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# Construction and validation of a risk prediction model for hypoglycemia in patients with gestational diabetes mellitus

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#### **Abstract**

**Objective** We explored the prevalence and determinants of hypoglycemia in patients with gestational diabetes mellitus (GDM), and we developed and validated a nomogram prediction model.

**Methods** We extracted data from the clinical records of 475 patients with GDM attending the tertiary class A specialized hospital in Zhuhai City between December 2021 and June 2023 for a modeling group, and we used data of another cohort of 204 GDM cases for a validation group. We conducted a logistic regression analysis to identify factors associated with hypoglycemia in patients with GDM and generated a risk prediction model presented as a nomogram. The model was validated using data from the patients in the validation group.

**Results** The prevalence of hypoglycemia in the study population was 25.5%. Our risk prediction model incorporated four predictors, including a fasting oral glucose tolerance test (OGTT) value, the number of fetuses, the presence or absence of intrahepatic cholestasis of pregnancy (ICP), and the blood glucose level self-monitoring frequency. The area under the receiver operating characteristic (ROC) curve was 0.786 for the modeling set and 0.742 for the validation set. The Brier score was 0.155, and the calibration slope was 0.750, demonstrating satisfactory clinical usefulness of the model. Moreover, a decision curve analysis further supported our model's clinical relevance.

**Conclusion** The prevalence of hypoglycemia in patients with GDM is considerable. Our nomogram prediction model demonstrated good performance for identifying high-risk individuals. The model could serve as a valuable tool for screening and managing hypoglycemia among patients with GDM.

Keywords Pregnancy, Hypoglycemia, Influencing factors, Risk prediction model and nomogram

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## Introduction

Gestational diabetes mellitus (GDM) is a common pregnancy complication, with a worldwide prevalence of approximately 16.7% [1, 2]. Globally, approximately 20% of hospitalized patients with diabetes mellitus experience at least one episode of hypoglycemia [3]. Patients with GDM are particularly susceptible to hypoglycemia due to the characteristic hormonal insulin resistance of pregnancy and the metabolic demands of the fetus, which lead to complex metabolic profiles and require strict glycemic control [4–6]. However, there is a lack of epidemiological



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data on hypoglycemia in patients with GDM in China. A study showed that approximately 51.73% of patients with GDM experience nocturnal blood glucose troughs between the hours of 1 and 5 am, often without noticeable symptoms [7]. Asymptomatic hypoglycemia poses a significant risk as it may not be detected and treated timely due to the lack of obvious symptoms. The harm it causes to the mother and fetus is characterized by its insidious nature and should be taken seriously. When hypoglycemia occurs, ketone bodies, which are secondarily produced due to hunger, insufficient food intake, fat breakdown, etc., may damage the fetus's nerves and even lead to intrauterine fetal death, endangering the health of both the mother and the fetus [8, 9]. Previous studies have shown that ketone bodies can pass through the placenta and can serve as an energy source for the fetus [10]. Kurepa et al's research [11] has indicated that maternal ketosis may lead to potentially harmful changes in the neurological condition of offspring in both animals and humans. DeCapo et al. [12] also found that pregnancy complicated by ketosis is associated with delayed intellectual development and decreased motor ability in offspring. Additionally, hypoglycemia may increase the risk of low birth weight infants [13]. Therefore, early identification of high-risk individuals for hypoglycemia and timely intervention are crucial to ensure the health and well-being of both mother and baby.

The increasing incidence of diabetes mellitus, has led healthcare professionals to become increasingly aware of the importance of hypoglycemia prevention. Most hypoglycemia risk assessment tools focus on patients with type 1 or type 2 diabetes mellitus and newborns [14–16], but these models are inappropriate to predict the hypoglycemia risk in patients with GDM. Therefore, we explored the influencing factors for hypoglycemia in patients with GDM and developed a predictive model for hypoglycemia risk, with the goal of providing a tool for early screening and prevention intervention among highrisk pregnant women.

