Diabetes, Metabolic Syndrome and Obesity

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

The Role of METS-IR in Early Screening for Gestational Diabetes Mellitus in Chinese Women: A Two-Center Prospective Study

Junxiang Gao[1], Shuoning Song[1], Yanbei Duo[1], Shihan Wang[1], Xiaolin Qiao[2], Yuemei Zhang[3], Jiyu Xu[4], Jing Zhang[5], Xiaorui Nie[2], Qiujin Sun[6], Xianchun Yang[6], Ailing Wang[7], Wei Sun[4], Yong Fu[1], Mengmeng Zhang[1], Yingyue Dong[1], Zechun Lu[7], Tao Yuan[1,*], Weigang Zhao[1,*]

[1]Department of Endocrinology, Key Laboratory of Endocrinology, Ministry of Health, Peking Union Medical College Hospital, Chinese Academy of Medical Science and Peking Union Medical College, Beijing, People's Republic of China; [2]Department of Obstetrics, Beijing Chaoyang District Maternal and Child Health Care Hospital, Beijing, People's Republic of China; [3]Department of Obstetrics, Haidian District Maternal and Child Health Care Hospital, Beijing, People's Republic of China; [4]Core Facility of Instrument, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences, School of Basic Medicine, Peking Union Medical College, Beijing, People's Republic of China; [5]Department of Laboratory, Haidian District Maternal and Child Health Care Hospital, Beijing, People's Republic of China; [6]Department of Clinical Laboratory, Beijing Chaoyang District Maternal and Child Health Care Hospital, Beijing, People's Republic of China; [7]National Center for Women and Children's Health, Chinese Center for Disease Control and Prevention, Beijing, People's Republic of China

*These authors contributed equally to this work

Correspondence: Tao Yuan; Weigang Zhao, Email t75y@sina.com; xiehezhaoweigang@163.com

Objective: This two-center prospective cohort study aimed to evaluate the predictive value of the Metabolic Score for Insulin Resistance (METS-IR) for gestational diabetes mellitus (GDM) in Chinese women during early pregnancy and compare its performance with conventional insulin resistance (IR) indices.

Methods: This prospective investigation evaluated 1450 Chinese gravidas (<12 gestational weeks) without pregestational diabetes from two obstetrical institutions. Baseline clinical-biochemical profiling occurred during the first trimester (6–12 weeks), with GDM confirmation via standardized 75g oral glucose tolerance testing at 24–28 weeks' gestation. Analytical methodologies incorporated multivariable regression modeling and ROC curve optimization to quantify the predictive validity of five metabolic indices (METS-IR, TyG index, TG/HDL-C ratio, HOMA-IR, TyG-BMI) for GDM risk stratification.

Results: Among participants, 378 (26.1%) developed GDM. The GDM group (n=378, 26.1%) was older (median age 31.0 vs 30.0 years, p<0.0001) and had higher prepregnancy BMI (22.62 vs 21.32 kg/m², p<0.0001), fasting glucose (4.7 vs 4.5 mmol/L, p<0.0001) compared to NGT. The GDM group exhibited significantly higher METS-IR (31.14 vs 29.03, p <0.001) and other IR indices (p <0.001). In unadjusted models, METS-IR quartile 4 (Q4) was strongly associated with GDM (OR=3.33, 95% CI:2.38–4.70), but this association attenuated after adjusting for age, weight gain, lipids, and insulin (adjusted OR=1.56, 95% CI:1.04–2.35). Comparatively, the TyG index (adjusted OR=3.06, 95% CI:2.03–4.66) and TG/HDL-C ratio (adjusted OR=2.02, 95% CI:1.38–2.99) retained robust predictive power. ROC analysis revealed a moderate discriminative capacity for METS-IR (AUC=0.629 unadjusted; 0.676 fully adjusted), outperformed by HOMA-IR (AUC=0.699) and TyG (AUC=0.699). METS-IR demonstrated high specificity (76.2%) in unadjusted screening but showed dependency on metabolic confounders in adjusted models.

Conclusion: METS-IR shows promise for early GDM screening and is outperformed by TyG and HOMA-IR in predictive value. METS-IR in early pregnancy reflects metabolic dysregulation linked to GDM risk, yet its predictive utility is partially mediated by lipid and insulin abnormalities. While METS-IR offers clinical feasibility through routine measurements, TyG and HOMA-IR exhibit superior independent predictive value. These findings highlight the importance of context-specific IR indices for early GDM risk stratification and underscore METS-IR's role as a composite marker of metabolically unhealthy obesity in pregnancy.

Keywords: gestational diabetes mellitus, METS-IR, early pregnancy, insulin resistance, prospective cohort, predictors

Received: 25 May 2025
Accepted: 17 September 2025
Published: 25 October 2025

Background

Gestational Diabetes Mellitus (GDM) denotes glucose intolerance newly identified in pregnancy, with standard diagnostic confirmation occurring during the second trimester (weeks 24–28) through systematic metabolic evaluation.[1] GDM confers immediate clinical risks to maternal well-being while potentially inducing developmental sequelae in offspring, such as macrosomia, dysregulated organogenesis, and heightened lifelong propensity for metabolic dysregulation.[2] Contemporary epidemiological surveillance reveals a pronounced global escalation in GDM prevalence, now recognized as a critical public health priority. Nationally representative data from the United States illustrate this trend, with GDM prevalence rates demonstrating a near-tripling increase from baseline estimates of 9% to current levels exceeding 25%.[3] Chinese epidemiological investigations reveal a gestational diabetes prevalence rate of 14.8%, with established risk determinants including advanced maternal age, prepregnancy adiposity, and genetic predisposition to diabetes.[4] GDM compromises maternal-fetal health by inducing perinatal complications such as neonatal hypoglycemia and macrosomia, while establishing lifelong metabolic vulnerabilities that heighten diabetes susceptibility in both maternal and offspring populations.[5] Elucidating the pathophysiological origins, modifiable risk determinants, and their mechanistic interactions with metabolic dysregulation patterns in GDM constitutes a critical research imperative for optimizing perinatal outcomes and preventive strategies. Early identification of GDM risk using accessible indices like METS-IR can enable timely interventions (eg, lifestyle modifications), reducing perinatal complications such as macrosomia and neonatal hypoglycemia. This is critical in resource-limited settings where complex tests are impractical.

The euglycemic–hyperinsulinemic clamp (EHC) is the gold standard for assessing insulin resistance; however, its complexity, high cost, and time-consuming nature limit its widespread application. In 2018, Bello-Chavolla OY et al developed METS-IR as a practical and effective surrogate biomarker for insulin resistance (IR), serving as an alternative to EHC.[6] Research indicates that METS-IR is more effective than other non-insulinogenic insulin resistance indices.[6] It combines body mass index (BMI), fasting plasma glucose (FPG), fasting triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C). The formula, Ln((2×FPG (mg/dL))+TG (mg/dL))×BMI)/(Ln(HDL-C (mg/dL))), integrates traditional indicators of reduced insulin sensitivity, dysglycemia and dyslipidemia) while incorporating pregnancy-specific metabolic adaptations. Besides METS-IR, several insulin resistance scores have been extensively researched, including the homeostatic model assessment for IR (HOMA-IR), the triglyceride-glucose index (TyG index), the TyG-BMI index, and the triglyceride to HDL-C ratio (TG/HDL-C ratio). The TyG index surpasses METS-IR in predicting type 2 diabetes, particularly among individuals with normal blood glucose levels.[7] Specifically, Harding et al pointed out that the TyG index is positively correlated with the risk of T2DM, providing a new perspective for its clinical application.[8] However, in the study of gestational diabetes mellitus, HOMA-IR, TyG, TG/HDL-C and TyG-BMI have their own advantages. As a traditional indicator, HOMA-IR provides a classical assessment method for insulin resistance,[9] while TyG,[10] TG/HDL-C[11] and TyG-BMI[12] provide a more flexible and multi-dimensional assessment method. TyG and HOMA-IR have shown strong GDM predictive value in prior studies,[10,12] but METS-IR's utility in pregnancy remains unexplored, warranting this investigation. Although METS-IR has shown good performance in assessing insulin resistance, its application value may vary in different clinical contexts.[6] Moreover, the mechanisms of insulin resistance are complex and involve multiple metabolic pathways, supporting the validity of different scores.[13] Currently, there are no studies on the application of METS-IR in GDM. Therefore, in this study, we aim to evaluate the relationship between indicators related to metabolic syndrome, and the occurrence of GDM during early pregnancy, and to explore the risk factors for gestational diabetes.

