

RESEARCH

Open Access



Integrating adipsin with novel cardiometabolic and inflammatory indices for enhanced early prediction of gestational diabetes mellitus: a prospective cohort study

Meizhi Cai^{1*}, Xuan Jiang^{2†}, Xinyi Xu^{2†}, Sidi Zhao¹, Yue Sun², Yushuo Yang², Ping Yang¹, Chen Fang¹ and Yifan Huang^{2*}

Abstract

Background Early identification of individuals at risk for gestational diabetes mellitus (GDM) is essential for mitigating its adverse effects on both maternal and foetal health. This study aimed to evaluate the predictive value of the cardiometabolic index (CMI), systemic inflammation response index (SIRI), and serum adipsin levels for GDM.

Methods A total of 1660 pregnant women were enrolled in this study conducted in Suzhou, China. Baseline clinical data, including blood glucose levels, lipid profiles, and blood cell counts, were collected at 12 weeks of gestation. GDM was diagnosed between 24 and 28 weeks of gestation. Logistic regression and receiver operating characteristic (ROC) curve analyses were performed to assess the associations and predictive performance of CMI, SIRI, and adipsin for GDM.

Results Compared with non-GDM participants, those with GDM exhibited significantly higher CMI and SIRI values and lower serum adipsin levels at baseline. Increased CMI and SIRI, as well as reduced adipsin levels, were independently associated with a higher risk of GDM in both unadjusted and adjusted models (all $P < 0.05$). The composite model incorporating all three biomarkers achieved a higher area under the curve (AUC) of 0.918 compared with the individual models for CMI (AUC = 0.825), SIRI (AUC = 0.802), and adipsin (AUC = 0.724).

Conclusions CMI, SIRI, and serum adipsin are independently associated with GDM risk, and their combination provides a promising multi-biomarker strategy for early GDM prediction. Further studies are needed to validate these findings in diverse populations.

Keywords Adipokines, Adipsin, Metabolic abnormalities, Glucose intolerance, Inflammation, Insulin resistance, Pregnancy-Diabetes

[†]Meizhi Cai, Xuan Jiang and Xinyi Xu contributed equally to this work.

*Correspondence:
Meizhi Cai
caimeizhi1987@hotmail.com
Yifan Huang
yyzhyf@hotmail.com

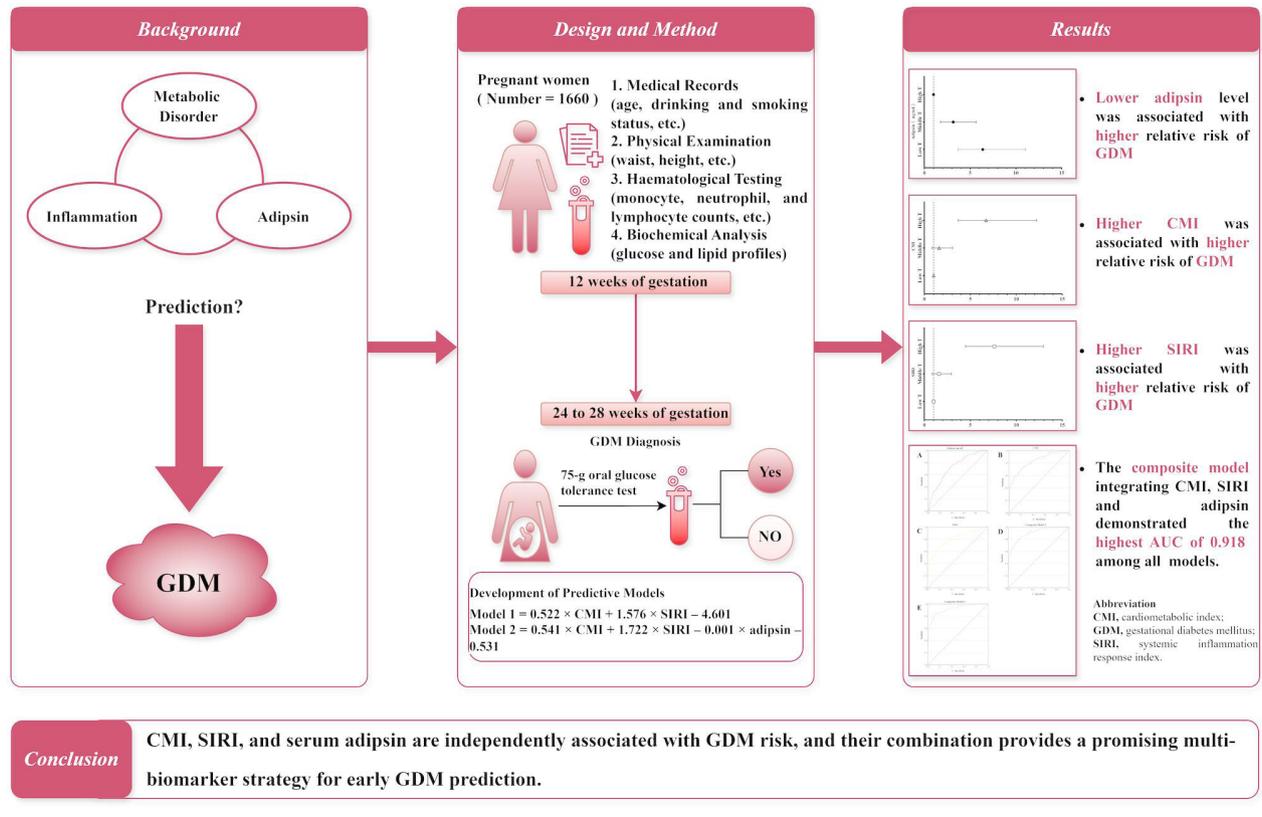
Full list of author information is available at the end of the article



© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

Graphical Abstract

Integrating adipsin with novel cardiometabolic and inflammatory indices for enhanced early prediction of gestational diabetes mellitus



Research insights

What is currently known about this topic?

- GDM increases risks of adverse maternal and foetal outcomes.
- Metabolic disorders and abnormal inflammation response are linked to GDM.
- Early identification and management of GDM risk factors may mitigate adverse outcomes.

What is the key research question?

- Can combining adipsin, CMI, and SIRI improve predictive accuracy for GDM?

What is new?

- This study investigates the predictive efficacy of CMI, SIRI, and adipsin for GDM.
- Adipsin improves the predictive accuracy of CMI and SIRI.