## **Objectives and methods**

## **Objectives**

We applied convenience sampling to recruit patients with GDM who visited a tertiary class A specialized hospital in Zhuhai City between December 2021 and June 2023. Inclusion criteria: Pregnant women with GDM diagnosed according to the "Guidelines for the Diagnosis and Treatment of Hyperglycemia in Pregnancy (2022)" [5]. Specifically, the 75 g oral glucose tolerance test (OGTT) was employed for screening. It is recommended to conduct this test during the 24 th to 28 th weeks of pregnancy. The blood glucose thresholds are as follows: fasting blood glucose should be 5.1

mmol/L or above, the blood glucose value 1 hour after oral glucose intake should be 10.0 mmol/L or above, and the blood glucose value 2 hours after oral glucose intake should be 8.5 mmol/L or above. A diagnosis of GDM is made if any one of these time points meets or exceeds the stipulated values. Additionally, when performing the OGTT, fasting blood must be drawn before 9 am to ensure accurate results. Moreover, the night before the OGTT, patients should avoid prolonged fasting to prevent reactive hyperglycemia in the morning, which could potentially skew the diagnosis. These pregnant women also needed to sign an informed consent. Exclusion criteria: Pregnant women with type 1 or type 2 diabetes mellitus and a history of mental illness or cognitive impairment, or complications such as malignant tumors or end-stage diseases. The Ethics Committee of our institution approved this study (approval number: 2022011012).

In this study, influencing factors were screened on the basis of literature review [17–22] and project team discussion, and finally included 18 influencing factors through expert opinions to construct A questionnaire of influencing factors for hypoglycemia (shown in Supplement 1). Specific influencing factors are shown in Table 1. We calculated the sample size by using the logistic variable event per predictor method [23], with a predicted hypoglycemia incidence rate of 23.96% (23/96) according to preliminary survey results. Considering a 20% sample loss rate, we determined the required sample size to be 451 cases. Ultimately, we enrolled 679 cases allocated in a 7:3 ratio, with 475 cases in the modeling group and 204 cases in the validation group.

#### Study methods

#### Diagnostic criteria for hypoglycemia

We defined hypoglycemia according to the recommendations in the American Diabetes Association (ADA) guidelines [24], setting grade 1 hypoglycemia (blood glucose levels between 3.0 and 3.9 mmol/L, with or without clinical symptoms) as the diagnostic criterion for this study.

#### Hypoglycemia event coding criteria

We classified hypoglycemic events using a binary system, with the hypoglycemia subgroup defined by one or more documented episodes meeting grade 1 criteria, while the non-hypoglycemia subgroup had no recorded episodes during observation. For participants with multiple events, only the chronologically first episode was registered to maintain data independence in subsequent analyses.

**Table 1** Univariate analysis of hypoglycemia in patients with gestational diabetes mellitus (n=475)

Name of variable	Categories	Hypoglycemia group $(n = 123)$	Non-hypoglycemia group $(n = 352)$	p-value
Age (years)		33.07±12.20	32.28±4.46	0.299 <sup>1)</sup>
BMI before Pregnancy (kg/m²)		21.64±3.58	22.99±3.90	0.0011)
Fasting OGTT value (mmol/L)		4.24±0.62	4.79±0.58	0.0011)
1-Hour OGTT value (mmol/L)		10.06±1.31	10.17±1.74	0.504 <sup>1)</sup>
2-Hour OGTT value (mmol/L)		9.01±1.24	9.09±1.50	0.577 <sup>1)</sup>
Gestational age in weeks(weeks)		30.54±5.24	31.95±5.73	0.087 <sup>1)</sup>
Educational background	Primary school and lower educational levels	1 (0.8)	3 (0.9)	0.456 <sup>2)</sup>
	Middle School and Vocational High School	37 (30.1)	90 (25.6)	
	Junior college	38 (30.9)	129 (36.6)	
	Undergraduate	45 (36.6)	116 (33)	
	Graduate	16 (3.4)	14 (4)	
Family history of diabetes mellitus	Yes	17 (13.8)	57 (16.2)	0.532 <sup>2)</sup>
	No	106 (86.2)	295 (83.8)	
Conception approach	Natural conception	110 (89.4)	317 (90.1)	0.843 <sup>2)</sup>
	Artificial insemination	13 (10.6)	35 (9.9)	
Maternal childbirth experience	Primipara	47 (38.2)	148 (42)	0.457 <sup>2)</sup>
	Multipara	76 (61.8)	204 (58)	
Number of fetuses	Singleton	113 (91.9)	340 (96.6)	0.032 <sup>2)</sup>
	Twins and multiple	10 (8.1)	12 (3.4)	
Diabetes mellitus education experience	Yes	99 (80.5)	166 (75.8)	0.286 <sup>2)</sup>
	No	24 (19.5)	85 (24.2)	
Self-monitoring of blood glucose	Regular monitoring	94 (76.4)	221 (62.8)	$0.006^{2)}$
	Irregular monitoring	25 (20.3)	90 (25.6)	
	No monitoring	4 (3.3)	41 (11.6)	
Daily exercise Time >45 min	Yes	20 (16.3)	41 (11.6)	0.188 <sup>2)</sup>
	No	103 (83.7)	311 (88.4)	
Use of insulin or metformin	Yes	29 (23.6)	92 (26.1)	0.575 <sup>2)</sup>
	No	94 (76.4)	260 (73.9)	
Additional meal 1–2 hour before bedtime	Yes	27 (22)	48 (13.6)	$0.029^{2)}$
	No	96 (78)	304 (86.4)	
Weekly weight gain	insufficient	84 (68.3)	186 (52.8)	0.012 <sup>2)</sup>
	normal	32 (26)	136 (38.6)	
	excessive	7 (7.8)	30 (8.5)	
Combined ICP	Yes	10 (8.1)	9 (2.6)	0.014 <sup>2)</sup>
	No	113 (91.9)	343 (97.4)	

