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Original Article

Construction and validation of risk prediction model for gestational diabetes based on a nomogram

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Abstract: Objective: To construct a model to predict the risk of gestational diabetes mellitus (GDM) based on a nomogram and verify it. Methods: Data from 182 patients with GDM treated in Xi'an International Medical Center Hospital from January 2018 to May 2021 were retrospectively analyzed. A total of 491 normal parturients who underwent physical examination in Xi'an International Medical Center Hospital during the same period were selected as controls. With a ratio of 7:3, patients with GDM were divided into a training group (n=128) and a verification (n=54) group, and 491 normal parturients were divided into a training control group (n=344) and a verification control group (n=147). Clinical data were collected, and risk factors for GDM were analyzed by logistic regression. R language was used to construct a prognostic prediction nomogram model for GDM, and a receiver operating characteristic curve was employed to evaluate the accuracy of this nomogram model in predicting the prognosis of GDM. Results: Univariate analysis revealed that age, body mass index (BMI), family history of diabetes, hemoglobin, triglycerides, serum ferritin, and fasting blood glucose in the first trimester were different between the training group and the training control group (P<0.05). Multivariate analysis revealed that age, BMI, hemoglobin, triglycerides, serum ferritin, and fasting blood glucose in the first trimester were independent risk factors for GDM (P<0.05). Based on a logistic regression equation, the risk formula was -5.971 + 1.054 * age + 1.133 * BMI + 1.763 * hemoglobin + 1.260 * triglycerides + 3.041 * serum ferritin + 1.756 * fasting blood glucose in the first trimester. The area under the curve for predicting the risk of GDM in the training group was 0.920, and that of the validation group was 0.753. Conclusion: Age, BMI, hemoglobin, serum ferritin, and fasting blood glucose in the first trimester are risk factors for GDM.

Keywords: Nomogram, gestational diabetes, risk prediction model, validation

Introduction

With the implementation of the "three-child policy", the number of patients with gestational diabetes mellitus (GDM) has been increasing, and the health status of women in the gestational age is becoming more concerning [1]. Data statistics show that GDM is a common complication during pregnancy, with an incidence of about 19% in China [2]. GDM is caused by impaired glucose tolerance during pregnancy and the symptoms should disappear afterwards, but studies have shown [3] that GDM can lead to major short-term and long-term health risks for both pregnant women and fetuses. To be specific, GDM may lead to adverse metabolic diseases in children, including obesity, lipid metabolism and fatty liver [4]. If the insulin level of pregnant women is affected by placental hormones, inflammatory factors, adipokines, endoplasmic reticulum stress, autoimmunity, genetics and other factors, the growth and development of the unborn child might be impacted [5]. According to a report [6], one in six newborns from mothers with high blood sugar levels during pregnancy would be at risk for adverse fetal outcome. Therefore, it is important to explore the risk factors for GDM

and to take preventive interventions in pregnant women.

Extensive studies have been conducted on the risk factors for GDM, and it has been identified that maternal age, ethnicity, previous history of gestational diabetes and family history of type 2 diabetes, behavioral lifestyle, biochemical values, and environmental endocrine disruptors are possible risk factors [7]. Currently, disease risk prediction models are well-established. Logistic regression analysis can comprehensively analyze multiple independent variables to screen for risk factors for outcome events and predict their probability [8]. Based on the mature risk prediction statistical model, the establishment of a model to predict GDM can provide an important reference for targeted prevention and control measures [9]. Predictive models for early identification of pregnant women at high risk for GDM have been developed. Zhang et al. [10] constructed a model to predict gestational diabetes risk based on maternal status combined with ultrasound and serological results using logistic regression models. However, in pregnant women, clinical biochemical tests and imaging examinations have rarely been implemented to reduce or avoid the impact on fetal and maternal health. Clinical biochemical indicators or imaging data in the above models are not usually available from ordinary pregnant women, which has restricted the applicability of the model [11].

Therefore, in this study, we included clinical indicators and constructed a model through nomograms to identify a high-risk GDM group, which should facilitate early prevention and timely control of GDM.

Materials and methods

Data from 182 patients with GDM who received treatment in Xi'an International Medical Center Hospital from January 2018 to May 2021 were analyzed retrospectively. Data from 491 normal parturients who underwent physical examination during the same period were collected as a control group. According to a ratio of 7:3, 182 patients were divided into a training group (n=128) and a verification group (n=54), and 491 normal parturients were divided into a training control group (n=344) and a verification control group (n=147). This study was approved by the medical ethics committee of Xi'an International Medical Center Hospital (Ethical batch No.: 20190846).