Materials and Methods

This study is part of a prospective, multicenter cohort study aimed at identifying biomarkers of GDM in early pregnancy and establishing an effective model for early prediction of GDM. Women were recruited during pre-pregnancy counseling or first antenatal visits, with clinical investigations (eg, BMI, blood tests) conducted at enrollment (6–12 weeks). Pre-pregnancy BMI was self-reported and verified using medical records, minimizing recall bias. OGTT at 24–28 weeks served as the diagnostic gold standard. This prospective study was initiated in 2019 at the Haidian Maternal and Child Health Hospital and Chaoyang Maternal and Child Health Hospital in China. Haidian and Chaoyang Maternal and Child Health Hospitals were chosen as high-volume urban centers with diverse socioeconomic populations, ensuring

generalizability to Chinese urban settings. All available clinical and laboratory data of all participants in this study were simultaneously recorded and verified by two researchers.

Study Participants

The study cohort selection criteria focused on three key inclusion elements: pregnant women ≤12 gestational weeks (confirmed by ultrasonography), aged ≥18 years, able to commit to regular antenatal visits from enrollment until delivery, and providing informed consent were enrolled. Participants were excluded for any of the following: (1) Non-singleton pregnancy; (2) Pre-existing diabetes mellitus (any type) or impaired glucose tolerance; (3) Severe systemic comorbidities, including but not limited to cardiovascular, endocrine, autoimmune, renal, pulmonary, hepatobiliary, gastrointestinal, or hematologic diseases; (4) Use of any medications during pregnancy except folic acid, prenatal vitamins, iron supplements, or progesterone; (5) Inability to comply with study protocols or attend follow-up visits; (6) Other conditions deemed unsuitable for participation by the investigators. Convenience sampling was used for pregnant women attending routine first-trimester visits, with consecutive enrollment to minimize selection bias. From an initial pool of 2,284 eligible participants with comprehensive first-trimester clinical data (6–12 gestational weeks), GDM diagnosis was subsequently determined through standardized oral glucose tolerance testing performed during 24–28 gestational weeks. Perinatal outcomes data for 1,450 subjects were subsequently extracted from institutional electronic health records (Figure 1). A power analysis indicated that with n=1,450, α=0.05, and effect size=0.3, power exceeded 90% for detecting GDM risk associations. Ethical approval was obtained from the National Center for Women and Children's Health Ethics Committee (Approval: FY2019-01). All participants provided written informed consent, with data anonymized and stored securely. The investigation received multicentric ethical review board approval and was executed in compliance with China's Major New Drug Development Initiative (ClinicalTrials.gov identifier: NCT03246295). All participants provided written informed consent prior to enrollment, with study procedures adhering to the ethical principles outlined in the 2013 revision of the Helsinki Declaration.

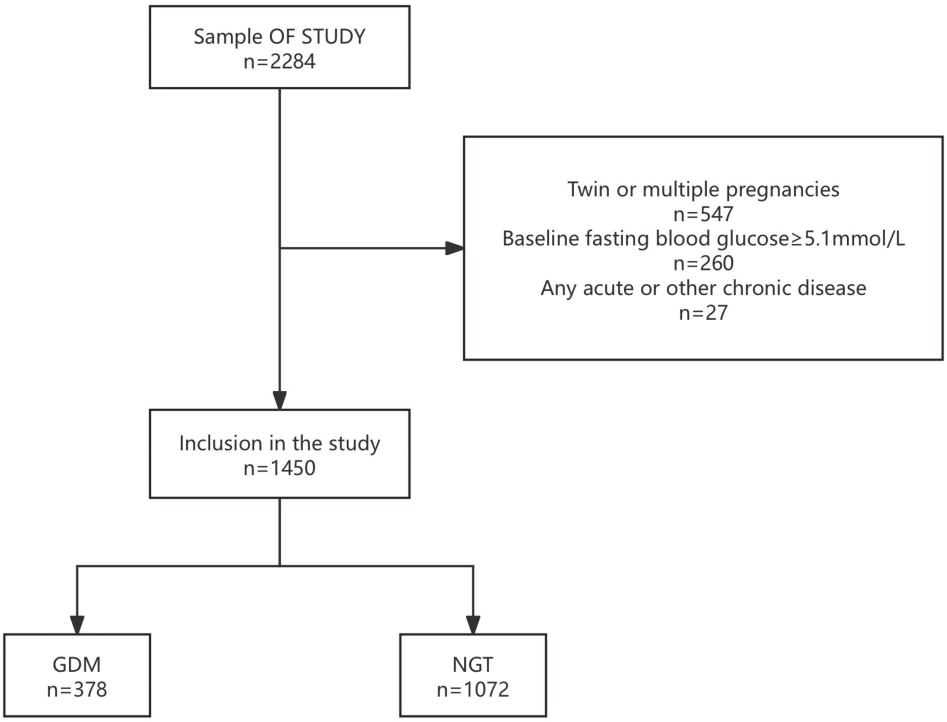

Figure 1 Population flow chart for predicting gestational diabetes using METS-IR score in the first trimester.
Abbreviations: GDM, gestational diabetes mellitus; NGT, non Gestational diabetes mellitus.

https://doi.org/10.2147/DMSO.S538992

Insulin Resistance Metrics

IR was assessed using five metrics: HOMA-IR, METS-IR, TyG index, TyG-BMI index, and TG/HDL-C. The HOMA-IR was calculated based on FPG and insulin levels using the formula: (FPG [mg/dL] × fasting insulin [μU/mL]) / 405.[14,15] METS-IR was calculated using the formula: (Ln[(2 × FPG) + TG] × BMI) / (Ln[HDL-C]), incorporating FPG, TG, HDL-C, and BMI. The TyG index is calculated using the formula: Ln(TG [mg/dL] × FPG [mg/dL] / 2).[16,17] BMI was determined by dividing weight in kilograms by the square of height in meters. The TyG-BMI was calculated using the formula: TyG-BMI = ln[(TG in mg/dL × glucose in mg/dL) ÷ 2] × BMI.[18] The TG/HDL-C ratio was derived from fasting triglycerides and high-density lipoprotein cholesterol using the formula: TG/HDL-C = TG in mg/dL ÷ HDL-C in mg/dL.[19]

Statistical Analysis

R software (version 4.3.1) was used for statistical analyses. Continuous variables with approximate normal distribution were presented as mean ± standard deviation, and independent t-tests were used for intergroup comparisons. Non-normally distributed metrics were summarized as medians with interquartile ranges and analyzed using Mann–Whitney *U*-tests. Categorical parameters were expressed as frequencies (percentages) and analyzed using Pearson's chi-square tests. Associations between variables were assessed using Pearson's correlation coefficients for normally distributed data and Spearman's rank correlation for non-normally distributed data. Independent risk factors for GDM were identified using both univariate and multivariate binary logistic regression models, with findings presented as odds ratios (OR) and 95% confidence intervals (CI). Predictive performance was evaluated using ROC curve analysis, measuring diagnostic accuracy through AUC, sensitivity, and specificity. A two-tailed $p<0.05$ defined statistical significance across all analytical procedures.