How might this study influence clinical practice?

Combined biomarker assessment could enhance personalized GDM prevention and management.

Background

Gestational diabetes mellitus (GDM) is a common metabolic disorder characterised by glucose intolerance that typically develops during the second or third trimester of gestation. GDM not only increases the risk of maternal preeclampsia and future type 2 diabetes but also contributes to foetal macrosomia and raises the likelihood of long-term metabolic complications in offspring [1, 2]. Identifying reliable and minimally invasive biomarkers for early GDM prediction is crucial for enhancing clinical outcomes and minimising long-term complications, as many existing early predictive indicators have suboptimal sensitivity and specificity [3].

The cardiometabolic index (CMI) is a recently proposed composite marker that reflects both metabolic and cardiovascular risk by incorporating measures of lipid levels and body fat distribution [4]. Similarly, the systemic inflammation response index (SIRI) is a novel biomarker that quantifies systemic inflammation based on neutrophil, monocyte, and lymphocyte counts [5]. Since

both metabolic dysregulation and chronic inflammation are implicated in GDM pathogenesis, it is plausible that CMI, SIRI, or both could serve as valuable predictive biomarkers for GDM.

Adipsin, also known as complement factor D, is an adipokine secreted by adipose tissue that plays a vital role in metabolic homeostasis and inflammation modulation [6]. It enhances insulin secretion, preserves β -cell function, and regulates lipid metabolism via the complement system. Although adipsin has been implicated in the pathogenesis of several metabolic diseases, the literature regarding adipsin's role in metabolic dysfunction remains controversial. Some studies, including meta-analysis, have reported the inverse associations of adipsin with several metabolic and cardiovascular diseases, such as type 2 diabetes [7, 8], insulin resistance [9], non-alcoholic fatty liver disease [10], and atherosclerosis [11]. In contrast, Pan et al. demonstrated that elevated serum adipsin level was associated with metabolic dysfunction-associated fatty liver disease, with both adipsin concentrations and the severity of fatty liver increasing as the number of metabolic risk factors rises [6]. Similarly, Wang et al. found a positive correlation between elevated serum adipsin and cardiovascular risk factors [12]. Although further verification is required, the potential role of adipsin in regulating glucose and lipid metabolism warrants investigation into its association with GDM, given that GDM shares some similar pathophysiological features with type 2 diabetes, including insulin resistance and metabolic dysregulation.

Given the substantial burden of GDM and its associated health complications, the identification of robust biomarkers for early prediction remains clinically pertinent. While previous studies have highlighted the potential individual roles of adipsin, CMI, and the SIRI in metabolic and inflammatory status, their combined predictive potential for GDM has not been thoroughly explored. This study aims to address this gap by assessing the predictive accuracy of these biomarkers, both individually and in combination, providing a novel multi-biomarker approach for early GDM prediction.

Methods

Population

This study initially enrolled all pregnant women ($N=2519$) who delivered at the Second Affiliated Hospital of Soochow University between 1 January 2023 and 31 December 2023. The inclusion criteria were as follows: (1) aged between 18 and 40 years; (2) first pregnancy; and (3) provision of signed informed consent. The exclusion criteria were as follows: (1) self-reported or clinically diagnosed glucose intolerance, insulin resistance, or diabetes at the first-trimester (12 weeks of gestation) prenatal check-up; (2) hepatic or renal metabolic disorders,

such as metabolic dysfunction-associated fatty liver disease; (3) history of drug, tobacco, or alcohol dependence; and (4) incomplete medical records or missing clinical data. The participant selection and follow-up flowchart is presented in Fig. 1. This study was approved by the Ethics Committee of The Second Affiliated Hospital of Soochow University. The design and all procedures of this study were in accordance with the Declaration of Helsinki.

Data collection

Basic demographic and clinical information was obtained from hospital medical records. Physical examination was conducted at 12 and 24–28 weeks of gestation. At 12 weeks of gestation, following an overnight fast, venous blood samples were collected for laboratory analysis. A 2 mL whole blood sample was collected into a vacuum tube containing EDTA as an anticoagulant for automated haematological testing. Additionally, a 5 mL whole blood sample was collected into an anticoagulant-free vacuum tube for serum biochemical analysis. For serum preparation, the 5 mL blood sample was left at room temperature for 30 min, after which the clotted blood was centrifuged at 2000 g for 10 min at 4 °C. The resulting serum was immediately aliquoted into separate tubes and stored at -80 °C to prevent degradation due to freeze-thaw cycles. Monocyte, neutrophil, and lymphocyte counts were measured using an automated haematology analyser (Mindray SAL 8000, Mindray Bio-Medical Electronics Co., Ltd., China). Serum glucose, triglyceride (TG), total cholesterol, and high-density cholesterol (HDL-c) levels were quantified using an automated biochemical analyser (Roche Cobas 501, Roche Diagnostics, USA) via enzymatic methods. Serum adipsin concentrations were determined using a commercial enzyme-linked immunosorbent assay kit (Multiscience Biotech Co., Ltd., China) following the manufacturer's protocol. The mean minimal detectable concentration of adipsin was 143.37 pg/mL, with intra- and inter-assay coefficients of variation of 5.4% and 6.0%, respectively. The CMI was calculated by multiplying the waist-to-height ratio by the TG-to-HDL-c ratio [4]. The SIRI was calculated as the product of the neutrophil count and monocyte count, divided by the lymphocyte count [5]. Smoking status was defined as lifetime cigarette consumption of ≥ 100 cigarettes, with smokers further categorised as current smokers (smoked within the past 30 days) or former smokers [13]. Alcohol consumption was defined as an average intake of at least 40 g per week over the past 12 months [14].