 $Continuous\ variables\ presented\ as\ mean \pm standard\ deviation;\ categorical\ variables\ as\ frequency\ (percentage)$ 

BMI body mass index, ICP intrahepatic cholestasis of pregnancy

Statistical tests: 1) Independent samples t-test; 2) Pearson chi-square test

#### Data collection methods

Two research team members, who underwent training using the questionnaire of influencing factors

for hypoglycemia and diagnostic criteria to ensure data homogeneity, collected the data. Subsequently,

designated researchers stored the data and randomly selected 10% of the patient data for verification.

#### Statistical methods

We conducted the statistical analysis using SPSS 22.0 and R software. Continuous data are described as means ± standard deviations or medians (interquartile ranges), and between-group comparisons were made using independent sample t-tests or Mann-Whitney U tests. Categorical data are described as frequencies and percentages (%), and between-group comparisons were made using Fisher's exact or Chi-square tests. We performed logistic regression analysis following a two-step approach: first including all variables showing statistical significance (p<0.05) in univariate analyses, then applying backward stepwise selection based on the Akaike Information Criterion (AIC) with a p<0.05 retention threshold to identify independent predictors and build the predictive model. The Youden Index (YI) was applied to determine the optimal model threshold value. We conducted a Hosmer-Lemeshow (H-L) test and determined the area under the receiver operating characteristic (ROC) curve to evaluate the model fit and its discriminative ability. Finally, we assessed the accuracy of the model using a calibration curve and its clinical effectiveness using decision analysis curves.

#### **Results**

# General characteristics and incidence of hypoglycemia in patients with GDM

We analyzed data from 679 patients with GDM in this study; 396 were primiparas (58.3%) and 283 were multiparas (41.7%). The patients' ages ranged from 18 to 48 years (mean age,  $32.12 \pm 4.43$  years) and their BMIs from 15.1 to 37.5 (mean BMI,  $22.63 \pm 3.87$ ). The gestational age in weeks at enrollment ranged from 24 to 40 weeks (mean gestational age in weeks:,  $31.56 \pm 5.69$  weeks). Additionally, 653 patients had singleton pregnancies (95%) and 34 had twin pregnancies (5%). Hypoglycemia occurred in 173 patients with GDM resulting in an incidence rate of

25.5%.The blood glucose levels at the time of hypoglycemia ranged from 2.9 to 3.8 mmol/L (mean blood glucose levels,  $3.60 \pm 0.23$  mmol/L).

#### Univariate analysis of hypoglycemia in GDM patients

Among the 475 patients in the modeling group, we subdivided those with GDM into hypoglycemia (n=123) and non-hypoglycemia (n=352) subgroups based on whether they had presented hypoglycemia. Table 1 presents the results of our univariate analysis of hypoglycemia in patients with GDM.

# Multivariable regression analysis for hypoglycemia in patients with GDM

Using hypoglycemia occurrence as the dependent variable (0 = did not occur; 1 = occurred), we conducted a logistic regression analysis on seven factors (BMI, fasting OGTT value, number of fetuses, blood glucose level self-monitoring, pre-bedtime fasting, weekly weight gain, and combined ICP) that had shown statistical significance (P < 0.05) in the univariate analysis.Our results (Table 2) indicate that the fasting OGTT value was a protective factor, while the number of fetuses, blood glucose level self-monitoring, and combined ICP variables were independent risk factors for hypoglycemia (P < 0.05).