Results

Study Population

Within the study cohort comprising 1,450 participants, 378 cases (26.1%) developed GDM. Table 1 presents a systematic comparison of demographic characteristics, obstetric outcomes, and infant parameters between individuals with GDM and those with normal glucose tolerance (NGT). Among the 1,450 pregnant women studied, the GDM group was older (median age 31.0 [IQR 28.0–34.0] years) compared to the NGT group (30.0 [27.0–32.0] years, $p<0.0001$). Additionally, the GDM group exhibited higher pre-pregnancy weight (58.25 [53.0–65.0] kg vs 56.0 [51.0–62.0] kg), BMI (22.62 [20.43–24.84] kg/m² vs 21.32 [19.60–23.15] kg/m²), fasting blood glucose levels (4.7 [4.3–5.1] mmol/L vs 4.5 [4.1–4.8] mmol/L), and insulin resistance index (HOMA-IR 1.59 [1.03–2.29] vs 1.20 [0.82–1.70]).51[1.19–2.16] vs 1.29[0.96–-1.80]) (all $p<0.0001$). Triglyceride levels were elevated in the GDM group (0.98 [0.75–1.29] vs 0.83 [0.64–1.09] mmol/L, $p<0.0001$), along with non Pregnancy-induced hypertension (2.12% vs 0.19%, $p=0.0004$). LDL-C (2.09 vs 1.98 mmol/L, $p=0.0002$), ALT (15.00 vs 12.60 IU/L, $p<0.0001$), and uric acid (217.00 vs 204.00 μmol/L, $p<0.0001$) were higher in GDM. LGA incidence was higher in GDM (15.3% vs 8.1%, $p<0.001$). However, no significant differences were observed between the groups regarding gestational distribution ($p=0.533$), diastolic blood pressure ($p=0.3842$), and blood urea nitrogen ($p>0.05$). The lack of association between family history and GDM in this cohort suggests that metabolic dysregulation, not genetics, drove risk stratification.

Biochemical Measures According to the Insulin Resistance Index

When the study population was stratified by METS-IR quartiles (Table 2), the Q4 group (highest insulin resistance group) exhibited significantly worse metabolic disturbances and an elevated trend of GDM risk compared to the Q1 group (lowest quartile). With increasing METS-IR quartiles, prepregnancy BMI (Q4: 25.68 ± 2.72 vs Q1: 18.63 ± 2.18 kg/m²), fasting glucose (Q4: 4.68 ± 0.63 vs Q1: 4.40 ± 0.63 mmol/L), fasting insulin (Q4: 10.26 ± 5.63 vs Q1: 5.49 ± 3.09 μIU/mL), and triglycerides (Q4: 1.40 ± 0.82 vs Q1: 0.71 ± 0.27 mmol/L) demonstrated progressive elevations (all $P < 0.001$). Concurrently, high-density lipoprotein (HDL-C) levels were markedly reduced in Q4 (1.43 ± 0.37 vs Q1: 1.47 ± 0.33 mmol/L, $P = 0.031$), strongly indicating a correlation between METS-IR and glucolipid metabolic dysfunction. Furthermore, systolic blood pressure (113.72 ± 10.50 vs 110.00 ± 9.89 mmHg, $P < 0.001$), uric acid levels (240.72 ± 59.63 vs 190.63 ± 49.89 μmol/L, $P < 0.001$), and GDM incidence (specific rates to be supplemented) were significantly

Table 1 Presents a Comparison of Sociodemographic Variables, Fasting Biochemical Measures, and Surrogate Fasting Insulin Resistance Indexes Between Subjects with Gestational Diabetes Mellitus and Those in the Discovery Sample

Parameter		Overall (n=1450)	NGT (n=1072)	GDM (n=378)	P-value
Age		30.000 [28.000, 33.000]	30.000 [27.000, 32.000]	31.000 [28.000, 34.000]	<0.0001
FDM	0	1121 (77.31)	833 (77.71)	288 (76.19)	0.5939
	1	329 (22.69)	239 (22.29)	90 (23.81)	
Prepregnancy weight (kg)		56.150 [52.000, 62.000]	56.000 [51.000, 62.000]	58.250 [53.000, 65.000]	<0.0001
Gestational weight gain rate (%)		0.218 [0.161, 0.287]	0.233 [0.176, 0.300]	0.187 [0.132, 0.250]	<0.0001
Prepregnancy BMI (kg/m^2)		21.514 [19.913, 23.508]	21.319 [19.603, 23.147]	22.623 [20.429, 24.840]	<0.0001
Systolic blood pressure (mmHg)		110.000 [105.000, 120.000]	110.000 [104.000, 120.000]	111.500 [106.250, 120.000]	0.0764
Diastolic blood pressure (mmHg)		70.000 [64.000, 75.000]	70.000 [64.000, 75.000]	70.000 [64.000, 75.000]	0.3842
Fasting glucose (mmol/L)		4.500 [4.200, 4.900]	4.500 [4.100, 4.800]	4.700 [4.300, 5.100]	<0.0001
Fasting insulin (μl/mL)		6.400 [4.400, 9.100]	6.100 [4.200, 8.400]	7.750 [4.900, 10.875]	<0.0001
Total cholesterol (mmol/L)		3.960 [3.490, 4.518]	3.930 [3.470, 4.480]	4.010 [3.580, 4.637]	0.0086
Triglycerides (mmol/L)		0.860 [0.650, 1.150]	0.830 [0.637, 1.090]	0.980 [0.750, 1.290]	<0.0001
HDL-C (mmol/L)		1.460 [1.240, 1.660]	1.460 [1.250, 1.670]	1.430 [1.210, 1.610]	0.1085
LDL-C (mmol/L)		2.005 [1.680, 2.438]	1.980 [1.660, 2.393]	2.090 [1.732, 2.578]	0.0002
ALT (IU/L)		13.000 [10.000, 18.675]	12.600 [10.000, 17.615]	15.000 [11.000, 20.890]	<0.0001
Serum creatinin (umol/L)		47.280 [43.000, 51.385]	47.000 [43.000, 51.000]	48.000 [43.000, 52.238]	0.036
Urea (umol/L)		3.000 [2.600, 3.547]	2.975 [2.587, 3.515]	3.070 [2.615, 3.610]	0.0996
Uric acid (umol/L)		207.000 [177.300, 240.280]	204.000 [173.000, 233.490]	217.000 [187.550, 261.638]	<0.0001
METS-IR		29.475 [26.628, 32.892]	29.026 [26.307, 31.970]	31.136 [27.808, 35.572]	<0.0001
TYG		8.045 [7.754, 8.345]	7.988 [7.707, 8.282]	8.186 [7.929, 8.496]	<0.0001
TYGBMI		172.514 [156.968, 192.079]	169.670 [154.900, 186.723]	183.599 [164.328, 209.623]	<0.0001
HOMAIR		1.268 [0.855, 1.848]	1.195 [0.821, 1.699]	1.593 [1.028, 2.289]	<0.0001
TGHDL		1.337 [1.015, 1.881]	1.285 [0.964, 1.803]	1.513 [1.187, 2.157]	<0.0001
Neonatal outcomes (%)	Normal infants	1380 (95.17)	1019 (95.06)	361 (95.50)	0.263
	Premature infants	42 (2.90)	32 (2.99)	10 (2.65)	
	Low birth weight infants	17 (1.17)	15 (1.40)	2 (0.53)	
	Asphyxia neonatorum	1 (0.07)	1 (0.09)	0 (0.00)	
	Neonatal defects	10 (0.69)	5 (0.47)	5 (1.32)	
Early eclampsia (%)	Early eclampsia	1413 (97.45)	1047 (97.67)	366 (96.83)	0.4817
	Non Early eclampsia	37 (2.55)	25 (2.33)	12 (3.17)	
Pregnancy-induced hypertension (%)	Pregnancy-induced hypertension	1440 (99.31)	1070 (99.81)	370 (97.88)	0.0004
	Non Pregnancy-induced hypertension	10 (0.69)	2 (0.19)	8 (2.12)	