Inclusion and exclusion criteria

Inclusion criteria of patients: Those who were diagnosed with gestational diabetes [12]; those who underwent all examinations and delivery in Xi'an International Medical Center Hospital; those who were age 20 to 45 years; those who had spontaneous conception of singleton pregnancy; those without major disease history; those with complete clinical data.

Exclusion criteria: Those with diabetes-related diseases before pregnancy; those with AIDS, hepatitis B or other infectious diseases; those with mental retardation, unclear language expression and communication disorders; those with cognitive impairment, affective disorders or other mental illness; those with heart, liver, kidney or other organ diseases; those with tumors; those with a history of drinking or smoking; those with other pregnancy complications.

Clinical data collection

The data were collected from maternal outpatient examination records and electronic medical record records, including age, occupation, education level, income, marital status, body mass index (BMI), family history of diabetes, family history of hypertension, parity, menstrual cycle, red blood cell count, hemoglobin, urea, creatinine, uric acid, cystatin C, triglycerides, serum ferritin and fasting blood glucose in the first trimester.

Outcome measures

Main outcome measures: Risk factors for GDM were analyzed by logistics regression. A model to predict the risk of gestational diabetes was constructed based on a nomogram. A receiver operating characteristic (ROC) curve was used to evaluate the model.

Secondary outcome measures: Differences in the clinical data between the groups.

Statistical analysis

R language 4.1.1 software [13] (R Foundation for Statistical Computing, Vienna, Austria) was

Table 1. Univariate analysis

Variable	Training Group (n=128)	Training Control Group (n=344)	χ^2 value	*P* value
Age				
≥30 years	78	124	23.609	<0.001
<30 years	50	220		
Occupation				
Fixed working	75	178	1.759	0.184
No fixed working	53	166		
Educational Level				
≥ High School	89	258	1.433	0.231
< High School	39	86		
Income				
≥3000 RMB/month	96	271	0.770	0.380
<3000 RMB/month	32	73		
Marital status				
Married	113	320	2.767	0.096
Remarriage	15	24		
BMI				
≥25 kg/m^2	23	30	8.004	0.005
<25 kg/m^2	105	314		
Family history of diabetes				
Yes	32	17	40.342	<0.001
No	96	327		
Family history of hypertension				
Yes	38	82	1.684	0.194
No	90	262		
Parity				
Primiparous	64	206	3.722	0.054
Multipara	64	138		
Menstrual cycle of women				
≥35 days	13	20	2.705	0.100
<35 days	115	324		

Note: Body Mass Index (BMI).

used for data cleaning, data analysis, and establishment of the model. Logistic regression was to analyze the risk factors for GDM. The model was verified by ROC curve. Data were visualized using Graph Pad Prism 8.0. A difference was considered significant when P<0.05.

Results

Analysis of clinical data

By comparing the clinical data of patients between the training group and the training control group, we found no significant difference in occupation, education level, income, marital status, family history of hypertension, parity, or menstrual cycle (P>0.05, **Table 1**). However, age, BMI, and family history of diabetes were statistically different between the two groups (P<0.05, **Table 1**).

Comparison of clinical values

By comparing the clinical laboratory values between patients in the training group and the training control group, we found no statistical difference in red blood cell count, urea, creatinine, uric acid, or cystatin C (P>0.05, **Table 2**). However, hemoglobin, triglyceride, serum ferritin, and fasting blood glucose in the first trimester were significantly different between the two groups (P<0.05, **Table 2**).

Table 2. Comparison of laboratory values of GDM patients

Variable	Training Group (n=128)	Training Control Group (n=344)	χ^2	*P*
Red blood cell count (10^9/L)	4.07±0.32	4.06±0.33	0.403	0.687
Hemoglobin (g/L)	124.06±9.36	117.14±9.97	6.813	<0.001
Urea (mmol/L)	2.92±0.60	2.93±0.58	0.212	0.832
Creatinine (μmol/L)	42.50±5.20	43.21±5.28	1.308	0.191
Uric acid (μmol/L)	205.79±40.60	202.79±3.95	0.722	0.470
Cystatin C (mg/L)	0.46±0.03	0.45±0.05	0.833	0.405
Triglycerides (mmol/L)	19.8±0.43	1.75±0.43	4.935	<0.001
Serum ferritin (ng/mL)	73.90±16.77	49.88±12.59	16.751	<0.001
Fasting blood glucose in the first trimester (mmol/L)	5.12±0.59	4.73±0.53	6.813	<0.001

Note: Body Mass Index (BMI).