# Construction of risk prediction model for hypoglycemia in patients with GDM

Based on the regression analysis results, we input the independent influencing factors for hypoglycemia in patients with GDM into R Studio (version 4.1.1) to construct a prediction model chart (Fig. 1). Each independent influencing factor's actual value was plotted upward against the score axis, and the intersection point corresponds to the score for that particular influencing factor. The sum of scores for all independent influencing factors is plotted downward as a vertical line, representing the risk of hypoglycemia in patients with GDM. For example, for a patient with GDM, a fasting OGTT value of 4.0 mmol/L, a singleton pregnancy, combined ICP, and

 Table 2
 Results of logistic regression analysis for hypoglycemia in patients with GDM

Variable	β	SE	Wald χ <sup>2</sup>	OR	95%CI	P
Constant	6.236	1.242	5.021	510.584	_	<0.001
Fasting OGTT value	-1.963	0.259	-7.588	0.140	0.083~0.228	<0.001
Number of fetuses	1.792	0.542	3.309	6.003	2.079~17.696	< 0.001
Combined ICP	1.551	0.545	2.846	4.715	1.634~14.199	0.004
Self-monitoring of blood glucose	1.543	0.572	2.699	4.679	1.698~16.824	0.007

Fasting OGTT value represents the original value; number of fetuses (singleton = 0, twins or more = 1); combined ICP (no = 0, yes = 1); Self-monitoring of blood glucose (no monitoring = 0, regular monitoring = 1, irregular monitoring = 2)

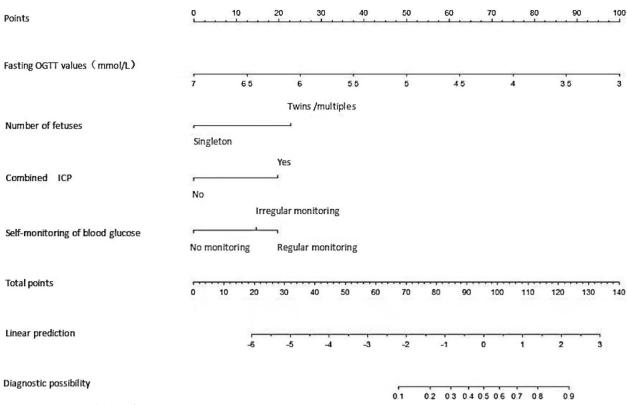


Fig. 1 Prediction model chart for hypoglycemia risk in patients with GDM

regular blood glucose monitoring, the risk scores were 75, 0, 20, and 20, respectively. The total score of 115 projected onto the 'risk' axis in the prediction model chart for this patient indicates an approximate probability of 80% for hypoglycemia occurrence.

# Assessment of risk prediction model for hypoglycemia in patients with GDM

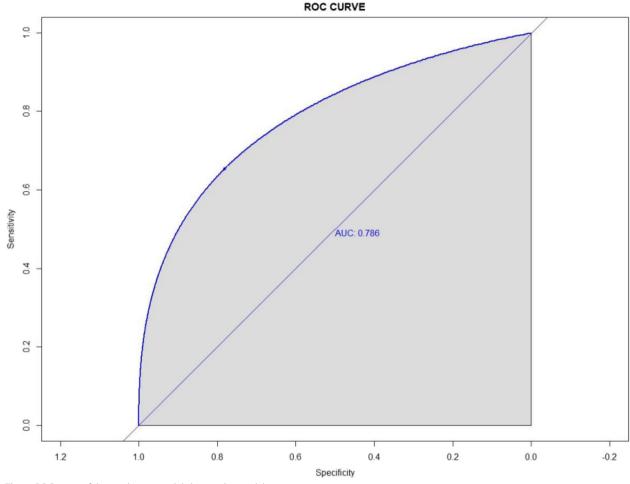
The area under the ROC curve (AUC) of the risk prediction model for hypoglycemia in patients with GDM was 0.786, with a specificity of 0.782 and a sensitivity of 0.654. The Youden Index was 0.436 at this point (Fig. 2). The calibration curve showed good fit between the two sets of columns, and the H-L test result was  $\chi^2 = 41.445$ , P =4.150 (Fig. 3). The AUC of the validation set was 0.742 (Fig. 4). The Brier score was 0.155, and the calibration slope was 0.750, indicating high consistency between the actual and predicted values on the calibration curve (Fig. 5). We conducted a decision curve analysis (DCA) to assess the model's clinical usefulness (Fig. 6). In the graph, the solid black horizontal line indicates a zero-net benefit, representing a scenario of no intervention for any patients. The gray diagonal line represents a scenario of intervention for all patients, and the black dashed line represents the net benefit of the model. The black dashed line is closer to the upper right corner, indicating the model's clinical usefulness.