Abbreviations: FDM, Family history of diabetes mellitus; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; BMI, Body mass index; LDL-C, Low-density lipoprotein cholesterol; HDL-C, High-density lipoprotein cholesterol; METS-IR, metabolic score for IR;HOMA-IR, homeostatic model assessment for IR; TG/HDL-C, Ratio of triglycerides and high-density lipoprotein cholesterol; TyG, TyG index; TyG-BMI, TyG*BMI index.

https://doi.org/10.2147/DMSO.S538992

https://doi.org/10.2147/DMSO.S538992

Table 2 Biochemical Measures According to Insulin Resistance Index (METS-IR (Table 2a), TYGBMI (Table 2b), HOMAIR (Table 2c), TGHDL (Table 2d), TYG (Table 2e)) Quartiles

Table 2a	Age	Prepregnancy Weight (kg)	Gestational Weight Gain Rate (%)	Prepregnancy BMI (kg/m^2)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Fasting Glucose (mmol/L)	Fasting Insulin (μl/mL)	Total Cholesterol (mmol/L)	Triglycerides (mmol/L)	HDL-c (mmol/L)	LDL-c (mmol/L)	ALT (IU/L)	Serum Creatinin (umol/L)	Urea (umol/L)	Uric Acid (umol/L)
METS-IR	30.38 ±3.96	57.62 ±8.91	0.23 ±0.10	21.90 ±3.21	111.56 ±10.76	69.93 ±8.74	4.53 ±0.62	7.31 ±4.35	4.01 ±0.80	0.98 ±0.56	1.47 ±0.33	2.09 ±0.63	18.80 ±34.31	47.42 ±6.68	3.43 ±8.00	211.21 ±55.32
Q1 (n=363)	29.81 ±3.72	49.16 ±4.50	0.29 ±0.11	18.61 ±2.14	110.65 ±10.45	69.50 ±8.13	4.45 ±0.59	5.31 ±3.03	4.03 ±0.74	0.83 ±0.37	1.65 ±0.34	1.95 ±0.53	16.54 ±20.02	46.58 ±6.07	3.10 ±0.84	189.47 ±48.75
Q2 (n=362)	30.28 ±3.75	54.74 ±4.38	0.25 ±0.10	20.80 ±1.04	110.97 ±10.34	69.20 ±8.91	4.52 ±0.59	6.11 ±2.85	3.97 ±0.80	0.89 ±0.42	1.52 ±0.29	2.02 ±0.60	19.41 ±57.99	46.91 ±7.11	3.08 ±0.69	200.88 ±47.58
Q3 (n=362)	30.17 ±3.93	59.10 ±4.84	0.22 ±0.09	22.52 ±1.23	110.85 ±11.17	69.28 ±8.84	4.55 ±0.65	7.29 ±3.39	3.94 ±0.82	0.94 ±0.43	1.44 ±0.30	2.06 ±0.57	16.77 ±13.48	47.50 ±6.83	3.65 ±8.81	212.70 ±50.56
Q4 (n=363)	31.28 ±4.28	67.46 ±8.69	0.16 ±0.09	25.66 ±2.76	113.78 ±10.78	71.73 ±8.84	4.61 ±0.64	10.52 ±5.58	4.10 ±0.84	1.27 ±0.79	1.26 ±0.28	2.32 ±0.73	22.49 ±27.43	48.69 ±6.51	3.88 ±13.31	241.74 ±59.56
P-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.01	<0.001	0.039	<0.001	<0.001	<0.001	0.066	<0.001	0.436	<0.001

Table 2b	AGE	Prepregnancy weight (kg)	Gestational weight gain rate (%)	Prepregnancy BMI (kg/m^2)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Fasting glucose (mmol/L)	Fasting insulin (μl/mL)	Total cholesterol (mmol/L)	Triglycerides (mmol/L)	HDL-c (mmol/L)	LDL-c (mmol/L)	ALT (IU/L)	Serum creatinin (umol/L)	Urea (umol/L)	Uric acid (umol/L)
TYGBMI	30.38 ±3.96	57.62 ±8.91	0.23 ±0.10	21.90 ±3.21	111.56 ±10.76	69.93 ±8.74	4.53 ±0.62	7.31 ±4.35	4.01 ±0.80	0.98 ±0.56	1.47 ±0.33	2.09 ±0.63	18.80 ±34.31	47.42 ±6.68	3.43 ±8.00	211.21 ±55.32
Q1 (n=363)	29.53 ±3.58	49.20 ±4.50	0.29 ±0.11	18.63 ±2.18	110.00 ±9.89	69.31 ±8.16	4.40 ±0.63	5.49 ±3.09	3.72 ±0.77	0.71 ±0.27	1.47 ±0.33	1.83 ±0.54	19.52 ±59.35	46.60 ±6.70	3.09 ±0.83	190.63 ±49.89
Q2 (n=362)	30.19 ±3.67	54.51 ±4.33	0.25 ±0.09	20.75 ±1.03	111.05 ±11.17	69.57 ±8.93	4.50 ±0.57	6.20 ±3.01	3.92 ±0.72	0.86 ±0.31	1.50 ±0.32	1.99 ±0.59	15.66 ±13.38	47.21 ±7.07	3.14 ±2.07	199.47 ±46.11
Q3 (n=362)	30.31 ±3.78	59.33 ±4.92	0.21 ±0.08	22.53 ±1.18	111.49 ±11.12	69.27 ±9.10	4.55 ±0.62	7.28 ±3.48	4.05 ±0.78	0.96 ±0.36	1.47 ±0.31	2.12 ±0.55	18.07 ±20.42	47.74 ±6.37	4.29 ±15.76	213.97 ±51.44
Q4 (n=363)	31.51 ±4.49	67.43 ±8.63	0.16 ±0.09	25.68 ±2.72	113.72 ±10.50	71.57 ±8.56	4.68 ±0.63	10.26 ±5.63	4.35 ±0.81	1.40 ±0.82	1.43 ±0.37	2.40 ±0.68	21.95 ±23.96	48.12 ±6.50	3.19 ±1.56	240.72 ±59.63
P-value	<0.001	<0.001	<0.001	<0.001	<0.001	0.001	<0.001	<0.001	<0.001	<0.001	0.031	<0.001	0.093	0.014	0.128	<0.001

Table 2c	AGE	Prepregnancy weight (kg)	Gestational weight gain rate (%)	Prepregnancy BMI (kg/m^2)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Fasting glucose (mmol/L)	Fasting insulin (μl/mL)	Total cholesterol (mmol/L)	Triglycerides (mmol/L)	HDL-c (mmol/L)	LDL-c (mmol/L)	ALT (IU/L)	Serum creatinin (umol/L)	Urea (umol/L)	Uric acid (umol/L)
HOMAIR	30.38 ±3.96	57.62 ±8.91	0.23 ±0.10	21.90 ±3.21	111.56 ±10.76	69.93 ±8.74	4.53 ±0.62	7.31 ±4.35	4.01 ±0.80	0.98 ±0.56	1.47 ±0.33	2.09 ±0.63	18.80 ±34.31	47.42 ±6.68	3.43 ±8.00	211.21 ±55.32
Q1 (n=363)	30.45 ±3.70	53.16 ±6.78	0.25 ±0.10	20.48 ±2.37	109.48 ±10.50	68.29 ±8.04	4.27 ±0.62	3.31 ±1.02	3.97 ±0.81	0.89 ±0.44	1.55 ±0.37	1.99 ±0.57	18.87 ±57.90	46.45 ±6.14	3.50 ±8.59	193.78 ±48.62
Q2 (n=362)	29.95 ±3.78	55.90 ±7.28	0.24 ±0.10	21.24 ±2.45	111.85 ±9.94	69.54 ±7.83	4.46 ±0.58	5.43 ±0.94	3.94 ±0.76	0.88 ±0.37	1.50 ±0.32	2.01 ±0.63	17.45 ±21.11	47.30 ±6.26	3.05 ±0.74	200.73 ±47.55
Q3 (n=363)	30.55 ±4.13	58.21 ±7.37	0.23 ±0.10	22.08 ±2.78	111.37 ±11.67	69.99 ±9.79	4.63 ±0.57	7.56 ±1.31	3.99 ±0.79	0.99 ±0.59	1.44 ±0.31	2.08 ±0.59	17.47 ±19.05	47.30 ±7.40	3.93 ±13.38	214.87 ±49.82
Q4 (n=362)	30.59 ±4.18	63.21 ±10.51	0.20 ±0.11	23.80 ±3.99	113.56 ±10.48	71.89 ±8.80	4.77 ±0.60	12.95 ±4.55	4.14 ±0.82	1.17 ±0.72	1.37 ±0.30	2.27 ±0.68	21.44 ±23.28	48.63 ±6.70	3.23 ±1.56	235.49 ±64.36
P-value	0.108	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.004	<0.001	<0.001	<0.001	0.355	<0.001	0.483	<0.001

