Baseline HbA1c to Identify High-Risk Gestational Diabetes: Utility in Early vs Standard Gestational Diabetes

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Context: The increasing prevalence of gestational diabetes mellitus (GDM) necessitates risk stratification directing limited antenatal resources to those at greatest risk. Recent evidence demonstrates that an early pregnancy glycated hemoglobin (HbA1c $\geq$5.9% (41 mmol/mol) predicts adverse pregnancy outcomes.

Objective: To determine the optimal HbA1c threshold for adverse pregnancy outcomes in GDM in a treated multiethnic cohort and whether this differs in women diagnosed $<$24 vs $\geq$24 weeks' gestation (early vs standard GDM).

Design and Setting: This was a retrospective cohort study undertaken at the Royal Prince Alfred Hospital Diabetes Antenatal Clinic, Australia, between 1991 and 2011.

Patients and Interventions: Pregnant women (N = 3098) underwent an HbA1c (single-laboratory) measurement at the time of GDM diagnosis. Maternal clinical and pregnancy outcome data were collected prospectively.

Main Outcome Measure: The association between baseline HbA1c and adverse pregnancy outcomes in early vs standard GDM.

Results: HbA1c was measured at a median of 17.6 $\pm$ 3.3 weeks' gestation in early GDM (n = 844) and 29.4 $\pm$ 2.6 weeks' gestation in standard GDM (n = 2254). In standard GDM, HbA1c $>$5.9% (41 mmol/mol) was associated with the greatest risk of large-for-gestational-age (odds ratio [95% confidence interval] = 2.7 [1.5–4.9]), macrosomia (3.5 [1.4–8.6]), cesarean section (3.6 [2.1–6.2]), and hypertensive disorders (2.6 [1.1–5.8]). In early GDM, similar HbA1c associations were seen; however, lower HbA1c correlated with the greatest risk of small-for-gestational-age (*P* trend = 0.004) and prevalence of neonatal hypoglycemia.

Conclusions: Baseline HbA1c $>$5.9% (41 mmol/mol) identifies an increased risk of large-for-gestational-age, macrosomia, cesarean section, and hypertensive disorders in standard GDM. Although similar associations are seen in early GDM, higher HbA1c levels do not adequately capture risk-limiting utility as a triage tool in this cohort. **(*J Clin Endocrinol Metab* 102: 150–156, 2017)**

Gestational diabetes mellitus (GDM) is one of the most common complications of pregnancy and is associated with substantial transgenerational maternal and neonatal morbidity (1–3). The prevalence of GDM is rising, due to both the increasing incidence of maternal risk factors such as obesity and advanced maternal age

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Abbreviations: BMI, body mass index; CI, confidence interval; GDM, gestational diabetes mellitus; HAPO, Hyperglycemia and Adverse Pregnancy Outcomes; HbA1c, glycated hemoglobin; LGA, large-for-gestational-age; NICU, neonatal intensive care unit; OGTT, oral glucose tolerance test; RPAH, Royal Prince Alfred Hospital; SGA, small-for-gestational-age.

(4–6) and the impact of the revised International Association for Diabetes in Pregnancy Study Group recommendations for the diagnosis and classification of GDM (7, 8). An increase in workload of 30% is predicted from the application of the new diagnostic criteria alone (9).

Given finite and often limited resources, this increased workload presents a challenge to the appropriate and effective delivery of antenatal health services. The identification of high vs lower risk GDM would enable health services to triage and dichotomize GDM patients based on their risk status (10). Pragmatic, easily applied risk stratification tools are therefore required to direct limited antenatal resources to those women at greatest risk. Glycated hemoglobin (HbA1c) measurement appeals as a potential triage tool: it requires a single nonfasting sample, is reproducible, and provides the best predictor of diabetes-related complications in the nonpregnancy setting (11–13). A recent prospective cohort study showed that an early pregnancy HbA1c level ≥5.9% (41 mmol/mol), measured at a median of 47 days' gestation, was a simple screening test to identify women with diabetes in pregnancy and predicted increased risk of adverse pregnancy outcomes, including major congenital anomaly, preeclampsia, shoulder dystocia, and perinatal death (14). It is unclear whether this HbA1c threshold has utility in predicting adverse outcomes in GDM, as distinct from diabetes in pregnancy, as women treated for GDM were explicitly excluded from analysis. It is also important to determine whether intervention for GDM attenuates the association between baseline HbA1c and pregnancy outcomes. Furthermore, it is unknown if such an HbA1c threshold exists and/or differs among women diagnosed and treated for GDM prior to 24 weeks' gestation—a cohort we have previously reported to be at particularly high risk for adverse pregnancy outcomes (15), given the physiological variability in blood glucose levels in early compared with later pregnancy (13, 16). Given the current recommendations for early testing for GDM among high-risk women, it has been argued that a clinical outcomes study assessing HbA1c levels in early pregnancy is "urgently required" (16).