Diagnosis of GDM

At 24–28 weeks of gestation, all participants underwent a 75-g oral glucose tolerance test for GDM diagnosis. Following an overnight fast of at least 8 h, a 5 mL fasting venous blood sample was collected into a vacuum

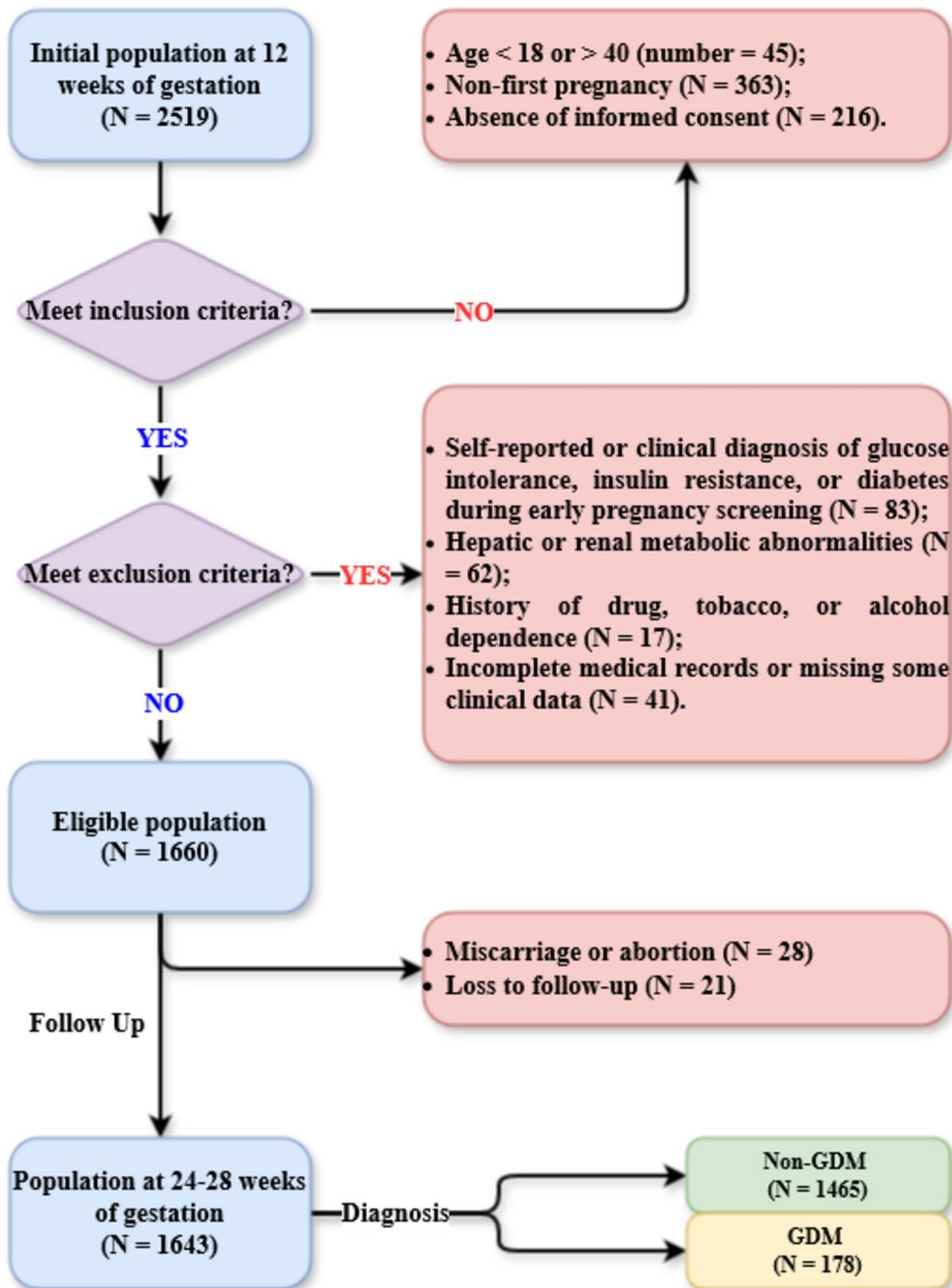


Fig. 1 Flow chart of participant selection and follow-up. N, number; GDM, gestational diabetes mellitus

tube containing sodium fluoride and potassium oxalate to inhibit glycolysis. Participants were then instructed to consume a 75-g glucose solution within 5 min. Additional 5 mL venous blood samples were collected at 1 h and 2 h post-ingestion using the same type of anticoagulant-containing tubes. All blood samples were immediately mixed to prevent clotting and then centrifuged at 2000 g for 10 min at 4 °C to separate plasma. Plasma glucose levels at each time point were measured using an automated biochemical analyser (Roche Cobas 501, Roche Diagnostics, USA) via enzymatic methods. According to the International Association of Diabetes and Pregnancy Study Groups criteria [15], GDM was diagnosed if any of the following conditions were met: (1) fasting plasma glucose level ≥ 5.1 mmol/L; (2) 1-hour plasma glucose level ≥ 10.0 mmol/L; or (3) 2-hour plasma glucose level ≥ 8.5 mmol/L.

Statistical analysis

Data are presented as numbers (percentages), means \pm standard deviations, or medians (interquartile ranges). Student's t-test and the Mann-Whitney U-test were used to compare normally and non-normally distributed continuous variables, respectively, between the

Table 1 Baseline characteristics of pregnant women at 12 weeks by GDM diagnosis at 24–28 weeks

Baseline characteristics at 12 weeks	Non-GDM at 24–28 weeks (Number = 1465)	GDM at 24–28 weeks (Number = 178)	P value
Age, years	27.6 \pm 3.9	31.2 \pm 4.2	< 0.001
Waist, cm	81.8 \pm 11.9	91.1 \pm 15.0	< 0.001
Height, cm	167.2 \pm 7.7	166.3 \pm 7.9	0.124
Smoking status, %			
No	1381 (94.3)	161 (90.4)	0.086
Former	56 (3.8)	13 (7.3)	
Yes	28 (1.9)	4 (2.2)	
Drinking status, %			
No	1118 (76.3)	141 (79.2)	0.388
Yes	347 (23.7)	37 (20.8)	
Fasting glucose, mmol/L	4.21 \pm 0.29	4.20 \pm 0.31	0.856
Triglyceride, mmol/L	1.01 (0.71–1.52)	2.64 (1.48–4.91)	< 0.001
HDL-c, mmol/L	0.67 (0.51–1.00)	0.46 (0.39–0.59)	< 0.001
CMI	0.78 (0.34–1.53)	3.28 (1.42–7.15)	< 0.001
Monocyte count, 10 ⁹ /L	0.30 (0.13–0.54)	0.73 (0.34–1.44)	< 0.001
Neutrophil count, 10 ⁹ /L	2.71 (2.06–3.49)	3.65 (2.70–4.60)	< 0.001
Lymphocyte count, 10 ⁹ /L	2.20 (1.70–2.80)	2.00 (1.63–2.57)	0.008
SIRI	0.34 (0.16–0.69)	1.15 (0.57–2.31)	< 0.001
Adipsin, ng/mL	4769.0 \pm 1076.7	3925.4 \pm 920.8	< 0.001