Table 2d	AGE	Prepregnancy weight (kg)	Gestational weight gain rate (%)	Prepregnancy BMI (kg/m^2)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Fasting glucose (mmol/L)	Fasting insulin (μl/mL)	Total cholesterol (mmol/L)	Triglycerides (mmol/L)	HDL-c (mmol/L)	LDL-c (mmol/L)	ALT (IU/L)	Serum creatinin (umol/L)	Urea (umol/L)	Uric acid (umol/L)
TGHDL	30.38 ±3.96	57.62 ±8.91	0.23 ±0.10	21.90 ±3.21	111.56 ±10.76	69.93 ±8.74	4.53 ±0.62	7.31 ±4.35	4.01 ±0.80	0.98 ±0.56	1.47 ±0.33	2.09 ±0.63	18.80 ±34.31	47.42 ±6.68	3.43 ±8.00	211.21 ±55.32
Q1 (n=363)	29.72 ±3.45	55.95 ±7.85	0.25 ±0.10	21.21 ±2.53	111.66 ±10.49	69.97 ±8.78	4.55 ±0.60	6.15 ±3.09	3.89 ±0.78	0.57 ±0.14	1.60 ±0.32	1.92 ±0.58	17.85 ±23.90	47.45 ±7.02	3.92 ±13.24	199.48 ±52.23
Q2 (n=362)	30.26 ±3.98	55.80 ±7.50	0.24 ±0.11	21.23 ±2.86	110.31 ±10.48	68.70 ±8.55	4.57 ±0.62	6.35 ±3.25	4.03 ±0.80	0.79 ±0.17	1.55 ±0.31	2.03 ±0.60	15.50 ±13.76	47.18 ±6.36	3.03 ±0.72	200.17 ±46.29
Q3 (n=362)	30.46 ±3.78	57.41 ±8.50	0.22 ±0.09	21.89 ±3.15	112.02 ±10.68	70.05 ±8.93	4.51 ±0.63	7.27 ±4.12	3.96 ±0.81	0.98 ±0.22	1.42 ±0.29	2.09 ±0.66	20.84 ±58.32	47.66 ±6.25	3.16 ±1.57	212.85 ±53.49
Q4 (n=363)	31.10 ±4.45	61.31 ±10.40	0.20 ±0.11	23.25 ±3.76	112.27 ±11.29	70.99 ±8.57	4.50 ±0.64	9.45 ±5.64	4.16 ±0.78	1.58 ±0.76	1.30 ±0.33	2.31 ±0.61	21.03 ±23.20	47.38 ±7.07	3.61 ±8.80	232.30 ±61.82
P-value	<0.001	<0.001	<0.001	<0.001	0.068	0.005	0.343	<0.001	<0.001	<0.001	<0.001	<0.001	0.092	0.817	0.412	<0.001
Table 2e	**AGE**	**Prepregnancy weight (kg)**	**Gestational weight gain rate (%)**	**Prep regnancyBMI (kg/m^2)**	**Systolic blood pressure (mmHg)**	**Diastolic blood pressure (mmHg)**	**Fasting glucose (mmol/L)**	**Fasting insulin (μl/mL)**	**Total cholesterol (mmol/L)**	**Triglycerides (mmol/L)**	**HDL-c (mmol/L)**	**LDL-c (mmol/L)**	**ALT (IU/L)**	**Serum creatinin (umol/L)**	**Urea (umol/L)**	**Uric acid (umol/L)**
TYG	30.38 ±3.96	57.62 ±8.91	0.23 ±0.10	21.90 ±3.21	111.56 ±10.76	69.93 ±8.74	4.53 ±0.62	7.31 ±4.35	4.01 ±0.80	0.98 ±0.56	1.47 ±0.33	2.09 ±0.63	18.80 ±34.31	47.42 ±6.68	3.43 ±8.00	211.21 ±55.32
Q1 (n=363)	29.45 ±3.24	56.10 ±7.88	0.25 ±0.11	21.38 ±2.66	110.77 ±10.63	69.47 ±8.79	4.26 ±0.61	6.39 ±3.26	3.51 ±0.71	0.54 ±0.12	1.38 ±0.31	1.77 ±0.50	19.14 ±58.26	47.65 ±7.41	3.84 ±13.24	204.78 ±50.32
Q2 (n=363)	30.20 ±3.86	55.82 ±7.78	0.24 ±0.10	21.29 ±2.89	110.57 ±10.52	68.92 ±8.51	4.49 ±0.54	6.64 ±3.60	3.90 ±0.69	0.77 ±0.11	1.49 ±0.33	1.99 ±0.56	16.00 ±13.06	47.32 ±5.96	3.08 ±0.76	198.97 ±48.43
Q3 (n=363)	30.48 ±4.05	57.51 ±8.38	0.22 ±0.10	21.81 ±3.16	112.11 ±10.53	70.22 ±8.84	4.62 ±0.57	7.03 ±3.72	4.13 ±0.69	0.99 ±0.15	1.50 ±0.32	2.16 ±0.67	19.53 ±25.13	47.16 ±6.83	3.26 ±2.47	213.00 ±53.48
Q4 (n=361)	31.41 ±4.37	61.06 ±10.39	0.20 ±0.10	23.12 ±3.72	112.81 ±11.22	71.11 ±8.69	4.75 ±0.65	9.18 ±5.80	4.50 ±0.77	1.63 ±0.73	1.50 ±0.36	2.43 ±0.58	20.54 ±22.51	47.55 ±6.45	3.53 ±8.61	228.16 ±63.65
P-value	<0.001	<0.001	<0.001	<0.001	0.013	0.005	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.315	0.752	0.6	<0.001

Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; BMI, Body mass index; LDL-C, Low-density lipoprotein cholesterol; HDL-C, High-density lipoprotein cholesterol; METS-IR, metabolic score for IR; HOMA-IR, homeostatic model assessment for IR; TG/HDL-C, Ratio of triglycerides and high-density lipoprotein cholesterol; TyG, TyG index; TyG-BMI, TyG*BMI index.

https://doi.org/10.2147/DMSO.S538992

higher in the Q4 group, further validating METS-IR as a predictor of gestational metabolic dysregulation and complications. These findings highlight that elevated METS-IR in early pregnancy may serve as a sensitive indicator for identifying high-risk GDM populations. The robust associations between METS-IR and GDM risk provide a critical theoretical foundation for early clinical interventions.