#### **Discussion**

# Analysis of influencing factors for hypoglycemia in patients with GDM

## Fasting OGTT value

Our findings indicate that the fasting OGTT value is a significant protective factor for hypoglycemia in patients with GDM, this is consistent with findings by Hu et al. [25]. Fasting blood glucose levels are a crucial indicator of the baseline glucose status of patients and they can be used to predict hypoglycemia [25, 26]. Fasting blood glucose levels primarily reflect pancreatic β-cell function, but they can also reflect the basal glucose metabolism in the body. Fasting OGTT values, based on standard requirements for fasting blood glucose monitoring in pregnant women, are only slightly altered by gestational weeks and dietary factors, and they are a good indicator of a patients' glucose levels. Therefore, healthcare professionals should pay attention to the fasting OGTT value of patients with GDM in their clinical practice and provide timely education on hypoglycemia prevention to highrisk individuals.



 $\textbf{Fig. 2} \ \ \mathsf{ROC} \ \mathsf{curve} \ \mathsf{of} \ \mathsf{the} \ \mathsf{prediction} \ \mathsf{model} \ \mathsf{chart} \ \mathsf{in} \ \mathsf{the} \ \mathsf{modeling} \ \mathsf{group}$ 

#### **Number of fetuses**

Our results suggest that the number of fetuses in a pregnancy is a risk factor for hypoglycemia in patients with GDM, with a higher incidence of hypoglycemia in patients with GDM carrying more than one fetus. The nature of the association between the number of fetuses and glucose levels in patients with GDM has remained controversial. In agreement with our findings, a study involving 684 twin and 1868 singleton pregnancies in women with GDM by Li et al. [27] showed that earlystage fasting blood glucose levels in twin pregnancies were lower than those in singleton pregnancies, but this research only focused on fasting blood glucose values in the early stages of pregnancy, which differs from the mid to late pregnancy stage investigated in our study. The decrease in fasting blood glucose levels in the early stages of twin pregnancies may be attributed to the increased demand for glucose by the mother due to the increased number of fetuses, while the placental function in the early stages of pregnancy is not fully developed, resulting in less impact on maternal insulin resistance. A different study [28] on women with GDM showed that twin pregnancies exhibit higher levels of insulin resistance and glycosylated hemoglobin than singleton pregnancies, but the OGTT test results were similar between both groups. The large placental area in twin pregnancies may lead to high levels of placental hormones and increased insulin resistance.

In this study, the risk of hypoglycemia in women with GDM and twin pregnancies was higher than that in women with singleton pregnancies, possibly due to the strict blood sugar control requirements and sample limitations of the former group of women. Studies have suggested that blood sugar management strategies for singleton and twin pregnancies should differ, large-scale studies on blood sugar control levels and maternal and infant outcomes in twin pregnancies with GDM in China are lacking. Therefore, the current clinical standards are the same for singleton and twin pregnancies, and this management strategy may be overly stringent for patients

