Can Common Clinical Parameters Be Used to Identify Patients Who Will Need Insulin Treatment in Gestational Diabetes Mellitus?

TANIA PERTOT, BSC[1]
LYNDA MOLYNEAUX, RN[2]
KRIS TAN, MSC[3]
GLYNIS P. ROSS, MD[2,3]
DENNIS K. YUE, MD, PHD[1,2,3]
JENCIA WONG, MD, PHD[1,2,3]

OBJECTIVE—To identify patients with gestational diabetes mellitus (GDM) who will need antenatal insulin treatment (AIT) by using a risk-prediction tool based on maternal clinical and biochemical characteristics at diagnosis.

RESEARCH DESIGN AND METHODS—Data from 3,009 women attending the Royal Prince Alfred Hospital GDM Clinic, Australia, between 1995 and 2010 were studied. A risk engine was developed from significant factors identified for AIT using a logistic regression model.

RESULTS—A total of 51% of GDM patients required AIT. Ethnicity, gestation at diagnosis, HbA_{1c}, fasting and 60-min glucose at oral glucose tolerance test, BMI, and diabetes family history were significant independent determinants of AIT. Notably, only 9% of the attributable risk for AIT can be explained by the clinical factors studied. A modeled risk-scoring system was therefore a poor predictor of AIT.

CONCLUSIONS—Baseline maternal characteristics including HbA_{1c} alone cannot predict the need for AIT in GDM. Lifestyle, compliance, or as yet unmeasured influences play a greater role in determining AIT.

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The treatment of gestational diabetes mellitus (GDM) is important to lower the risk of perinatal complications (1) and, to achieve this, a proportion of women require intensive antenatal insulin treatment (AIT). The rising incidence of GDM (2), coupled with the recent revision of GDM diagnostic criteria (3), is predicted to conservatively increase the incidence of GDM by ~30%, with significant implications for the numbers requiring AIT and clinical workload (4). With this looming spectre, it has been suggested that improved efficiency of health care delivery in GDM relies on improved risk stratification that would allow for triage to low- or higher-risk clinics (4). Consequently, there is interest in the ability to predict GDM in early pregnancy (5), and because AIT is the most resource-intensive management component in GDM, a risk-prediction tool that identifies patients likely to need AIT would have theoretical utility. Thus, the aim of this large cohort study was to determine if, using commonly available maternal clinical and biochemical characteristics at the time of GDM diagnosis, it was possible to develop an effective and easily implemented AIT prediction tool.

RESEARCH DESIGN AND METHODS

—Women (n = 3,009) attending the Royal Prince Alfred Hospital antenatal diabetes clinic between 1995 and 2010 were studied. GDM was defined by the Australasian Diabetes in Pregnancy Society criteria (6). Baseline maternal clinical and biochemical data taken at the time of GDM diagnosis were collected prospectively in a standardized manner (7). Ethics committee approval and informed consent was obtained. AIT was commenced on the basis of the pattern of home blood glucose monitoring and response to dietary treatment. Blood glucose thresholds above which insulin was commenced were 5 mmol/L at fasting and 7.2 mmol/L at 1 h and are standard practice at Royal Prince Alfred Hospital in keeping with previous studies (8,9). Univariate analysis was performed on maternal historical and antenatal risk factors to determine the associations with AIT. Significant factors were included in a stepwise logistic regression model (risk engine) to calculate the probability of requiring AIT. Receiver operating curve analysis was also used to evaluate the predictive ability of the risk engine.

RESULTS—A total of 51% (n = 1,535) of women required AIT (see Supplementary Tables for demographic details). Univariate analysis identified significant associations between AIT and gestation at diagnosis, ethnicity, GDM diagnosed at ≤25/40 gestational weeks, prepregnancy weight, BMI, diabetes family history, oral glucose tolerance test (OGTT) area under the curve glucose, fasting glucose, OGTT 60-min glucose, HbA_{1c} (all $P < 0.0001$), and age ($P = 0.02$). In the logistic regression model, HbA_{1c} (odds ratio [OR] 2.2), family history of diabetes (OR 1.4), fasting glucose (OR 1.3), OGTT 60-min glucose (OR 1.06), and BMI (OR 1.04) were identified to be statistically significant contributors to the requirement for AIT. Diagnosis of GDM after 25 weeks was identified as a significant protective factor for the need for AIT (OR 0.5). Asian (OR 0.7) and Arabic (OR 0.6) ethnicity were protective compared with Europeans. Using a cutoff value of 50% probability of AIT, the