The aims of the current study were therefore to examine the relationship of antenatal HbA1c at GDM diagnosis with adverse pregnancy outcomes and to determine if this HbA1c risk threshold differs in women diagnosed with early (<24 weeks' gestation) vs standard (≥24 weeks' gestation) GDM, in a large treated multiethnic cohort.

Materials and Methods

Women (N = 3098) attending the Royal Prince Alfred Hospital (RPAH) Antenatal Diabetes Clinic between 1991 and 2011 were studied. GDM was defined by the Australasian Diabetes in Pregnancy diagnostic criteria, with all women undergoing universal testing between 24 and 28 weeks' gestation with either the diagnostic 2-hour, 75-g oral glucose tolerance test (OGTT) or a screening 50-g glucose challenge test and, if positive, a subsequent OGTT (17, 18). A very small number (estimated to be <5%) of women at RPAH refuse GDM testing. At RPAH, women at high risk for GDM—defined by the presence of previous GDM, macrosomia or unexplained stillbirth, family history of type 2 diabetes, maternal age ≥35 years, obesity [body mass index (BMI) >30 kg/m^2], and non-white ethnicity—have been advised to undergo early testing with the OGTT generally soon after the first antenatal appointment, due to their greater risk of adverse pregnancy outcomes (15). These high-risk criteria are in alignment with current Australian guidelines (19). HbA1c analysis was performed in a single laboratory using a Diabetes Control and Complications Trial–aligned method (variant II cation-exchange BioRad instrument; Bio-Rad, Hercules, CA), following the initial Antenatal Diabetes Clinic assessment and generally within 2 to 3 weeks of GDM diagnosis.

Women with known preexisting diabetes or who fulfilled the World Health Organization diagnostic criteria for diabetes mellitus in pregnancy (13) (retrospectively applied) were excluded to ensure the study cohort was restricted to a true GDM population. Baseline maternal clinical and biochemical data taken at the time of GDM diagnosis was collected prospectively in a standardized manner (20). Ethics committee approval and informed consent were obtained.

As previously published, our treatment approach was standardized (20) and involved a multidisciplinary team, lifestyle intervention, and addition of insulin therapy if self-monitored blood glucose targets were not achieved with lifestyle modification alone.

Pregnancy outcomes of interest were macrosomia (defined as birth weight ≥4000 g); large-for-gestational-age (LGA) and small-for-gestational-age [SGA; defined as gender- and gestational age–specific birth weight >90th centile and <10th centile, respectively, for New South Wales, Australia, population (21), and (22) for secondary analysis, see later], neonatal intensive care unit (NICU) admission, respiratory distress syndrome, hypoglycemia (blood glucose level <2.5 mmol/L detected at any stage postpartum; blood glucose levels were routinely checked within 24 hours postpartum in all offspring of women with GDM), preterm delivery (<37 weeks' gestation), cesarean section, and hypertensive disorders in pregnancy (defined as preeclampsia or systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg in a previously normotensive pregnant woman who is ≥20 weeks of gestation and has no proteinuria or new signs of end-organ dysfunction).