Table 3. Value assignment

Factor	Assignment value
Age	≥30 years =1, <30 years =0
BMI	≥25 kg/m^2 =1, <25 kg/m^2 =0
Family history of diabetes	Present =1, Absent =0
Hemoglobin (g/L)	≥119.69=1, <119.69=0
Triglycerides (mmol/L)	≥1.71=1, <1.71=0
Serum ferritin (ng/mL)	≥60.00=1, <60.00=0
Fasting blood glucose in the first trimester (mmol/L)	≥5.01=1, <5.01=0
Disease condition	Training Group =1, Training Control Group =0

Note: Body Mass Index (BMI).

Table 4. Multivariate analysis

Factor	β	Standard Error	Chi-square value	*P* value	OR value	95% CI	
						Lower limit	Upper limit
Age	1.054	0.305	11.947	0.001	2.870	1.578	5.218
BMI	1.133	0.433	6.850	0.009	3.104	1.329	7.248
Family history of diabetes	0.331	0.359	0.848	0.357	1.392	0.688	2.815
Hemoglobin (g/L)	1.763	0.325	29.502	<0.001	5.832	3.087	11.02
Triglycerides (mmol/L)	1.260	0.334	14.208	<0.001	3.526	1.831	6.788
Serum ferritin (ng/mL)	3.041	0.33	84.961	<0.001	20.933	10.964	39.965
Fasting blood glucose in the first trimester (mmol/L)	1.756	0.317	30.619	<0.001	5.787	3.108	10.779

Note: Body Mass Index (BMI).

Analysis of independent risk factors affecting GDM

We first assigned values based on the results obtained from univariate analysis (**Table 3**). Subsequently, we used logistic regression analysis and chose backward LR for regression. It was found that age, BMI, hemoglobin, serum ferritin, triglyceride, and fasting blood glucose in the first trimester were independent risk factors for GDM (**Table 4**).

Construction of risk model

Based on logistic regression equation, we established a risk model with the following formula: -5.971 + 1.054 * age + 1.133 * BMI + 1.763 * hemoglobin + 1.260 * triglycerides + 3.041 * serum ferritin + 1.756 * fasting blood glucose in the first trimester. By calculating the risk score, we found that the risk score of patients in the training control group was significantly lower than that of patients in the

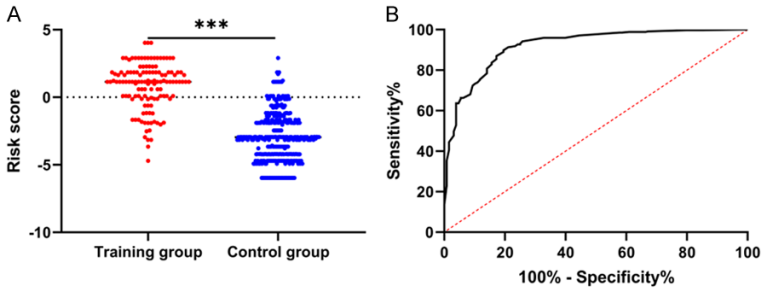

Figure 1. Risk model built based on logistic regression. A. Comparison of risk scores between the training group and the training control group; B. Area under the curve of the score for predicting the risk of gestational diabetes mellitus. Note: *** means P<0.001.

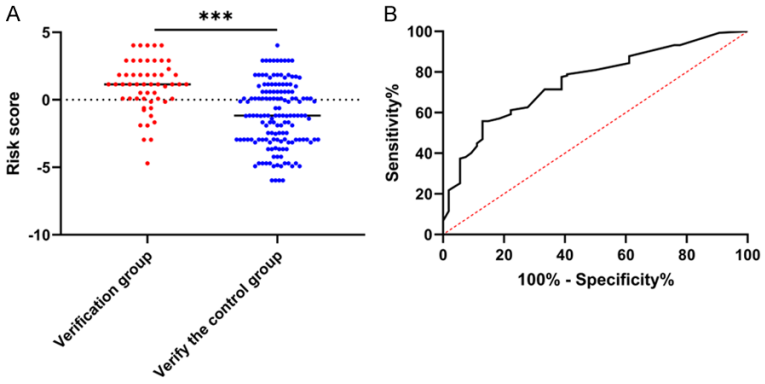

Figure 2. Validation of the risk model. A. Comparison of patient risk scores between the validation group and the validation control group; B. Area under the curve of the score for predicting the risk of gestational diabetes mellitus. Note: *** means P<0.001.