Data are presented as the mean \pm standard deviation, median (interquartile range), or number (percentage). P values are derived from the results of Student's t test, Mann-Whitney U test, or Chi-square test. CMI, cardiometabolic index; GDM, gestational diabetes mellitus; HDL-c, high density lipoprotein cholesterol; SIRI, systemic inflammation response index

GDM and non-GDM groups. Categorical variables were compared using the chi-square test. The CMI, SIRI, and adipsin were categorised into tertiles for further analysis, as this approach facilitates clinical and epidemiological interpretation by expressing results as odds ratios for different risk groups, accounts for potential non-linear relationships by avoiding the assumption of linearity, and minimises the influence of extreme values. Multi-variable logistic regression analysis was performed to evaluate the associations of CMI, SIRI, and adipsin with GDM, and to develop two predictive composite models for GDM. In the predictive model 1, CMI and SIRI were incorporated as independent variables, with GDM status as the dependent variable. Based on the logistic regression analysis, the equation for predictive model 1 in terms of the log-odds of GDM was generated as follows: $\text{logit}(p) = 0.522 \times \text{CMI} + 1.576 \times \text{SIRI} - 4.601$. The probability (p) of GDM was then derived from this equation using the inverse logit transformation: $p = \exp(\text{logit}(p)) / (1 + \exp(\text{logit}(p)))$. This generated probability was saved as a new variable (PRE_1) in the statistical software. In the predictive model 2, CMI, SIRI, and serum adipsin levels were entered as independent variables, with GDM as the dependent variable in the logistic regression analysis. Similarly, the equation for predictive model 2 in terms of the log-odds of GDM was: $\text{logit}(p) = 0.541 \times \text{CMI} + 1.722 \times \text{SIRI} - 0.001 \times \text{adipsin} - 0.531$. Following the same inverse logit transformation as in predictive model 1, the probability of predictive model 2 was generated and saved as another new variable (PRE_2) in the statistical software. These two predicted probabilities (PRE_1 and PRE_2) were subsequently used in receiver operating characteristic (ROC) curve analysis to assess and compare the predictive performance of the two composite models for identifying subsequent GDM. All statistical tests were two-tailed, and a P value < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS 20.0 software (IBM Corp., USA).

Results

Characteristics of the participants

A total of 1643 participants, with a mean age of 28.0 years, were included in the study. The baseline characteristics of women who underwent clinical examinations at 12 weeks of gestation are presented in Table 1, categorised by those with and without GDM at 28 weeks of gestation. Compared with their non-GDM counterparts, women with GDM were significantly older (31.2 \pm 4.2 years *versus* 27.6 \pm 3.9 years, $P < 0.001$) and had a greater waist circumference (91.1 \pm 15.0 cm *versus* 81.8 \pm 11.9 cm, $P < 0.001$). However, height did not differ significantly between the two groups ($P = 0.124$). There was also no significant difference in smoking status or alcohol consumption between groups. Although baseline fasting

glucose levels were comparable between groups, lipid and inflammatory markers, including TG, HDL-c, and monocyte count, were significantly higher in the GDM group. Additionally, serum adipsin levels were significantly lower in the GDM group compared with the non-GDM group (3925.4 ± 920.8 ng/mL versus 4769.0 ± 1076.7 ng/mL, $P < 0.001$).

Associations of adipsin, SIRI and CMI with GDM

The crude and adjusted relative risks (RRs) with 95% confidence intervals (CIs) are presented in Table 2. For CMI, women in the highest tertile had a significantly higher risk of GDM compared with those in the lowest tertile (crude RR=12.43, 95% CI: 7.06–21.87; adjusted RR=6.71, 95% CI: 3.68–12.23; both $P < 0.001$). The middle tertile was associated with increased risk in the crude model (crude RR=2.11, 95% CI: 1.10–4.03, $P = 0.024$), though this was not statistically significant after adjustment (adjusted RR=1.60, 95% CI: 0.83–3.07, $P = 0.169$). For the SIRI, the highest tertile was strongly associated with GDM (crude RR=9.92, 95% CI: 5.89–16.70; adjusted RR=7.61, 95% CI: 4.47–12.95; both $P < 0.001$). The middle tertile was not significantly associated with GDM in either model (crude RR=1.75, 95% CI: 0.95–3.22, $P = 0.073$; adjusted RR=1.59, 95% CI: 0.85–2.95, $P = 0.145$). For adipsin, women in the lowest tertile had a significantly increased risk (crude RR=8.53, 95% CI: 4.97–14.61; adjusted RR=6.37, 95% CI: 3.67–11.05; both $P < 0.001$). Similarly, the middle tertile was also associated with increased risk (crude RR=3.33, 95% CI: 1.87–5.93; adjusted RR=3.15, 95% CI: 1.75–5.67; both $P < 0.001$).

Table 2 Logistic regression analyses of cardiometabolic index, SIRI, and adipsin associations with gestational diabetes mellitus

Variable	Tertiles	Crude RR (95%CI)	P	Adjusted RR (95%CI)	P
Adipsin, ng/mL	T3 (≥ 5118.6)	Reference		Reference	
	T2 (4185.2–5118.6)	3.33 (1.87–5.93)	<0.001	3.15 (1.75–5.67)	<0.001
	T1 (<4185.2)	8.53 (4.97–14.61)	<0.001	6.37 (3.67–11.05)	<0.001
CMI	T1 (<0.53)	Reference		Reference	
	T2 (0.53–1.36)	2.11 (1.10–4.03)	0.024	1.60 (0.83–3.07)	0.169
	T3 (≥ 1.36)	12.43 (7.06–21.87)	<0.001	6.71 (3.68–12.23)	<0.001
SIRI	T1 (<0.23)	Reference		Reference	
	T2 (0.23–0.62)	1.75 (0.95–3.22)	0.073	1.59 (0.85–2.95)	0.145
	T3 (≥ 0.62)	9.92 (5.89–16.70)	<0.001	7.61 (4.47–12.95)	<0.001

Variables are divided into tertiles (T1, T2, and T3). RR, 95%CI, and P values are derived from the results of multivariable logistic regression analyses. Age, drinking status, and smoking status are included as covariates in the adjusted model. CI, confidence interval; CMI, cardiometabolic index; RR, relative risk; SIRI, systemic inflammation response index.