Statistical methods

Data were analyzed using NCSS 2007. Continuous data were checked for normality and presented as mean or median. Data not normally distributed were transformed for analysis. Analysis of variance or Kruskal–Wallis tests were used to compare means or medians. Categorical data were presented as a percentage. χ^2 was used to compare groups. Data were grouped according to timing of GDM diagnosis <24 (early GDM) or ≥24 weeks' (standard GDM) gestation and then stratified by HbA1c according to the following clinically relevant categories: HbA1c ≤4.5% (≤26 mmol/mol), 4.6% to

4.9% (27 to 30 mmol/mol), 5.0% to 5.5% (31 to 37 mmol/mol), 5.6% to 5.9% (38 to 41 mmol/mol), and >5.9% (>41 mmol/mol). Specifically, the HbA1c threshold >5.9% (41 mmol/mol) was selected to facilitate comparison with Hughes *et al.* (14), and HbA1c of 5.5% (37 mmol/mol) reflects the uppermost normal HbA1c reference in the nonpregnant female population and in the first and second trimesters in pregnant women (23). Two HbA1c categories above and below this HbA1c of 5.5% (37 mmol/mol) reference level were set to demonstrate stepwise associations and trends in HbA1c and outcomes, ensuring an even spread of glycemia encompassing known range in pregnancy (23). The independent association between HbA1c categories and pregnancy outcomes was assessed in both unadjusted and adjusted models using odds ratios and the associated confidence intervals (CIs), with HbA1c ≤4.5% (26 mmol/mol) nominated as the reference group. Model adjustments for LGA and SGA were maternal age, ethnicity, prepregnancy BMI, and hypertensive disorders of pregnancy. An Armitage proportion trend test calculated any trend in outcomes according to HbA1c levels. The Benjamini–Hochberg procedure was used to control the false discovery rate. An additional sensitivity analysis was also undertaken using the Perinatal Institute's customized centile calculator accounting for maternal ethnicity, BMI, and parity in addition to gender and gestational age for an Australian population (22) to establish LGA and SGA. As the results using this centile calculator and conclusions arising are similar to the primary analysis, these are presented as supplemental only (Supplemental Table 1). Statistical significance was accepted at $P < 0.05$.

Results

HbA1c was measured at a median of 17.6 ± 3.3 weeks' gestation in early GDM (n = 844) and 29.4 ± 2.6 weeks' gestation in standard GDM (n = 2254). Mean baseline HbA1c was 5.3% (±0.6%; 34 mmol/mol) for women with early GDM and 5.3% (±0.5%; 34 mmol/mol) for standard GDM. Characteristics of women stratified by timing of GDM diagnosis are shown in Table 1. Women diagnosed with GDM early were older, had a higher BMI, had a higher prevalence of family history of diabetes, and were more likely to have required insulin treatment than those with standard GDM. These differences largely reflect the clinical selection criteria used for early screening for GDM at our institution.

HbA1c in standard GDM and pregnancy outcomes

Adverse pregnancy outcomes stratified by HbA1c group are shown in Table 2 and Supplemental Fig. 1.

In women with standard GDM, there was a clear positive association between increasing baseline HbA1c and LGA, macrosomia, cesarean section, and hypertensive disorders of pregnancy ($P < 0.0001$ for all Table 2; P trend ≤ 0.002 for all; Supplemental Fig. 1). A baseline HbA1c threshold >5.9% (41 mmol/mol) captured the greatest risk of these outcomes. Specifically, a baseline HbA1c >5.9% (41 mmol/mol) was associated with a 3.5-fold and 3.6-fold increased risk of macrosomia and cesarean section, respectively, and an almost threefold increased risk of LGA and hypertensive disorders of pregnancy, compared with the referent HbA1c category (Table 3). The risk of LGA associated with a baseline HbA1c >5.9% (41 mmol/mol) persisted even after adjustment for maternal age, ethnicity, and prepregnancy BMI (Supplemental Table 2). A baseline HbA1c of >5.6% to 5.9% (38 to 41 mmol/mol) was also associated with an approximate twofold increased risk of macrosomia and hypertensive disorders of pregnancy and was statistically significant for cesarean section (Table 3).