training group (**Figure 1A**, P<0.001). Subsequently, we found by ROC curve analysis that the area under the curve for predicting the of risk GDM was 0.920 (**Figure 1B**), suggesting a high value of the risk model we constructed. To validate our risk model, we imported the data from the verification groups into the risk model to obtain a validation risk score. As a result, the risk scores of patients in the verification group were found to be consistently higher than those in the verification control group (**Figure 2A**, P<0.001). ROC curve analysis revealed that the area under the curve for predicting the risk of GDM in the validation groups was 0.753 (**Figure 2B**).

Risk nomogram model for gestational diabetes

According to the results of logistic regression analysis, nomogram models predicting the risk of GDM were drawn by R software. The plotted nomogram model (**Figure 3**) had an age of 8 and a BMI of 7, and hemoglobin, serum ferritin and fasting blood glucose in the first trimester increased the corresponding scores of the nomogram model, corresponding to an increased risk of GDM. For example, a patient older than 30 years, with BMI less than 25 kg/m^2, hemoglobin (g/L) 109.2, serum ferritin (ng/mL) 73.8, and fasting blood glucose (mmol/L) 5.2 in the first trimester were calculated to have a total score of 100 points, and the probability of this patient to have GDM was about 45%.

Discussion

The incidence of GDM is 3.96%-6.8% worldwide and up to 17.5% in China. GDM has become an important pregnancy complication affecting both maternal and child health [14]. Gestational diabetes guidelines recommend that women with impaired glucose tolerance or impaired fasting glucose should consult before pregnancy, preferably with an oral glucose tolerance test before pregnancy, to reduce the risk of GDM [15]. Previous studies [16, 17] found a single screening index for GDM in the first trimester, but did assess GDM occurrence well due to the complex pathogenesis of GDM. Therefore, active analysis of the risk factors for GDM is helpful for prevention, early clinical screening, and active intervention for GDM.

In this study, we collected a total of 673 pregnant subjects who underwent examinations in Xi'an International Medical Center Hospital from January 2018 to May 2021. GDM was found in 182 of 673 the pregnant women, with an incidence of 27.04%. Previous reports in Sacks et al. [18] showed that the overall incidence of GDM ranged from 9.3% to 25.5%, which is basically consistent with our results. Subsequently, we found that age, BMI, hemo-

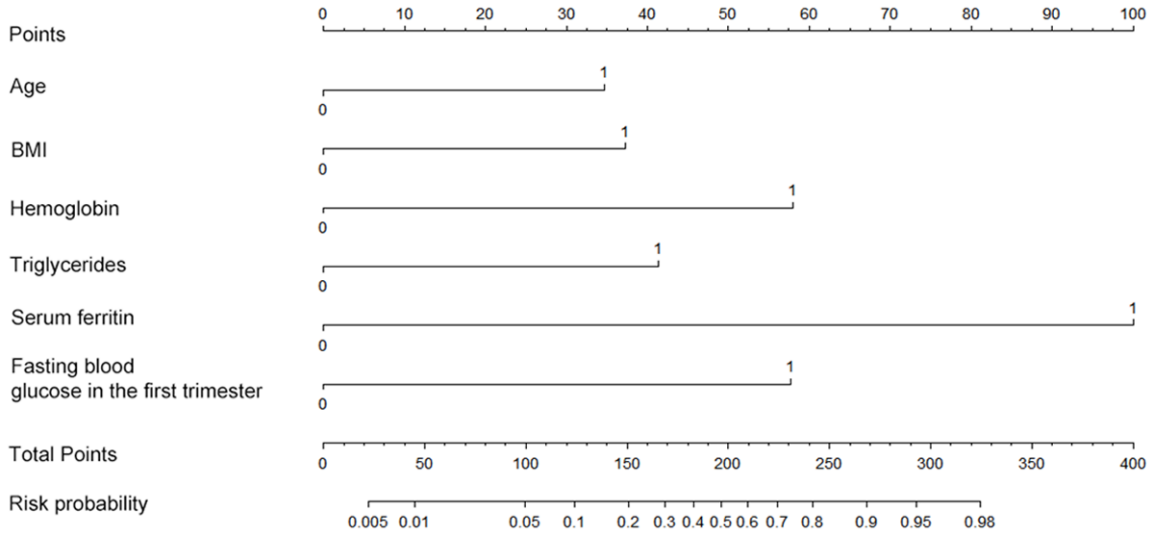

Figure 3. Nomogram model for predicting gestational diabetes mellitus.