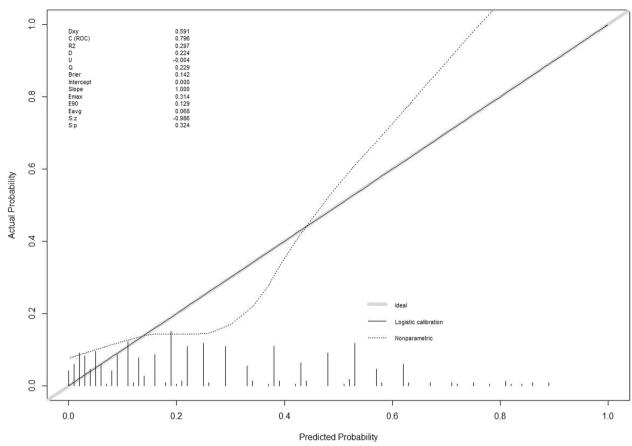


Fig. 3 Calibration curve of the prediction model chart in the modeling group

with GDM and twin pregnancies. The increased insulin resistance and strict blood sugar control targets pose stringent requirements for blood sugar management in patients with GDM and twin pregnancies, increasing the risk of blood sugar fluctuations and hypoglycemia. In our study, the overall BMI of patients with GDM and twin pregnancies was relatively low, with only 17.6% of them being overweight and 5.8% being obese; the proportions of overweight and obese patients in the total sample were higher. Moreover, the rate of insufficient weight gain in patients with twin pregnancies was as high as 94%, suggesting that most patients with twin pregnancies had inadequate energy intakes. Therefore, clinical healthcare workers should monitor the weight and supervise the blood sugar management strategies of patients with twin pregnancies, develop personalized dietary plans for those with GDM, and explore more appropriate blood sugar control targets than those used for patients with singleton pregnancies.

#### Combined ICP with GDM

Our results indicate that combined ICP is a risk factor for hypoglycemia in patients with GDM. ICP is a common liver disease during pregnancy characterized by symptoms such as pruritus, scratching, jaundice, elevated serum bile acid levels, and mild liver dysfunction [29]. The liver is the primary insulin degradation organ, and liver cell dysfunction can impair insulin degradation, leading to excessive insulin entering various tissues of the body and causing blood sugar fluctuations. A study by He et al. [30] on patients with liver failure demonstrated that these patients are prone to hypoglycemia due to reduced liver insulin deactivation and decreased liver glycogen breakdown. Patients with combined ICP rarely exhibit severe liver damage, and their high hypoglycemia risk may be related to abnormal serum bile acid levels.

Studies have found that bile acids act as signaling molecules, binding to receptors such as farnesoid X to regulate bile acid synthesis and participate in glucose, lipid, and energy metabolism, pathways that are closely related to the maintenance of glucose homeostasis [31]. A study involving 45 women with a history of GDM found that an increase in the ratio of  $12\alpha$ -hydroxylated bile acids to non- $12\alpha$ -hydroxylated bile acids reduces insulin sensitivity, and an increase in the proportion of non- $12\alpha$ -hydroxylated bile acids is more conducive to blood sugar

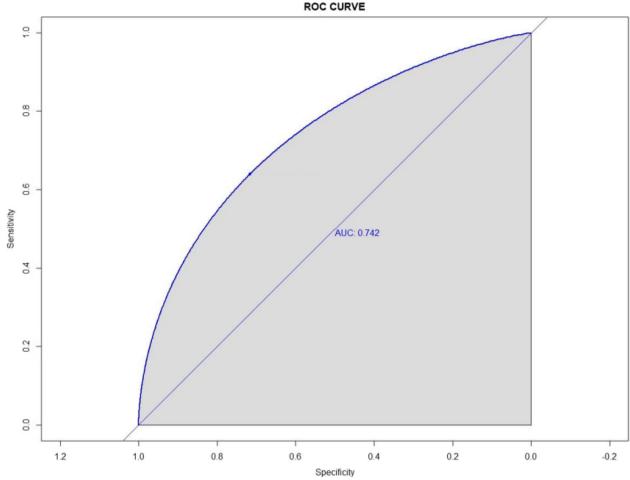


Fig. 4 ROC curve of the prediction model chart in the validation group

control [32]. Tang et al.'s [33] investigation of 173 ICP patients confirmed that they are prone to abnormal carbohydrate and lipid metabolism. Bile acid levels are associated with carbohydrate and lipid metabolic processes. However, the hospital in this study has not conducted tests on biochemical indicators such as 12α-hydroxylated or non-12α-hydroxylated bile acids, carrying out such projects in the future and elucidating the specific indicators of 12α-hydroxylated and non-12α-hydroxylated bile acids in patients with GDM and combined ICP is important. In this study, all GDM patients with ICP were treated with ursodeoxycholic acid (UDCA). UDCA is a first-line treatment for ICP recommended by clinical guidelines [34], and its primary mechanisms include inhibiting hepatic cholesterol synthesis, reducing hepatic lipid deposition, and promoting bile excretion. Although UDCA is primarily indicated for ICP, some studies suggest that it may also influence glucose metabolism. For example, Qin Guoding et al. [35] found that empagliflozin combined with UDCA significantly reduced insulin resistance in patients with type 2 diabetes mellitus (T2DM) and non-alcoholic fatty liver disease (NAFLD). Additionally, animal studies [36] have shown that UDCA can improve blood glucose levels and pancreatic  $\beta$ -cell function in T2DM mice. However, clinical studies on the independent hypoglycemic effects of UDCA remain limited, and its specific mechanisms are not yet fully understood.