In standard GDM, we also found a significantly lower risk of neonatal hypoglycemia associated with a baseline HbA1c in the 5.0% to 5.5% (31 to 37 mmol/mol) and 5.6% to 5.9% (38 to 41 mmol/mol) ranges, but otherwise, a uniform risk was seen throughout the other HbA1c categories (Table 3). No significant difference in risk of neonatal hypoglycemia was evident in those with HbA1c >5.9% (41 mmol/mol) compared with the lowest referent HbA1c category. There were no significant differences between HbA1c categories and risk of NICU admission, preterm delivery, or SGA, even after adjustment for maternal age, ethnicity, and hypertensive disorders of pregnancy (Supplemental Table 2).

HbA1c in early GDM and pregnancy outcomes

In the early GDM cohort, the association between baseline HbA1c and adverse outcomes was less clear and nonlinear for some outcomes. As with standard GDM, increasing HbAlc levels at diagnosis positively correlated with risk of macrosomia, LGA, cesarean section, and hypertensive disorders of pregnancy ($P \leq 0.004$ for all Table 2 and Supplemental Fig. 1) HbA1c threshold >5.9% (41 mmol/mol) was associated with the greatest risk of these outcomes with an approximate three- to fivefold increase in risk above the referent HbA1c category ($P \leq 0.006$ for all; Table 4). However, after adjustment for maternal age, ethnicity, and prepregnancy BMI, the association between LGA and baseline HbA1c >5.9% (41 mmol/mol) did not remain statistically significant (Supplemental Table 3). Furthermore, women with the lowest HbA1c category had the highest risk of SGA (P trend = 0.004; Supplemental Fig. 1). This independent association for HbA1c and SGA remained even after adjustment for maternal age and hypertensive disorders of pregnancy (Supplemental Table 3). Furthermore, the HbA1c associated risk of neonatal hypoglycemia was nonlinear (P trend nonsignificant), with the highest risks seen at both ends of the HbA1c spectrum (Table 2). The highest prevalence of neonatal hypoglycemia (21.9%) was seen in those with the lowest baseline HbA1c.

Table 1. Baseline Maternal Characteristics and Insulin Requirements Stratified by Timing of GDM Diagnosis

Maternal Characteristics	Early GDM (n = 844)	Standard GDM (n = 2254)	*P* Value
Ethnicity, %			<0.0001
Anglo-Celtic	16.6	24.1	
Mediterranean	9.0	10.9	
Middle Eastern	5.2	5.2	
Asian	47.7	40.3	
Indian	12.4	10.5	
Australian Aboriginal	1.2	1.0	
Pacific Islander	3.2	2.4	
Other	4.6	5.5	
Age, y	35.1 ± 4.9	33.2 ± 5.0	<0.0001
Initial BMI, kg/m^2	25.5 ± 6.3	24.0 ± 5.1	<0.0001
Initial weight, kg	65.4 ± 18.4	66.6 ± 15.2	0.0001
Family history of diabetes,[a] %	57.0	47.4	<0.0001
Parity, %			<0.0001
Nulliparous	34.5	44.3	
Multiparous	65.5	55.8	
Gestation at GDM diagnosis, wk	17.6 ± 3.3	29.4 ± 2.6	
OGTT, min			
0	4.8 ± 1.0	4.7 ± 1.9	0.3
60	10.0 ± 8.7	9.8 ± 1.6	0.0002
120	8.7 ± 2.6	8.4 ± 2.0	0.002
Baseline HbA1c, %	5.3 ± 0.6	5.3 ± 0.5	0.0003
Insulin treatment, %	64.8	45.9	<0.0001
Gestation insulin commenced, wk	24.5 ± 6.0	32.9 ± 3.3	<0.0001
Maximum dose insulin, units	34 [30–36]	20 [18–26]	<0.0001

Data are mean ± standard deviation or median [interquartile range]. Statistical significance was accepted at $P < 0.05$.

[a]First degree relative with type 2 diabetes and/or sibling with GDM.

Discussion

In women with GDM diagnosed at the standard of 24 to 28 weeks' gestation, an HbA1c >5.9% (41 mmol/mol) taken at diagnosis despite subsequent treatment still predicts an increased risk of several adverse pregnancy outcomes including macrosomia, LGA, cesarean section, and hypertensive disorders of pregnancy. This threshold also captured comparable high rates of neonatal hypoglycemia to that seen in the lowest HbA1c category. Interestingly, an HbA1c threshold >5.9% (41 mmol/mol) did not significantly correlate with increased risk of neonatal hypoglycemia, preterm delivery, or NICU admission, suggesting that HbA1c is a more sensitive predictor for specific as opposed to all adverse pregnancy outcomes associated with GDM. Overall, however, our data support the pragmatic use of a single baseline HbA1c measurement taken at the time of diagnosis of standard GDM to inform triage decisions toward a low- or high-risk model of care.