Statistical significance and model fit of predictive composite models

The statistical significance of variables in the predictive composite models was evaluated using the Wald test, and model fit was assessed with the Hosmer-Lemeshow test. In the model 1, the Wald values for CMI, SIRI, and the constant term were 127.61, 113.76, and 453.73, respectively ($P < 0.001$ for all); in the model 2, the Wald values for CMI, SIRI, adipsin, and the constant term were 115.64, 109.24, 67.76, and 1.21, respectively ($P < 0.001$ for all except for the constant term, $P = 0.271$). The Hosmer-Lemeshow test results demonstrated an adequate fit for both composite model 1 ($P = 0.517$) and composite model 2 ($P = 0.459$), indicating good agreement between the predicted and observed outcomes.

Combined adipsin, CMI, and SIRI for predicting GDM

As presented in Fig. 2; Table 3, the area under the curve (AUC) values for adipsin, the CMI, and the SIRI were 0.724, 0.825, and 0.802, respectively. The composite model 1 integrating CMI and SIRI has achieved an AUC of 0.898, while the composite model 2 additionally incorporated adipsin further improving the AUC to 0.918. The Youden index method was used to determine the optimal predicted probability cut-off points. For adipsin, the optimal cut-off was 4385.84 ng/mL, with a sensitivity of 0.730 and a specificity of 0.630. The optimal cut-off for CMI was 1.71, yielding a sensitivity of 0.713 and a specificity of 0.789. For SIRI, the optimal cut-off was 0.83, with corresponding sensitivity and specificity values of 0.669 and 0.831, respectively. The composite model 1 had an optimal cut-off of 0.075, with a sensitivity of 0.837 and a specificity of 0.802. For composite model 2, the optimal cut-off was 0.098, achieving a sensitivity of 0.843 and a specificity of 0.861.

Discussion

In this study, we investigated the associations of CMI, SIRI, and serum adipsin levels with the risk of GDM in a cohort of pregnant women. Our results indicate that reduced adipsin and elevated CMI and SIRI are significantly associated with an increased risk of GDM. These results suggest that these biomarkers could serve as potential predictors for GDM, with their combination improving predictive accuracy.

According to previous studies, the global prevalence of GDM varies considerably, with rates in the Western Pacific region ranging from 4.5 to 20.3% and a median prevalence of 10.3% [16]. In our study, the incidence of GDM was approximately 10.8% in 2023, which aligns with data from this region but is slightly lower than the 14.8% average reported for mainland China [17]. Possible explanations for this discrepancy include: (1) differences in inclusion and exclusion criteria—for instance,

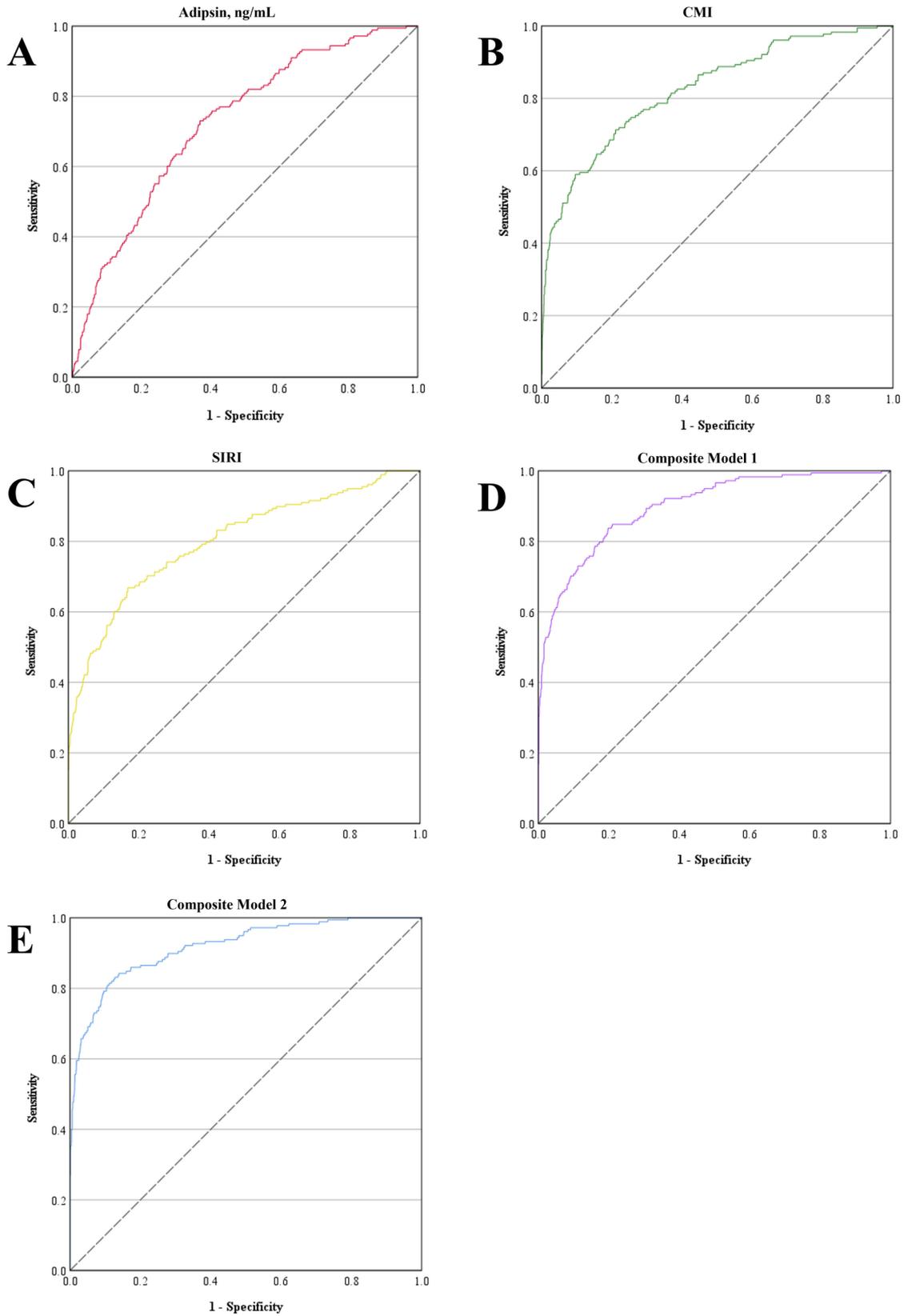


Fig. 2 ROC curves for predicting gestational diabetes mellitus. ROC curves were generated to assess the diagnostic performance of **A** adipsin, **B** CMI, **C** SIRI, **D** the predicted probability of composite model 1, and **E** the predicted probability of composite model 2. The composite model 1 integrates the CMI and SIRI, whereas the composite model 2 integrates the CMI, SIRI and adipsin. CMI, cardiometabolic index; ROC, receiver operating characteristic; SIRI, systemic inflammation response index