In this study, detailed information on the dosage and duration of UDCA treatment in ICP patients was not recorded, which limits our ability to fully assess the potential impact of UDCA on hypoglycemia risk. This represents a significant limitation of our research. Nevertheless, we recommend that in clinical practice, GDM patients with ICP should undergo enhanced hypoglycemia risk assessment, dietary management, and medication management. Specific measures include optimizing dietary structure, ensuring adequate daily caloric intake, and providing health education on rational medication use to reduce the risk of hypoglycemia.

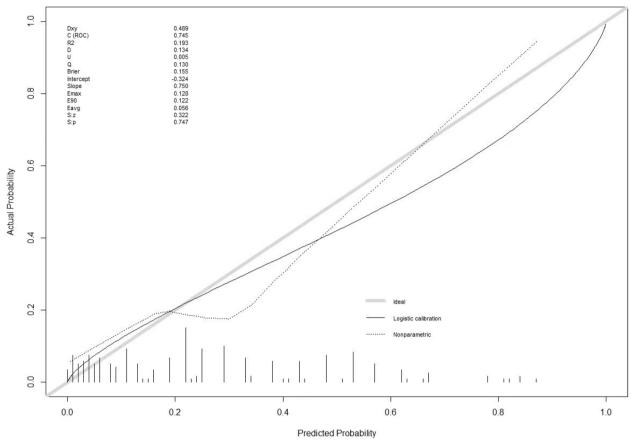
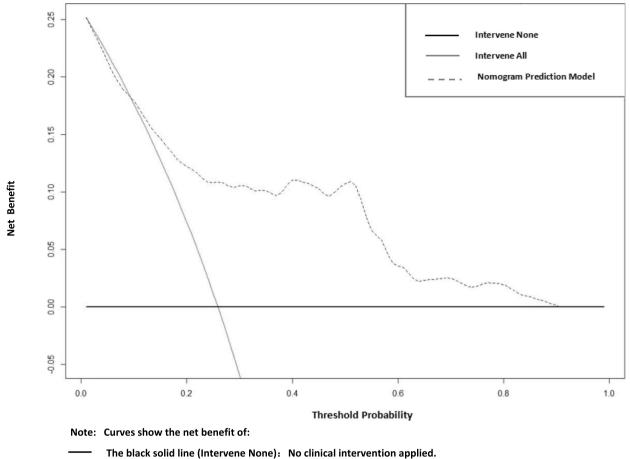


Fig. 5 Calibration curve of the prediction model chart in the validation group

## Self-monitoring of blood glucose levels

Blood glucose level self-monitoring is a crucial component of the comprehensive GDM management [37]. The results of our study indicate that regular blood glucose level self-monitoring is a risk factor for the occurrence of hypoglycemia in patients with GDM. In a meta-analysis consistent with our findings, researchers reported that regular blood glucose level self-monitoring increases the incidence of asymptomatic hypoglycemic events among the study population [38]. In addition, compared to those who did not perform self-monitoring, individuals who did demonstrated varying degrees of reductions in BMI, weight, fasting blood glucose, and waist circumference. The increased incidence of hypoglycemic events in that study may primarily be attributed to asymptomatic episodes being detected more frequently with regular self-monitoring than without it, rather than to an actual increase in the occurrence rate of hypoglycemic episodes. Additionally, regular blood glucose level self-monitoring often reflects a higher level of disease awareness and treatment adherence among patients. In our study, individuals in the group practicing regular self-monitoring exhibited significantly higher rates of insufficient weight gain (P < 0.05) and diabetes mellitus education (P < 0.001) compared with those who did not self-monitor or did so irregularly. This suggests that patients engaging in regular blood glucose level self-monitoring may adhere more strictly to blood glucose control measures. The goal of blood glucose level self-monitoring should be to facilitate timely awareness of blood glucose levels and provide a reference value for healthcare professionals to adjust the patient's blood glucose management plan. Therefore, during clinical education, patients should be guided to avoid the misconception of pursuing lower blood glucose levels, and they should be taught how to respond to high or low blood glucose levels and to seek medical assistance. Moreover, efforts should be made to improve the compliance and enthusiasm of patients with GDM to self-monitor their blood glucose levels to promptly prevent and detect hypoglycemic events, thereby improving maternal and neonatal outcomes.