Our findings in women with standard GDM concord with that of Hughes *et al.* (14), who identified a specific HbA1c threshold ≥5.9% (41 mmol/mol) in early pregnancy, which effectively identified women at increased risk of major congenital anomaly, preeclampsia, shoulder dystocia, perinatal death, preterm delivery, induction of labor, and LGA. Similarly, the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study group has also previously shown significant associations between higher levels of HbA1c and frequencies of HAPO outcome measures in their cohort, albeit poorer correlation overall in comparison with the diagnostic OGTT (24). Specifically, odds ratios for risk of cesarean section, preeclampsia, and preterm delivery were comparable between the HbA1c and OGTT (24).

In contrast, this HbA1c >5.9% (41 mmol/mol) threshold did not adequately capture all the risks associated with early GDM. Although increased risks of macrosomia, cesarean section, and hypertensive disorders of pregnancy were seen at HbA1c >5.9% (41 mmol/mol), this HbA1c threshold was not significantly associated with a risk of LGA after adjustment for maternal ethnicity and BMI. Furthermore, the greatest risks of neonatal hypoglycemia and SGA were seen in those with the lowest baseline HbA1c ≤4.5% (26 mmol/mol) at GDM diagnosis. Given these findings, the utility of a specific HbA1c threshold in early GDM to stratify women at greatest overall risk is likely to be limited. It is also notable that for most adverse outcomes, at any given baseline HbA1c the proportion of women affected are higher in early GDM.

These findings are consistent with our previous research showing that women with early GDM, despite

Table 2. Rates (%) of Adverse Pregnancy Outcomes According to HbA1c Categories for Standard GDM and Early GDM

	Standard GDM					
HbA1c (%)	≤4.5 (n = 116)	4.6–4.9 (n = 333)	5.0–5.5 (n = 1124)	5.6–5.9 (n = 468)	>5.9 (n = 213)	*P* Value
Macrosomia	5.2	6.8	6.7	10.8	16	<0.0001
LGA	15.5	21.3	20.7	22.8	33	<0.0001
Cesarean section	18.3	25.2	25.4	34.8	44.6	<0.0001
Hypertensive disorders of pregnancy	7	5.9	9.8	13.6	16.1	<0.0001
Neonatal hypoglycemia	14.7	11.3	8.6	6.8	11	0.03
NICU	31	29.1	27.6	28.8	29.6	0.2
Preterm delivery	4.3	5.2	4.9	6.2	8.5	0.3
SGA	5.5	8.2	7.9	6.7	5.7	0.7
	Early GDM					
	≤4.5 (n = 67)	4.6–4.9 (n = 174)	5.0–5.5 (n = 396)	5.6–5.9 (n = 141)	>5.9 (n = 66)	*P* Value
Macrosomia	7.7	4.2	7.2	10.4	22.4	0.003
LGA	15.4	14.7	19	31.9	42.4	<0.0001
Cesarean section	37.9	31.5	37.4	39	62.7	0.001
Hypertensive disorders of pregnancy	7.6	10.9	12.7	14.5	29.6	0.004
Neonatal hypoglycemia	21.9	7.7	9.1	12.3	14	0.02
NICU	38.8	29.9	27.8	39.7	33.3	0.06
Preterm delivery	7.6	10.1	9.3	13.1	13.6	0.6
SGA	15.4	11	6.8	4.4	6.8	0.04

LGA and SGA: gender and gestational age specific birth weight >90th centile and <10th centile for Australia population (21). Statistical significance was accepted at $P < 0.05$.

early diagnosis and intensive intervention, have poorer pregnancy outcomes (15) and furthermore support the heterogeneity in outcomes within a GDM cohort. Taken together, these data would suggest that early GDM be considered a high-risk cohort, irrespective of baseline HbA1c and triaged accordingly.