Mathematical Modeling of Insulin Resistance Index

In a multifactorial logistic regression model (Table 3), all five insulin resistance indicators demonstrated a dose-response relationship with GDM risk. Notably, the association with METS-IR significantly weakened after adjusting for metabolic confounders. In the unadjusted model, the highest quartile of METS-IR (Q4) showed a significant association with increased GDM risk (OR = 3.328, 95% CI 2.375–4.704, $p < 0.001$). However, the risk was reduced by 35.1% after adjustment for age and rate of change of total body weight during pregnancy (Multivariable-adjusted 2) (OR = 2.159, 95% CI:1.486–3.155). After adjusting for fasting insulin, low-density lipoprotein cholesterol, and pre-pregnancy diastolic blood pressure, the association weakened to OR=1.559 (95% CI 1.037–2.352, p=0.034), indicating that METS-IR's predictive effect on GDM is partially mediated by lipid metabolism abnormalities and insulin secretion dysregulation. After multifactorial adjustment, the TG/HDL-C ratio (adjusted OR=2.019, 95% CI 1.375–2.988) and the TYG index (adjusted OR=3.062, 95% CI 2.034–4.664) demonstrated strong associations, indicating a higher independent predictive value for GDM risk. Notably, none of the corrected ORs of METS-IR were statistically significant in the intermediate tertile groups (Q2-Q3) (Q2:1.021, 95% CI:0.699–1.494; Q3:1.055, 95% CI:0.721–1.549), highlighting that its risk-predictive efficacy was concentrated in the higher tertiles with more severe metabolic disturbances. In the fully adjusted model (Multivariable-adjusted 3), all five insulin resistance indices (HOMAIR, METS-IR, TGHDL, TYG, TYGBMI) showed statistically significant positive associations with the outcome in their highest quartile (Q4), with odds ratios (ORs) ranging from 1.573 (METS-IR) to 3.022 (TYG). However, the pattern across quartiles varied: the TGHDL and TYG indices exhibited significant associations in all quartiles (Q2-Q4), with TYG showing a progressively increasing risk (Q2: OR=1.875, Q3: OR=2.555, Q4: OR=3.022). In contrast, significant associations for HOMAIR (Q4: OR=2.413), METS-IR (Q4: OR=1.573), and TYGBMI (Q4: OR=1.888) were only observed in Q4; the associations in the lower quartiles (Q2 and Q3) for these three indices were not statistically significant, with ORs close to 1.0.

METS-IR and Risks of Maternal and Neonatal Outcomes

Multivariable logistic regression analyses revealed significant associations between insulin resistance indices and adverse pregnancy outcomes (Table 4). The METS-IR index demonstrated robust associations with preterm delivery across all models: unadjusted model (OR=21.06, 95% CI: 1.22–363.95; P=0.036), age- and weight-adjusted model (Multivariable-adjusted 1, OR=87.99, 95% CI: 6.87–1127.33; P=0.00058), and fully adjusted models (Multivariable-adjusted 2: OR=24.26, 95% CI: 3.41–172.57; P=0.00144; Multivariable-adjusted Model 3: OR=24.29, 95% CI: 3.41–172.92; P=0.00145). For preeclampsia, METS-IR showed consistent risk elevation: unadjusted (OR=49.16, 95% CI: 1.79–1352.13; P=0.021) and fully adjusted (Multivariable-adjusted Model 3: OR=45.67, 95% CI: 4.55–457.99; P=0.00116). However, no significant association was observed between METS-IR and pregnancy-induced hypertension in any model ($P \geq 0.242$). Regarding adverse neonatal outcomes, METS-IR demonstrated significant associations in adjusted models: age- and weight-adjusted (OR=62.16, 95% CI: 5.22–740.30; P=0.001) and fully adjusted (Multivariable-adjusted Model 3: OR=14.03, 95% CI: 1.97–100.06; P=0.008). The TyG index consistently showed strong associations with pregnancy-induced hypertension risk across all models (Multivariable-adjusted Model 3: OR=205.66, 95% CI: 2.71–15,614.36; P=0.016). HOMA-IR was significantly associated with preeclampsia risk in both unadjusted (OR=21.06, 95% CI: 1.22–363.95; P=0.036) and fully adjusted models (Multivariable-adjusted Model 3: OR=20.84, 95% CI: 2.75–158.19; P=0.003). These findings demonstrate distinct predictive patterns for different insulin resistance indices across pregnancy complications, with METS-IR showing particularly strong associations with preterm delivery and preeclampsia.

Table 3 Linear Regression Analyses to Evaluate the Association of METS-IR and Surrogates of Insulin Resistance, Adjusted for Age, Prepregnant Weight Gain Rate, Diastolic Blood Pressure, Fasting Insulin and Low-Density Lipoprotein Cholecterol

	Crude			Multivariable-Adjusted[1]			Multivariable-Adjusted[2]			Multivariable-Adjusted[3]		
HOMAIR	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value
Q2	0.867	(0.594, 1.261)	0.4548	0.856	(0.583, 1.254)	0.4252	0.85	(0.572, 1.26)	0.418	0.852	(0.574, 1.263)	0.4266
Q3	1.336	(0.94, 1.905)	0.1076	1.217	(0.849, 1.747)	0.2856	1.188	(0.792, 1.786)	0.4049	1.172	(0.781, 1.761)	0.4436
Q4	3.08	(2.216, 4.312)	<0.005	2.629	(1.87, 3.721)	<0.005	2.455	(1.417, 4.261)	0.0014	2.413	(1.395, 4.178)	0.0016
METS-IR	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value
Q2	1.221	(0.843, 1.772)	0.2915	1.075	(0.737, 1.571)	0.7066	1.021	(0.699, 1.494)	0.9153	1.023	(0.7, 1.497)	0.9078
Q3	1.5	(1.047, 2.159)	0.0277	1.197	(0.824, 1.746)	0.3466	1.055	(0.721, 1.549)	0.7816	1.061	(0.724, 1.56)	0.7607
Q4	3.328	(2.375, 4.704)	<0.005	2.159	(1.486, 3.155)	0.0001	1.559	(1.037, 2.352)	0.0335	1.573	(1.047, 2.373)	0.0298
TGHDL	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value
Q2	1.865	(1.286, 2.727)	0.0011	1.75	(1.198, 2.574)	0.0041	1.715	(1.171, 2.529)	0.0059	1.716	(1.172, 2.531)	0.0059
Q3	2.276	(1.581, 3.306)	<0.005	1.944	(1.34, 2.844)	0.0005	1.812	(1.244, 2.66)	0.0021	1.845	(1.267, 2.708)	0.0015
Q4	3.27	(2.294, 4.714)	<0.005	2.526	(1.751, 3.68)	<0.005	2.019	(1.375, 2.988)	0.0004	2.032	(1.384, 3.007)	0.0003
TYG	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value
Q2	2.043	(1.383, 3.049)	0.0004	1.881	(1.265, 2.823)	0.002	1.886	(1.264, 2.842)	0.0021	1.875	(1.256, 2.827)	0.0023
Q3	2.957	(2.03, 4.366)	<0.005	2.58	(1.758, 3.834)	<0.005	2.583	(1.743, 3.875)	<0.005	2.555	(1.723, 3.833)	<0.005
Q4	4.366	(3.022, 6.403)	<0.005	3.427	(2.345, 5.079)	<0.005	3.062	(2.034, 4.664)	<0.005	3.022	(2.008, 4.602)	<0.005
TYGBMI	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value	Odds ratio	95% CI	P-value
Q2	1.203	(0.828, 1.751)	0.3328	1.04	(0.711, 1.524)	0.8401	0.997	(0.68, 1.464)	0.9875	0.998	(0.68, 1.466)	0.9899
Q3	1.351	(0.936, 1.956)	0.1092	1.049	(0.715, 1.542)	0.8068	0.938	(0.634, 1.39)	0.7483	0.946	(0.639, 1.403)	0.7831
Q4	3.838	(2.74, 5.428)	<0.005	2.464	(1.69, 3.617)	<0.005	1.88	(1.243, 2.858)	0.0029	1.888	(1.248, 2.871)	0.0028

Notes: Data are OR (95% CI). 1 Adjusted for age and prepregnant weight gain rate. 2 Adjusted for age, prepregnant weight gain rate, diastolic blood pressure, fasting insulin and Low-density lipoprotein cholesterol. 3 Adjusted for age, prepregnant weight gain rate, diastolic blood pressure, fasting insulin, Low-density lipoprotein cholesterol and Family history of diabetes mellitus.