From the [1]Sydney Medical School, University of Sydney, Sydney, Australia; the [2]Diabetes Centre, Royal Prince Alfred Hospital, Sydney, Australia; and the [3]Department of Endocrinology, Royal Prince Alfred Hospital, Sydney, Australia.
Corresponding author: Jencia Wong, jencia.wong@email.cs.nsw.gov.au.
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receiver operating curve only has a sensitivity of 66% and 1 − specificity of 37%. Notably, only 9% ($R^2 = 0.09$) of the attributable risk for AIT can be explained by the clinical factors studied. For example, as shown in Table 1, despite ~50% of the cohort requiring AIT, only 1.3% had a predicted probability of insulin usage of 90.1–100%, and many groups with a low calculated risk had a relatively high rate (20–30%) of insulin use. We also performed similar receiver operating curve analysis using HbA_{1c} alone. An HbA_{1c} threshold of ≥7% provides 99% specificity for requiring AIT but would only identify 17 such patients. At the other end of the spectrum, using an HbA_{1c} cutoff of ≤4%, 84 patients would still require AIT and only 174 patients could be correctly triaged to a "low-risk clinic." Thus, the numbers of patients who could be correctly identified by this approach are so low that there is little practical impact on workflow.

CONCLUSIONS—We identified a number of significant independent risk factors for AIT, particularly measures of glycemia, time of diagnosis, and family history of diabetes. These factors are intuitive, given that they represent severity of and propensity for hyperglycemia. The surprising finding was the lack of predictive power encompassed by these risk factors, with only 9% of the risk for AIT being attributable. The few previous studies have been limited by the small number of subjects and confined to the predictive value of glycemia alone (10,11). Nevertheless, although the performance of this risk tool based on many commonly available clinical and biochemical factors is disappointing, the results are informative on a number of fronts.

First, it is clear from our data that a risk-stratification approach based on baseline measures of glycemia alone would not have predictive utility. The inference is that individuals with measurements in the lower glucose ranges at diagnosis do not necessarily track in the lower ranges during the rest of the pregnancy and, conversely, some individuals in the higher glucose ranges at diagnosis are able to modify their levels of glycemia to avoid insulin treatment. This putative lack of glycemic stability over time may embody some of the risk in the lower glucose ranges seen in the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study (12). Our data suggest that additional factors have a more significant impact on the need for insulin, over and above irreversible factors such as family history, prior GDM, or baseline glycemia at diagnosis. One such possibility is that dietary compliance has the greatest impact on the need for insulin; however, this was not assessed. Also, unmeasured fetal or placental factors that influence insulin resistance may have a greater impact on AIT. The fact that a prior history of GDM was not an independent significant factor for insulin use supports both these possibilities.

The strengths of our study include the large cohort with prospectively collected standardized data in a multiethnic Australian population and the use of commonly available clinical and biochemical measures. Our data suggest that baseline maternal characteristics including glycemia alone cannot predict AIT and suggest the primacy of lifestyle or as yet unmeasured influences in determining this higher-risk cohort.

Table 1—*Probability of antenatal insulin treatment as generated by risk model compared with actual insulin use*

	Low risk					Medium risk		High risk	Total
Probability (%) of insulin treatment predicted by risk model	0–10	10.1–20	20.1–30	30.1–40	40.1–50	50.1–60	60.1–70	70.1–80	80.1–90	90.1–100	
Percentage of whole cohort with this calculated risk	0.1	1.9	9.7	18.7	22.7	18.3	14.5	8.0	4.8	1.3	100
Percentage of patients actually requiring insulin in each risk band	33.3	20.8	27.6	35.7	46.0	55.3	65.8	76.0	83.6	97.3	
Percentage of patients requiring insulin	0.1	0.7	5.2	13.0	20.4	19.8	18.6	11.9	7.9	2.4	100

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