The association of neonatal hypoglycemia and SGA with the lowest baseline HbA1c category in women with early GDM is difficult to account for. Factors such as early intervention, excessive carbohydrate restriction, and poor nutrition in the context of only minimally elevated glucose levels in early pregnancy could all potentially contribute. This would be consistent with the known association between maternal hypoglycemia in pregnancy, fetal growth restriction, and increased risk of perinatal mortality (25); although, this association has not previously been examined in early pregnancy. Unfortunately, we were unable to assess (potential over-) compliance with glycemic intervention in this study. Alternatively, it may be that factors other than the degree of maternal dysglycemia at baseline are implicated in the development of SGA and neonatal hypoglycemia. It is also notable that in the HAPO cohort, the risk of neonatal hypoglycemia was lowest in those with the highest HbA1c category [HbA1c ≥5.8% (40 mmol/mol)] (24). Neonatal hypoglycemia was not assessed in the Hughes *et al.* (2014) cohort; however, the rate of SGA was similarly higher among women with HbA1c <5.9% (41 mmol/mol) [15.1% compared with 11.1% for HbA1c ≥5.9% (41 mmol/mol); relative risk (95% CI) = 0.71 (0.46–1.10)] (14). These observations would tend to support our assertion that a baseline HbA1c has limited utility as a triage tool to dichotomize risk in early onset GDM.

The strengths of our study include the large numbers of subjects and a multiethnic cohort likely to be translatable to different populations. The prospectively collected standardized data, the well-validated and standardized treatment intervention, and the single laboratory measuring HbA1c provide for a robust investigational data set.

A key limitation of our study was that we were unable to account for the presence of hemoglobinopathy or iron deficiency, which would have impacted the accuracy of HbA1c assessment. Nonetheless, investigation and active management of iron deficiency is a routine component of antenatal care at our institution. We also acknowledge that the early GDM cohort was preselected, and thus, it is possible the data may not be representative of all with early onset GDM. Nevertheless, our high-risk selection criteria are aligned with current guidelines (19). It is also possible that there may be subsets within the early GDM cohort that have stronger associations between HbA1c and adverse pregnancy outcomes. In the absence of published data in this area, we therefore note this as a study limitation. Finally, we were unable to compare

Table 3. Standard GDM: Odds Ratio [95% CI] for Association Between HbA1c Categories and Pregnancy Outcomes

HbA1c (%)	≤4.5	4.6–4.9	5.0–5.5	5.6–5.9	>5.9	*P* Value
Macrosomia	1	1.3 [0.5–3.4]	1.3 [0.6–3.2]	2.2 [0.9–5.3]	3.5 [1.4–8.6][a]	0.006[a]
LGA	1	1.5 [0.8–2.7]	1.4 [0.8–2.4]	1.6 [0.9–2.8]	2.7 [1.5–4.9][a]	0.001[a]
Cesarean section	1	1.5 [0.9–2.6]	1.5 [0.9–2.5]	2.4 [1.4–4.0][b]	3.6 [2.1–6.2][a]	0.0008[b]; <0.0001[a]
Hypertensive disorders of pregnancy	1	0.8 [0.4–2.0]	1.5 [0.7–3.1]	2.1 [1.0–4.5]	2.6 [1.1–5.8][a]	0.02[a]
Neonatal Hypoglycemia	1	0.7 [0.4–1.4]	0.5 [0.3–0.9][b]	0.4 [0.2–0.8][a]	0.7 [0.4–1.4]	0.00[a]; 0.04[b]
NICU	1	0.9 [0.6–1.4]	0.8 [0.6–1.3]	0.9 [0.6–1.4]	0.9 [0.6–1.5]	NS
SGA	1	1.5 [0.6–3.8]	1.5 [0.6–3.5]	1.2 [0.5–3.1]	1.1 [0.4–2.9]	NS
Preterm delivery	1	1.2 [0.4–3.3]	1.1 [0.4–2.9]	1.5 [0.6–3.9]	2.0 [0.7–5.6]	NS

Unadjusted model. *P* values using category HbA1c ≤4.5% as reference group. LGA and SGA: gender and gestational age specific birth weight >90th centile and <10th centile for Australia population (21).

