI ≥33.5 kg/m^2 groups were statistically significant. Continuity-adjusted χ^2 test (after adjustment for overlapping membership): FM: IADPSG vs. FPG, $P = 0.37$; IADPSG vs. BMI, $P = 0.83$; FPG vs. BMI, $P = 0.71$. Pre-eclampsia/eclampsia: IADPSG vs. FPG, $P > 0.9$; IADPSG vs. BMI, $P = 0.07$; FPG vs. BMI, $P = 0.14$. †FM was defined as birth weight >90th percentile, adjusted for sex and gestational age. Birth weight percentiles were calculated for the Israeli participants' offspring, using national birth weight standards (15). §Pre-eclampsia was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on ≥2 occasions a minimum of 6 h apart, and proteinuria of ≥1+ on a dipstick test or a protein level in the urine of ≥300 mg for a 24-h period (9).

Acknowledgments—No potential conflicts of interest relevant to this article were reported.

O.K.-L researched the data and wrote the manuscript. L.S.F researched the data, contributed to discussion, and reviewed the manuscript. L.O. researched the data and reviewed the manuscript. N.L., A.H., O.T., L.L.-G., N.M., and M.H. contributed to discussion and reviewed the manuscript. O.K.-L. is the guarantor of this work and, as such, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Parts of this work were presented in oral form at the 6th International Symposium on Diabetes in Pregnancy Scientific Meeting, Salzburg, Austria, 23–26 March 2012.

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