Abbreviations: METS-IR, metabolic score for IR;HOMA-IR, homeostatic model assessment for IR; TG/HDL-C, Ratio of triglycerides and high-density lipoprotein cholesterol; TyG, TyG index; FDM, Family history of diabetes mellitus; TyG-BMI, TyG*BMI index.

https://doi.org/10.2147/DMSO.S538992

Table 4 METS-IR and Risks of Maternal and Neonatal Outcomes

		Crude		Multivariable-Adjusted[1]		Multivariable-Adjusted[2]		Multivariable-Adjusted[3]	
	Predictor	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
Preterm Delivery	METS-IR	21.06 (1.22–363.95)	0.0361	87.99 (6.87–1127.33)	0.00058	24.26 (3.41–172.57)	0.00144	24.29 (3.41–172.92)	0.00145
	TYG	25.77 (2.25–295.25)	0.00901	68.33 (8.36–558.27)	<0.0001	22.09 (3.83–127.31)	0.000533	22.09 (3.83–127.37)	0.000534
	TYGBMI	27.86 (2.59–300.12)	0.00608	80.39 (7.59–851.12)	0.000269	23.75 (3.49–161.62)	0.0012	23.79 (3.49–162.18)	0.00121
	TGHDL	21.82 (1.52–312.54)	0.0232	80.74 (8.85–736.76)	<0.0001	26.06 (3.96–171.49)	0.000696	25.97 (3.96–170.32)	0.000689
	HOMAIR	2.86 (0.27–29.92)	0.381	11.74 (1.82–75.73)	0.00963	7.57 (1.26–45.48)	0.0269	7.30 (1.20–44.30)	0.0308
Preeclampsia	METS-IR	49.16 (1.79–1352.13)	0.0213	72.24 (3.13–1665.99)	0.00751	45.65 (4.56–457.24)	0.00115	45.67 (4.55–457.99)	0.00116
	TYG	1.85 (0.06–53.55)	0.719	8.56 (0.56–130.91)	0.123	13.56 (1.49–123.77)	0.0208	13.56 (1.49–123.78)	0.0209
	TYGBMI	32.68 (1.88–569.70)	0.0168	54.27 (2.96–995.86)	0.00714	40.62 (4.23–389.98)	0.00133	40.65 (4.22–391.15)	0.00134
	TGHDL	0.63 (0.00–97.66)	0.858	11.42 (0.58–225.76)	0.11	26.75 (2.69–266.09)	0.00505	26.71 (2.70–264.49)	0.00498
	HOMAIR	49.94 (6.09–409.57)	0.00027	57.85 (7.59–440.95)	<0.0001	21.48 (2.86–161.32)	0.00287	20.84 (2.75–158.19)	0.00331
Pregnancy-Induced Hypertension	METS-IR	0.30 (0.00–4512.33)	0.808	51.37 (0.06–43,516.37)	0.252	25.52 (0.11–5794.80)	0.242	25.55 (0.11–5820.12)	0.242
	TYG	1536.31 (5.61–420,682.26)	0.0104	3203.25 (16.20–633,377.23)	0.00277	205.39 (2.71–15,583.00)	0.0159	205.66 (2.71–15,614.36)	0.0159
	TYGBMI	6.92 (0.01–5321.07)	0.568	81.20 (0.20–32,124.03)	0.15	24.97 (0.13–4653.60)	0.228	25.03 (0.13–4689.45)	0.228
	TGHDL	37.44 (0.04–37,162.18)	0.303	350.12 (1.70–72,054.08)	0.0311	44.99 (0.28–7156.96)	0.141	44.74 (0.28–7041.74)	0.141
	HOMAIR	3.22 (0.01–1870.08)	0.719	23.11 (0.19–2790.60)	0.199	15.24 (0.17–1401.45)	0.238	15.06 (0.16–1408.97)	0.242
Adverse Neonatal Outcome	METS-IR	12.44 (0.73–210.70)	0.0808	62.16 (5.22–740.30)	0.00109	14.00 (1.97–99.74)	0.00843	14.03 (1.97–100.06)	0.0084
	TYG	0.79 (0.05–12.17)	0.865	9.14 (1.07–77.68)	0.0427	5.89 (0.94–36.92)	0.0582	5.89 (0.94–36.95)	0.0582
	TYGBMI	14.84 (1.37–160.50)	0.0264	50.07 (4.99–502.75)	0.000883	14.04 (2.06–95.68)	0.00696	14.10 (2.07–96.24)	0.00692
	TGHDL	0.66 (0.01–35.23)	0.838	22.98 (2.35–225.16)	0.00709	10.42 (1.50–72.45)	0.0179	10.34 (1.49–71.70)	0.0181
	HOMAIR	1.48 (0.13–16.73)	0.751	8.32 (1.32–52.44)	0.024	4.59 (0.76–27.72)	0.0967	4.56 (0.75–27.76)	0.0996

Notes: Data are OR (95% CI). 1 Adjusted for age and prepregnant weight gain rate. 2 Adjusted for age, prepregnant weight gain rate, diastolic blood pressure, fasting insulin and Low-density lipoprotein cholesterol. 3 Adjusted for age, prepregnant weight gain rate, diastolic blood pressure, fasting insulin, Low-density lipoprotein cholesterol and Family history of diabetes mellitus.

Abbreviations: METS-IR, metabolic score for IR;HOMA-IR, homeostatic model assessment for IR; TG/HDL-C, Ratio of triglycerides and high-density lipoprotein cholesterol; TyG, TyG index; TyG-BMI, TyG*BMI index.

https://doi.org/10.2147/DMSO.S538992

ROC Analysis

Among the five insulin resistance indices evaluated, the METS-IR index exhibited evolving discrimination patterns for GDM across sequential adjustment models (Table 5). Compared to HOMA-IR and TyG, METS-IR uses routine measures but shows less independence from confounders. In the unadjusted analysis (Crude Model) (Figure 2), METS-IR demonstrated moderate discrimination (AUC=0.629) with 44.7% sensitivity and 76.2% specificity, accompanied by a significant positive association (OR=1.076, 95% CI:1.053–1.100; P<0.001). Following adjustment for age and total gestational weight gain rate (Multivariable-adjusted Model 1) (Figure 3), discrimination improved (AUC=0.668) with substantially increased sensitivity (73.0%) but decreased specificity (52.9%), while maintaining significant association (OR=1.040, 95% CI:1.015–1.066; P=0.002). Subsequent adjustment for fasting insulin, LDL cholesterol, and preconception diastolic blood pressure (Multivariable-adjusted Model 2) (Figure 4) resulted in non-significant association (OR=1.006, 95% CI:0.979–1.034; P=0.678) despite minor AUC improvement (0.676). In the fully adjusted model (Multivariable-adjusted Model 3) (Figure 5) incorporating family diabetes history, METS-IR maintained non-significance (OR=1.005, 95% CI:0.977–1.034; P=0.712) with stable discriminative capacity (AUC=0.678), while achieving 75.2% sensitivity at 49.8% specificity. This progressive attenuation contrasted with HOMA-IR, which maintained robust significance through Multivariable-adjusted Model 3 (OR=3.38, 95% CI:1.17–9.75; P=0.025). Of note, METS-IR exhibited the highest baseline specificity (76.2%) and preserved substantial sensitivity in fully adjusted analyses (75.2% in Multivariable-adjusted Model 3), suggesting clinical utility as a preliminary screening tool in settings lacking insulin assays.

