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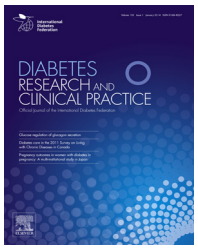

Validation of early risk-prediction models for gestational diabetes based on clinical characteristics

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ABSTRACT

Aims: Gestational diabetes (GDM) is generally diagnosed late in pregnancy, precluding early preventive interventions. This study aims to validate, in a large Caucasian population of pregnant women, models based on clinical characteristics proposed in the literature to identify, early in pregnancy, those at high risk of developing GDM in order to facilitate follow up and prevention.

Methods: This is a cohort study including 7929 pregnant women recruited prospectively at their first prenatal visit. Clinical information was obtained by a self-administered questionnaire and extraction of data from the medical records. The performance of four proposed clinical risk-prediction models was evaluated for identifying women who developed GDM and those who required insulin therapy.

Results: The four models yielded areas under the receiver operating characteristic curve (AUC) between 0.668 and 0.756 for the identification of women who developed GDM, a performance similar to those obtained in the original studies. The best performing model, based on ethnicity, body-mass index, family history of diabetes and past history of GDM, resulted in sensitivity, specificity and AUC of 73% (66–79), 81% (80–82) and 0.824 (0.793–0.855), respectively, for the identification of GDM cases requiring insulin therapy.

Conclusions: External validation of four risk-prediction models based exclusively on clinical characteristics yielded a performance similar to those observed in the original studies. In our cohort, the strategy seems particularly promising for the early prediction of GDM requiring insulin therapy. Addition of recently proposed biochemical markers to such models has the potential to reach a performance justifying clinical utilization.

1. Introduction

Gestational diabetes mellitus (GDM) is traditionally defined as the onset or first recognition of glucose tolerance disorder during pregnancy [1,2]. Prevalence of GDM in pregnant women varies widely from <1% to 28% in different populations and is highly dependent on the screening and diagnosis strategies used [3–5]. It is estimated to be around 4% in Canada [6] and between 2% and 8% in Europe [5]. The rising of both maternal age and rate of overweight/obesity lead to an escalating number of GDM cases [7].

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Abbreviations: GCT, glucose challenge test; GDM, gestational diabetes mellitus; IADPSG, International Association of Diabetes and Pregnancy Study Groups; IGT, impaired glucose tolerance; LR−, negative likelihood ratios; LR+, positive likelihood ratios; NPV, negative predictive value; PPV, positive predictive value; Se, sensitivity; Sp, specificity; WG, weeks of gestation.

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GDM is associated with increased rates of obstetric and neonatal complications such as preeclampsia, cesarean delivery, neonatal hypoglycemia and macrosomia [8,9]. It is well recognized that lifestyle changes and treatment with insulin or hypoglycemic agents can reduce the risks of these adverse outcomes [10,11]. Accumulating evidence also links GDM with later emergence of obesity, type-2 diabetes and metabolic syndrome in the woman and her offspring [12,13], all known risk factors for cardiovascular disease.

In Canada, screening for GDM is currently a universal two-step process. Women are screened at 24–28 weeks of gestation (WG) with an oral 50 g glucose challenge test (GCT) and those with positive results are then submitted to a 2 h 75 g oral glucose tolerance test (OGTT) for diagnosis [1,14]. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) recently recommended a new approach: screening high-risk women for overt diabetes at the first prenatal visit and performing a 75 g OGTT at 24–28 WG in all pregnant women [4,15]. These recommendations are being strongly debated [16–18], but GDM is nevertheless diagnosed late in pregnancy in most existing screening programs.

Numerous GDM risk factors have been recognized and are included in clinical practice recommendations [14,19–21]. The most important ones are maternal age, ethnicity, body mass index (BMI), family history of diabetes, past history of GDM, previous delivery of a macrosomic infant and multiple pregnancy [3].