Table 3 The predictive efficacy of biomarkers for GDM development risk based on ROC analysis

Variable	AUC (95% CI)	Cut-off point	Sensitivity	Specificity
Adipsin	0.724 (0.687–0.762)	4385.84	0.730	0.630
CMI	0.825 (0.790–0.860)	1.71	0.713	0.789
SIRI	0.802 (0.764–0.841)	0.83	0.669	0.831
Composite model 1	0.898 (0.873–0.924)	0.075	0.837	0.802
Composite model 2	0.918 (0.894–0.941)	0.098	0.843	0.861

AUC, area under the curve; CI, confidence interval; CMI, cardiometabolic index; GDM, gestational diabetes mellitus; ROC, receiver operating characteristic; SIRI, systemic inflammation response index.

our study excluded women with early insulin resistance and abnormal glucose tolerance, which may have led to a lower reported incidence of GDM; (2) variations in confounding factors such as diet, socioeconomic status, and lifestyle across studies; and (3) our hospital's long-standing comprehensive health education and pregnancy guidance programme.

The association between CMI and GDM aligns with the role of metabolic dysregulation in the development of type 2 diabetes. A previous large population-based study reported that high CMI was strongly associated with diabetes [4], and this association has also been demonstrated in several recent studies [18–20]. However, few studies have examined the relationship between CMI and GDM. In our study, the positive association between CMI and GDM remained statistically significant after adjusting for age, alcohol consumption status, and smoking status, although the strength of association was slightly attenuated. This observation aligns with several previous studies linking lipid disorders to glucose intolerance and insulin resistance during pregnancy [21, 22]. For instance, in a study of 67 pregnant women, Daniel et al. demonstrated that elevated TG levels in early pregnancy were positively associated with insulin resistance and β -cell dysfunction during pregnancy [23]. Given the rising prevalence of metabolic disorders, CMI may serve as a non-invasive, cost-effective tool for the early identification of women at high risk of GDM.

Our findings also highlight the role of systemic inflammation, as measured by SIRI, in the development of GDM. Inflammation is widely recognised as a key factor in the pathogenesis of insulin resistance [24], which is central to the pathophysiology of GDM. We found that women in the highest SIRI tertile had a more than sevenfold increased risk of GDM. These findings support previous studies that link chronic low-grade inflammation to insulin resistance and glucose metabolism abnormalities. Prolonged inflammatory responses,

characterised by elevated levels of TNF- α and IL-6, disrupt insulin signalling pathways, reduce insulin sensitivity, and impair pancreatic β -cell function. TNF- α and other cytokines interfere with insulin receptor function by promoting serine phosphorylation of insulin receptor substrate-1, impairing glucose uptake in peripheral tissues such as muscle and adipose tissue. The inflammatory markers that constitute SIRI—neutrophils, lymphocytes, and monocytes—may play distinct roles in GDM-related immune dysregulation. Studies have shown that elevated neutrophil counts in pregnant women with GDM reflect a heightened state of systemic inflammation, as neutrophils are major contributors to reactive oxygen species (ROS) and proinflammatory cytokine production, which exacerbate insulin resistance [25, 26]. In contrast, a reduced lymphocyte count in GDM may indicate immune suppression, consistent with findings that pregnant women with hyperglycaemia exhibit altered adaptive immune responses [27]. Regarding monocytes, increased monocyte levels in GDM have been linked to heightened inflammatory activity, as monocytes can differentiate into macrophages and promote chronic low-grade inflammation by secreting IL-1 β , IL-6, and TNF- α . Nevertheless, findings on the association between monocytes and GDM remain inconsistent. Two population-based studies reported significantly elevated monocyte counts in GDM patients [28, 29], while another study found that a decreased gestational monocyte count was associated with GDM development [30]. These discrepancies highlight the limitations of using a single biomarker to predict GDM. The significant association between SIRI and GDM in our study underscores the critical role of inflammation in GDM development and management, reinforcing the potential of composite inflammatory markers like SIRI in GDM risk assessment.

To date, research on adipsin level changes and the mechanisms through which adipsin influences GDM remains limited. Two population-based studies reported that women with GDM have higher circulating adipsin levels than those with normal glucose tolerance. This suggests a possible compensatory mechanism to support insulin secretion and maintain glycaemic control during pregnancy, especially considering that both these studies used blood samples collected on the day of caesarean section at the end of pregnancy [31, 32]. Conversely, another study of 426 pregnant women found that GDM women aged over 35 years had lower adipsin levels, which partially aligns with our findings [33]. The inconsistent results regarding adipsin levels in GDM highlight the complexity of adipokine regulation during pregnancy. This complexity is influenced by factors such as maternal age, gestational stage, and study design, reinforcing the need for further research to clarify the role of adipsin and

other adipokines in GDM and their potential as biomarkers or therapeutic targets.

Both SIRI and CMI demonstrated good predictive accuracy for GDM ($0.8 \leq AUC < 0.9$), whereas the combination of SIRI, CMI, and serum adiponin markedly improved predictive accuracy to an excellent level ($0.9 \leq AUC < 1.0$), although adiponin alone exhibited only fair predictive accuracy ($0.7 \leq AUC < 0.8$) [34]. These findings suggest that a multibiomarker approach could enhance the early detection of GDM risk, allowing for timely intervention to mitigate adverse pregnancy outcomes. The clinical implications of CMI and SIRI are substantial. Unlike adiponin, all variables required to calculate CMI and SIRI are routinely measured during pregnancy, eliminating the need for additional invasive or costly tests. Given that the composite model incorporating only CMI and SIRI without adiponin still demonstrated near-excellent predictive accuracy ($AUC = 0.898$), these two indices alone may provide a practical alternative in clinical settings where adiponin measurement is not feasible.