Abbreviation: NS, not significant.

Statistical significance was accepted at $P < 0.05$. [a] or [b] correspond to where odds ratio *P* value for HbA1c category statistically significant compared with referent HbA1c category. All remained significant after using the Benjamini–Hochberg procedure (corrected significance level = 0.04).

these associations between HbA1c and outcomes with a control (normoglycemic) cohort; however, the clinical rationale for this study was to determine the utility of baseline HbA1c in identifying higher risk pregnancies in women with GDM, as opposed to examining the diagnostic utility of HbA1c.

Our data suggest that a single HbA1c taken at diagnosis may be a useful pragmatic guide for identifying women at risk for specific adverse outcomes including macrosomia, LGA, cesarean section, and hypertensive disorders in pregnancy in standard GDM. Thus, a single HbA1c taken at the time of universal screening for GDM at 24 to 28 weeks' gestation can be used in clinical management approaches that seek to dichotomize GDM into high- and low-risk models of care at diagnosis. Pragmatically, a threshold HbA1c >5.9% (41 mmol/mol)

Table 4. Early GDM: Odds Ratio [95% CI] for Association Between HbA1c Categories and Pregnancy Outcomes

HbA1c (%)	≤4.5	4.6–4.9	5.0–5.5	5.6–5.9	>5.9	*P* Value
Macrosomia	1	0.52 [0.2–1.7]	0.92 [0.3–2.5]	1.40 [0.5–4.1]	3.6 [1.8–7.2][a]	0.0002[a]
LGA	1	0.9 [0.4–2.1]	1.3 [0.6–2.7]	2.6 [1.2–5.5][b]	3.2 [2.0–5.2][a]	0.02[b]; 0.000[a]
Cesarean section	1	0.8 [0.4–1.4]	1.0 [0.6–1.7]	1.0 [0.6–1.9]	2.8 [1.3–5.7][a]	0.006[a]
Hypertensive disorders of pregnancy	1	1.5 [0.5–4.2]	1.8 [0.7–4.7]	2.1 [0.7–5.8]	5.1 [1.7–15.2][a]	0.003[a]
NICU	1	0.7 [0.4–1.2]	0.6 [0.4–1.04]	1.0 [0.6–1.9]	0.8 [0.4–1.6]	NS
Preterm delivery	1	1.4 [0.5–3.9]	1.2 [0.5–3.3]	1.8 [0.7–5.2]	1.9 [0.6–6.2]	NS
Neonatal hypoglycemia	1	0.3 [0.1–0.7][b]	0.4 [0.2–0.7][a]	0.5 [0.2–1.1]	0.7 [0.4–1.2]	0.003[b]; 0.004[a]
SGA	1	0.7 [0.3–1.6]	0.4 [0.2–0.9][b]	0.3 [0.9–0.7][a]	0.4 [0.1–1.4]	0.02[b]; 0.01[a]

Unadjusted model. *P* values using category HbA1c ≤4.5% as reference group. LGA and SGA: gender and gestational age specific birth weight >90th centile and <10th centile for Australia population (21).

Abbreviation: NS, not significant.

Statistical significance was accepted at $P < 0.05$. [a] or [b] correspond to where odds ratio *P* value for HbA1c category statistically significant compared with referent HbA1c category. All remained significant after using the Benjamini–Hochberg procedure (corrected significance level = 0.04).

identifies women with a greater need for surveillance given their increased risk of certain adverse outcomes and, arguably, where management resources are limited, those who should be prioritized. Importantly for this cohort, the association with adverse pregnancy outcomes is not fully attenuated by treatment of GDM. Further studies comparing this pragmatic approach against more sophisticated risk engine approaches are warranted.

Our study also adds a perspective to the utility of a baseline HbA1c in the context of early GDM. In contrast to standard GDM, for early GDM, higher HbA1c levels do not adequately capture the increased risk of certain adverse pregnancy outcomes also seen at lower HbA1c levels, limiting its utility as a triage tool in this cohort. These data are consistent with a growing body of evidence suggesting that early GDM may not in itself be appropriate for low-risk models of care.

Acknowledgments

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