globin, serum ferritin, and fasting blood glucose in the first trimester were independent risk factors for GDM by logistics regression analysis. Age is internationally recognized as a risk factor for GDM, so it was included in this study [19]. Metabolism decreases with increasing age, affecting the function of islet β cells and causing decrease of insulin secretion, thereby making pregnant women prone to GDM [20]. In recent decades, due to cultural forces, the age of pregnant women has risen. oupled with the implemented three-child policy in China and the increasingly strict GDM diagnostic criteria for IADPSG, an increase in the incidence of GDM is inevitable [21, 22]. A previous survey found [23] that the probability of GDM increased 1.125-fold with increasing maternal age. Other studies have also pointed out that pregnant women over the age of 40 are more likely to develop GDM. The Canadian Society of Obstetricians and Gynecologists (SOGC) [24] recommends in *Gestational Diabetes Guidelines* that pregnant women aged over 35 years should undergo blood glucose screening as early as possible and get early intervention. Therefore, age is taken as a risk assessment indicator for GDM, and medical workers should carry out risk assessment and screening for women who intend to have children as early as possible, so as to allow timely intervention and carry out regular follow-up.

In our study, the odds of GDM were found to be 2.537 times higher in parturients with BMI≥25 kg/m^2 than that in those with BMI<25 kg/m^2. This is consistent with the results of a meta-analysis study by Najafi et al. [25], who explored the effect of pre-pregnancy BMI on GDM. *British Diabetes Guidelines* state that [26] BMI≥30 kg/m^2 increases the risk of GDM, while China takes BMI≥25 kg/m^2 as a risk entry point for GDM in the 2020 edition of *Clinical Practice Nursing Guidelines For Gestational Diabetes* [27]. We believe that this variation is due to the different ethnic groups, environment, and other factors. At present, it is believed that high pre-pregnancy BMI hinders the body from making full use of islet β cells, which in turn cannot regulate blood glucose and leads to GDM [28]. Due to a sedentary lifestyle, poor weight management is commonly seen in the modern population [29]. In the first prenatal examination of pregnant women, medical workers should measure the pre-pregnancy BMI of pregnant women to identify those at risk for GDM, and to prevent or control it. Lipid metabolism during pregnancy is associated with estrogen and insulin resistance. Abnormal lipid metabolism is mainly caused by increased estrogen levels and insulin resistance. Increased estrogen levels in pregnant women in the first trimester can lead to increased triglycerides, and elevated free fatty acid levels can exacerbate the degree of insulin resistance [30]. Therefore, the higher the triglyceride level, the higher the insulin resistance index, and pregnant women under such conditions are more likely to have GDM. In addition, hemoglo-

bin and serum ferritin were also found to be risk factors for GDM in pregnant women in our study. Serum ferritin is an indicator of iron storage in the body. In recent years, relevant studies have shown that methemoglobin and glycosylated hemoglobin in the first trimester are significantly associated with the risk of GDM [31, 32]. Therefore, monitoring the serum ferritin and hemoglobin levels during pregnancy has important clinical significance in predicting GDM. In addition, we constructed a risk model by logistic regression and validated the model. It was found that the area under the curve of the risk model for predicting GDM was 0.920, and the area under the curve of the validation data was 0.729, which indicated a successful model. In clinical application, the scores corresponding to risk factors can be summed to obtain a total score, and the risk of GDM can be evaluated by the total score.

In this study, we successfully constructed a risk model to predict GDM by logistic regression. However, this study has some limitations. First, we used single-center internal data for validation, which may lead to biased results. Second, patients were not followed up since it was a retrospective study, so whether there is an effect on the final outcome of pregnant women and fetuses needs to be further investigated. Therefore, we hope to carry out a multicenter retrospective analysis in future studies and collect maternal outcomes to supplement our findings.

In summary, age, BMI, hemoglobin, serum ferritin, and fasting blood glucose in the first trimester are risk factors for the development of GDM.

Disclosure of conflict of interest

None.

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