Our study has several strengths, including a large real-world sample size and cost-effective multibiomarker prediction models. However, certain limitations should be considered. All participants were recruited from a single institution in China, limiting the generalizability of our findings to populations with different genetic and environmental backgrounds. In addition, the underlying mechanistic pathways linking these biomarkers to GDM development were not fully elucidated in this study. Future studies should aim to validate these biomarkers in diverse populations and further explore their underlying mechanisms.

In conclusion, our findings suggest that low adiponin levels, high CMI and SIRI in early pregnancy are significant risk factors for GDM. The combination of these biomarkers provides a promising approach for the early identification of women at risk for GDM, potentially facilitating timely interventions and improving maternal and foetal outcomes. Further research is warranted to confirm these findings and explore their clinical applications in GDM screening.

Abbreviations

CMI	cardiometabolic index
GDM	gestational diabetes mellitus
HDL-c	high-density lipoprotein cholesterol
RR	relative risk
ROC	receiver operating characteristic
SIRI	systemic inflammation response index
TG	triglyceride

Acknowledgements

We would like to thank all the participants for their participation and cooperation.

Author contributions

M.C., C.F., and Y.H. contributed to the conception and design of the study. M.C., X.J., X.X., S.Z., Y.S., and P.Y. performed the experiments and collected and

organized the original data. M.C. and X.J. performed the statistical analysis. Y.Y. prepared the tables and figures. M.C., X.J., and X.X. contributed to the discussion and wrote the first draft of the manuscript. C.F. and Y.H. edited the final manuscript. All the authors reviewed and approved the final version of the manuscript.

Funding

This study was supported by grants from the Suzhou Science and Education Strengthening Health Youth Project (KJXW2021011), the Suzhou Medical Innovation and Application Research Project (SKY2023119), the Extracurricular Academic Research Fund for Undergraduates (KY2024266B), and the Priority Academic Program Development of Jiangsu Higher Education Institutions.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request and with the permission of the Second Affiliated Hospital of Soochow University.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of The Second Affiliated Hospital of Soochow University, and signed informed consent forms were obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Clinical Nutrition Division, The Second Affiliated Hospital of Soochow University, No.1055 San Xiang Road, Suzhou 215000, Jiangsu, China

²School of Public Health, Suzhou Medical College of Soochow University, No.199 Ren Ai Road, Suzhou 215000, Jiangsu, China

Received: 25 January 2025 / Accepted: 17 April 2025

Published online: 02 May 2025

References

- Dennison RA, Chen ES, Green ME, Legard C, Kotecha D, Farmer G, et al. The absolute and relative risk of type 2 diabetes after gestational diabetes: A systematic review and meta-analysis of 129 studies. *Diabetes Res Clin Pract.* 2021;171:108625. <https://doi.org/10.1016/j.diabres.2020.108625>.
- Murray SR, Reynolds RM. Short-and long-term outcomes of gestational diabetes and its treatment on fetal development. *Prenat Diagn.* 2020;40(9):1085–91. <https://doi.org/10.1002/pd.5768>.
- Karami M, Mousavi SH, Rafiee M, Heidari R, Shahrokhi SZ. Biochemical and molecular biomarkers: unraveling their role in gestational diabetes mellitus. *Diabetol Metab Syndr.* 2023;15(1):5. <https://doi.org/10.1186/s13098-023-00980-8>.
- Wakabayashi I, Daimon T. The cardiometabolic index as a new marker determined by adiposity and blood lipids for discrimination of diabetes mellitus. *Clin Chim Acta.* 2015;438:274–8. <https://doi.org/10.1016/j.cca.2014.08.042>.
- Zhou YY, Wang YQ, Wu TT, Zhang AQ, Li YS. Association between obesity and systemic immune inflammation index, systemic inflammation response index among US adults: a population-based analysis. *Lipids Health Dis.* 2024;23(1):245. <https://doi.org/10.1186/s12944-024-02240-8>.
- Pan J, Li QY, Sun Y, Gu YY, Ding YJ, Pang NZ, et al. Increased serum adiponin correlates with MAFLD and metabolic risk abnormalities. *Diabetes Metab Syndr Obes.* 2023;16:187–200. <https://doi.org/10.2147/Dmso.S396335>.
- Tafere GG, Wondafrash DZ, Zewdie KA, Assefa BT, Ayza MA. Plasma adiponin as a biomarker and its implication in type 2 diabetes mellitus. *Diabetes Metab Syndr Obes.* 2020;13:1855–61. <https://doi.org/10.2147/Dmso.S253967>.
- Bansal A, Honnapurmath VK, Singh A. Serum adiponin levels as a new marker in type 2 diabetes mellitus: A meta-analysis. *Int J Diabetes Dev Ctries.* 2025;1–7. <https://doi.org/10.1007/s13410-025-01449-2>