- The gray solid line (Intervene All): Universal clinical intervention for all patients.
- The gray dotted line (Nomogram Prediction Model): Risk-stratified intervention based on the nomogram model.

Threshold Probability: The minimum probability of hypoglycemia at which intervention is considered justified (x-axis).

Axes: - X-axis: Threshold probability (%) - Y-axis: Standardized net benefit

Fig. 6 Decision curve analysis of the prediction model chart

#### Strengths and limitations

To our knowledge, this is the first study about hypoglycemia risk prediction model for GDM patients. We developed and validated a prediction model chart for hypoglycemia in patients with GDM, demonstrating its clinical usefulness. However, we are aware of this study's limitations: 1) Our investigation of influencing factors was limited, and we failed to survey biochemical indicators such as specific bile acids in patients with GDM, precluding the assessment of the impact of ICP severity on the hypoglycemia risk. 2) Another limitation of this study is the lack of detailed data on UDCA use in ICP patients, including dosage and duration. Although all ICP patients received UDCA treatment, the potential influence of this medication on hypoglycemia risk could not be fully assessed. Future studies should consider collecting detailed medication data to further explore this relationship. 3) This was a single-center study with a small sample size based on convenience sampling; thus, improved sample representativeness is needed. Future studies should expand the sample size and conduct multicenter surveys, while analyzing more comprehensive influencing factors to improve the predictive efficacy of the model, enhance the effectiveness of clinical hypoglycemia prevention education, and promote maternal and neonatal health.

#### **Conclusion**

For this study, we analyzed data from 475 patients with GDM, among whom the incidence of hypoglycemia was relatively high with many cases being asymptomatic. Due to the endocrine feedback regulation changes influenced by pregnancy factors in patients with GDM, hypoglycemia often goes unnoticed, making timely screening, identification, and education of high-risk populations particularly important. Our multivariate regression analysis results identified the fasting OGTT value, number of fetuses, combined ICP, and frequency of blood glucose level self-monitoring as influencing factors for hypoglycemia in patients with GDM. In addition, we generated a prediction model chart for hypoglycemia in patients with GDM on the basis of these factors. External validation of our prediction model chart showed an area under the ROC curve value of 0.742; the predictive and calibration curves were relatively consistent with the ideal curve, indicating good clinical applicability of the risk prediction model.

#### Abbreviations

ADA American Diabetes Association Atherosclerosis risk in communities Area under the ROC curve ALIC DCA Decision curve analysis GDM Gestational diabetes mellitus ICP Intrahepatic cholestasis of pregnancy OGTT Oral glucose tolerance test ROC Receiver operating characteristic Youden Index

YI Youden Index UDCA Ursodeoxycholic acid NAFLD Non-alcoholic fatty liver disease

#### **Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s12884-025-07740-8.

Supplementary Material 1.

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We would like to thank all the participants in this study. Thanks to everyone for their help in study design, questionnaire distribution, recycling, input, and analysis.

## Clinical trial number

Not applicable.

#### Authors' contributions

All authors contributed to the study conception and design. Jie-mei Yang: Conceptualization, Methodology, Data analysis, Writing-original draft, Writing-review & editing. Li-zhi Wan & Xiang-feng Zhao: Methodology, Data analysis. Cui Wan & Rui-fen Huang & Rong-rong Peng: Data collection. Qian-cheng Ye: Data analysis. Xiu-zhen Li: Conceptualization, Data collection. Cai-xia Liu: Supervision, Writing- review & editing. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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#### Data availability

The datasets generated and analysed during the current study are not publicly available due we may have further research related to the data but are available from the corresponding author on reasonable request.

#### **Declarations**

#### Ethics approval and consent to participate

This study was performed in line with the principles of the Declaration of Helsinki. Approved by the ethics committee of the author's institution: Medical Ethics Committee of Zhuhai Center For Maternal And Child Health Care (Ref. 2022011012)

Informed consent was obtained from all individual participants included in the study.

#### Consent for publication

Not applicable in the declarations section.

#### Competing interests

The authors declare no competing interests.

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