Several authors have proposed clinical risk-prediction tools based on these risk factors available early in pregnancy to identify women at high risk of developing GDM [22–25], but not specifically for those requiring insulin therapy. This cohort study aims to validate, in a large Caucasian population, the performance of these models for identifying women who developed GDM and those who required insulin therapy in order to improve risk stratification and facilitate follow up and prevention.

2. Subjects

This is a cohort study including 7929 pregnant women recruited prospectively at their first prenatal visit (before 20 WG) between March 2005 and April 2010 in the Quebec City metropolitan area. Women were eligible if they were at least 18 years old and without renal and hepatic disease.

Exclusion criteria for the present study were pregestational diabetes ($n = 65$), multiple pregnancy ($n = 107$), uncertain diagnosis (absence of screening and/or diagnostic tests and gestational age at delivery unknown or before 32 WG, $n = 395$) and delivery outside of our centers ($n = 91$). Data from 63 patients were removed from the databank at their request.

3. Materials and methods

After giving written consent, the 7929 participants followed a well-defined protocol authorized by the Institutional Ethics Review Board. Between 24 and 28 WG, they completed a self-administered questionnaire allowing the collection of socio-demographic and biomedical information on various health risk factors. We have used validated questions on health [26,27] and dietary habits [28,29]. Anthropometric measurements have been determined as described earlier [27,29]. After delivery, the medical records were reviewed to complete clinical information, including the use of insulin therapy during pregnancy. According to practice guidelines [1], insulin therapy was initiated if, within 2 weeks, nutrition therapy alone did not allow to attain the following glycemic targets: fasting glucose <5.3 mmol/L, 1-h post-prandial glucose <7.8 mmol/L and 2-h post-prandial glucose < 6.7 mmol/L.

GDM diagnosis was established according to the recommendations provided by the Canadian Diabetes Association in 2008 [1] (50 g GCT in all women followed by 75 g OGTT if GCT between 7.8 and 10.2 mmol/L). Among the 381 women with GDM who were included, 87 were diagnosed based on the result of the GCT (≥10.3 mmol/L) alone and 172 were diagnosed after the OGTT (≥2 values exceeding the thresholds of 5.3, 10.6 and 8.9 mmol/L at 0, 1 and 2 h, respectively). We also used the information retrieved in the medical records to establish another GDM subgroup of 122 women who received insulin during pregnancy without undergoing an OGTT. This group consisted of patients for whom (1) the screening and diagnostic tests were either not performed, results were unavailable or borderline, and (2) frankly abnormal results on glucose monitoring led to the decision to start insulin therapy during pregnancy. This allowed us to identify all women with severe GDM and mitigate the false negative rate of the GCT. Finally, 151 women were diagnosed with impaired glucose tolerance (IGT) after the OGTT (1 value exceeding the thresholds).

Table 1 summarizes the methodology and risk-scoring systems used in the four predictive models that were evaluated [22–25]. Risk factors included in the models were maternal age, BMI, ethnicity, family history of GDM, past history of GDM, macrosomic infant and adverse obstetric outcomes. The models were developed in populations from Canada, Turkey, Netherlands and Australia. Risk factors were selected after multivariate logistic regression and different strategies were used for the weighting of each factor. Naylor et al. used the rounded adjusted odd ratios [22]; Caliskan et al. assigned a score of one to all risk factors that remained significant in logistic regression [23]; van Leeuwen et al. used the equation of the logistic regression model modified by a shrinkage factor to calculate the probability of GDM [24]; Teede et al. used the rounded log of the adjusted odd ratios [25].

The performance of the four models was evaluated for identifying women who developed GDM. We also evaluated the capacity of the models to identify GDM cases who required insulin therapy, dietary intervention only and participants who developed IGT.

4. Statistical analyses

Characteristics of the participants who developed GDM ($n = 381$) were compared to the rest of the study cohort ($n = 6827$) using Student t test for continuous variables and Chi-square or Fisher exact test for categorical variables. Differences were considered significant at $P < 0.05$ (two-sided). The risk score or probability for each participant was