9. Wang J-S, Lee W-J, Lee I-T, Lin S-Y, Lee W-L, Liang K-W, et al. Association between serum adipsin levels and insulin resistance in subjects with various degrees of glucose intolerance. *J Endocr Soc.* 2019;3(2):403–10. <https://doi.org/10.1210/je.2018-00359>.
10. Zhang J, Li K, Pan L, Teng F, Zhang P, Lin B, et al. Association of Circulating adipsin with nonalcoholic fatty liver disease in obese adults: a cross-sectional study. *BMC Gastroenterol.* 2021;21:1–9. <https://doi.org/10.1186/s12876-021-01721-9>.
11. Zhang JH, Teng F, Pan LL, Guo D, Liu JF, Li KL, et al. Circulating adipsin is associated with asymptomatic carotid atherosclerosis in obese adults. *BMC Cardiovasc Disord.* 2021;21(1):1–9. <https://doi.org/10.1186/s12872-021-0232-9-3>.
12. Wang Y, Zheng X, Xie X, Qian W, Zhang L, Ren W. Correlation of increased serum adipsin with increased cardiovascular risks in adult patients with growth hormone deficiency. *Endocr Pract.* 2019;25(5):446–53. <https://doi.org/10.4158/EP-2018-0541>.
13. Ryan H, Troscclair A, Gfroerer J. Adult current smoking: differences in definitions and prevalence Estimates—NHIS and NSDUH, 2008. *J Environ Public Health.* 2012;2012:1–11. <https://doi.org/10.1155/2012/918368>.
14. Fan JG, Farrell GC. Epidemiology of non-alcoholic fatty liver disease in China. *J Hepatol.* 2009;50(1):204–10. <https://doi.org/10.1016/j.jhep.2008.10.010>.
15. Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PM, Damm P, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care.* 2010;33(3):676–82. <https://doi.org/10.2337/dc09-1848>.
16. McIntyre HD, Catalano P, Zhang C, Desoye G, Mathiesen ER, Damm P. Gestational diabetes mellitus. *Nat Reviews Disease Primers.* 2019;5(1):47. <https://doi.org/10.1038/s41572-019-0098-8>.
17. Gao CH, Sun X, Lu L, Liu FW, Yuan J. Prevalence of gestational diabetes mellitus in Mainland China: A systematic review and meta-analysis. *J Diabetes Investig.* 2019;10(1):154–62. <https://doi.org/10.1111/jdi.12854>.
18. Zha FB, Cao CC, Hong MR, Hou HL, Zhang QH, Tang B, et al. The nonlinear correlation between the cardiometabolic index and the risk of diabetes: A retrospective Japanese cohort study. *Front Endocrinol (Lausanne).* 2023;14:1120277. <https://doi.org/10.3389/fendo.2023.1120277>.
19. Song JM, Li YM, Zhu JX, Liang J, Xue S, Zhu ZZ. Non-linear associations of cardiometabolic index with insulin resistance, impaired fasting glucose, and type 2 diabetes among US adults: a cross-sectional study. *Front Endocrinol (Lausanne).* 2024;15:1341828. <https://doi.org/10.3389/fendo.2024.1341828>.
20. Hewage N, Wijesekara U, Perera R. Effectiveness of cardiometabolic index, lipid accumulation product, visceral adiposity index and waist-to-thigh ratio for the early diagnosis of diabetes in young females at childbearing age who were obese or non-obese. *Clin Epidemiol Global Health.* 2024;30:101783. <https://doi.org/10.1016/j.cegh.2024.101783>.
21. Rico JE, Specker B, Perry CA, McFadden JW. Plasma ceramides and triglycerides are elevated during pregnancy in association with markers of insulin resistance in hutterite women. *Lipids.* 2020;55(4):375–86. <https://doi.org/10.1002/lipd.12247>.
22. Zhu HY, He D, Liang N, Lai AL, Zeng JB, Yu HL. High serum triglyceride levels in the early first trimester of pregnancy are associated with gestational diabetes mellitus: A prospective cohort study. *J Diabetes Investig.* 2020;11(6):1635–42. <https://doi.org/10.1111/jdi.13273>.
23. Eppel D, Feichtinger M, Lindner T, Kotzaeridi G, Rosicky I, Yerlikaya-Schatten G, et al. Association between maternal triglycerides and disturbed glucose metabolism in pregnancy. *Acta Diabetol.* 2021;58(4):459–65. <https://doi.org/10.1007/s00592-020-01644-z>.
24. Wu HZ, Ballantyne CM. Metabolic inflammation and insulin resistance in obesity. *Circ Res.* 2020;126(11):1549–64. <https://doi.org/10.1161/Circresaha.119.315896>.
25. Saucedo R, Ortega-Camarillo C, Ferreira-Hermosillo A, Díaz-Velázquez MF, Meixueiro-Calderón C, Valencia-Ortega J. Role of oxidative stress and inflammation in gestational diabetes mellitus. *Antioxidants.* 2023;12(10):1812. <https://doi.org/10.3390/antiox12101812>.
26. Sun T, Meng F, Zhao H, Yang M, Zhang R, Yu Z, et al. Elevated First-Trimester neutrophil count is closely associated with the development of maternal gestational diabetes mellitus and adverse pregnancy outcomes. *Diabetes.* 2020;69(7):1401–10. <https://doi.org/10.2337/db19-0976>.
27. McElwain C, McCarthy F, McCarthy C. Gestational diabetes mellitus and maternal immune dysregulation: what we know so far. *Int J Mol Sci.* 2021;22(8):4261. <https://doi.org/10.3390/ijms22084261>.
28. Yang HL, Zhu CY, Ma QL, Long Y, Cheng Z. Variations of blood cells in prediction of gestational diabetes mellitus. *J Perinat Med.* 2015;43(1):89–93. <https://doi.org/10.1515/jpm-2014-0007>.
29. Wang J, Zhu QW, Cheng XY, Sha CX, Cui YB. Clinical significance of neutrophil-lymphocyte ratio and monocyte-lymphocyte ratio in women with hyperglycemia. *Postgrad Med.* 2020;132(8):702–8. <https://doi.org/10.1080/00325481.2020.1764235>.
30. Huang X, Zha B, Zhang M, Li Y, Wu Y, Zhang R, et al. Decreased monocyte count is associated with gestational diabetes mellitus development, macrosomia, and inflammation. *J Clin Endocrinol Metabolism.* 2022;107(1):192–204. <https://doi.org/10.1210/clinem/dgab657>.
31. Saucedo R, Valencia J, Moreno-González LE, Peña-Cano MI, Aranda-Martínez A, García Y, et al. Maternal serum adipokines and inflammatory markers at late gestation and newborn weight in mothers with and without gestational diabetes mellitus. *Ginekol Pol.* 2022;93(2):126–33. <https://doi.org/10.5603/GP.a2021.0083>.
32. McElwain CJ, Manna S, Musumeci A, Sylvester I, Rouchon C, O'Callaghan AM, et al. Defective visceral adipose tissue adaptation in gestational diabetes mellitus. *J Clin Endocrinol Metabolism.* 2024;109(5):1275–84. <https://doi.org/10.1210/clinem/dgad699>.
33. Tangjittipokin W, Narkdontri T, Teerawattanapong N, Thanatummat B, Wardati F, Sunsaneevithayakul P, et al. The variants in ADIPOQ are associated with maternal Circulating adipokine profile in gestational diabetes mellitus. *J Multidisciplinary Healthc.* 2023;309–19. <https://doi.org/10.2147/JMDH.S396238>.
34. Carter JV, Pan JM, Rai SN, Galandiuk S. ROC-ing along: evaluation and interpretation of receiver operating characteristic curves. *Surgery.* 2016;159(6):1638–45. <https://doi.org/10.1016/j.surg.2015.12.029>.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.