Table 5 AUC for Each Assessed Parameter in Determining GDM

Crude	AUC	Sensitivity	Specificity	OR	CI	P-value
METS-IR	0.629	0.447	0.762	1.076	(1.053, 1.1)	<0.005
TYG	0.641	0.653	0.57	2.9	(2.234, 3.791)	<0.005
TYGBMI	0.645	0.429	0.814	1.015	(1.011, 1.019)	<0.005
TGHDL	0.617	0.722	0.462	1.39	(1.236, 1.571)	<0.005
HOMAIR	0.634	0.553	0.674	1.672	(1.475, 1.902)	<0.005
Multivariable-adjusted[1]	AUC	Sensitivity	Specificity	OR	CI	P-value
METS-IR	0.668	0.73	0.529	1.04	(1.015, 1.066)	0.0018
TYG	0.688	0.659	0.646	2.35	(1.795, 3.096)	<0.005
TYGBMI	0.676	0.672	0.598	1.009	(1.005, 1.014)	0.0001
TGHDL	0.671	0.611	0.659	1.257	(1.116, 1.422)	0.0002
HOMAIR	0.688	0.675	0.621	1.548	(1.361, 1.765)	<0.005
Multivariable-adjusted[2]	AUC	Sensitivity	Specificity	OR	CI	P-value
METS-IR	0.676	0.735	0.527	1.006	(0.979, 1.034)	0.6784
TYG	0.699	0.685	0.635	2.103	(1.57, 2.833)	<0.005
TYGBMI	0.679	0.616	0.648	1.004	(0.999, 1.009)	0.1582
TGHDL	0.681	0.786	0.477	1.135	(1.001, 1.29)	0.0492
HOMAIR	0.699	0.717	0.59	3.442	(2.076, 5.838)	<0.005
Multivariable-adjusted[3]	AUC	Sensitivity	Specificity	OR	CI	P-value
METS-IR	0.677	0.537	0.717	1.006	(0.979, 1.033)	0.676
TYG	0.698	0.685	0.625	2.08	(1.55, 2.793)	<0.001
TYGBMI	0.679	0.717	0.54	1.003	(0.999, 1.008)	0.168
TGHDL	0.681	0.762	0.502	1.133	(0.999, 1.285)	0.053
HOMAIR	0.698	0.788	0.512	3.499	(2.082, 5.88)	<0.001

Notes: Data are OR (95% CI). 1 Adjusted for age and prepregnant weight gain rate. 2 Adjusted for age, prepregnant weight gain rate, diastolic blood pressure, fasting insulin and Low-density lipoprotein cholesterol. 3 Adjusted for age, prepregnant weight gain rate, diastolic blood pressure, fasting insulin, Low-density lipoprotein cholesterol and Family history of diabetes mellitus.

Abbreviations: METS-IR, metabolic score for IR;HOMA-IR, homeostatic model assessment for IR; TG/HDL-C, Ratio of triglycerides and high-density lipoprotein cholesterol; TyG, TyG index; TyG-BMI, TyG*BMI index.

https://doi.org/10.2147/DMSO.S538992

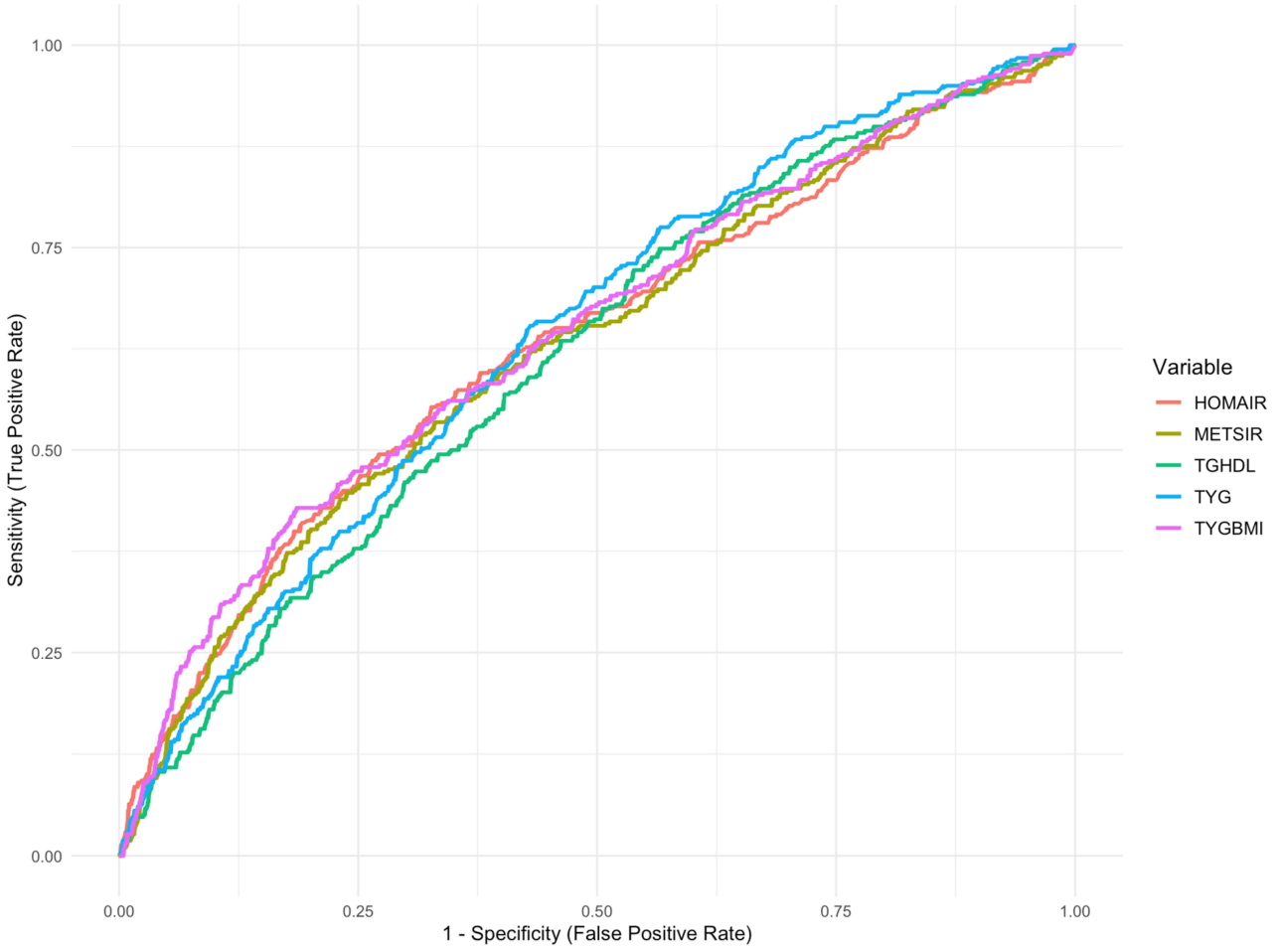

Figure 2 Crude ROC curve of insulin resistance index for predicting GDM risk.

Discussion

GDM, a common metabolic complication of pregnancy, poses significant clinical implications for maternal health globally.[20,21] Beyond immediate obstetric risks such as pregnancy-induced hypertension and macrosomia, this condition elevates long-term susceptibility to type 2 diabetes progression postpartum.[22,23] Recent epidemiological studies highlight pronounced geographical variations in GDM prevalence, with International Diabetes Federation estimates indicating an age-standardized global rate of 14%—ranging from 7.1% in Northern European populations to 27.6% in Southeast Asian cohorts.[24] The elevated GDM incidence observed in this study cohort relative to national averages in China may reflect regional socioeconomic factors, potentially associated with Beijing's urbanized setting and advanced healthcare infrastructure, not selection bias. Established clinical predictors of GDM—advanced maternal age, dyslipidemia, genetic predisposition to diabetes, and elevated prepregnancy body mass index—were corroborated in this investigation.[25,26] Urbanization in Beijing correlates with sedentary lifestyles and dietary shifts, increasing obesity and GDM risk. Comparative analyses revealed statistically significant differences between GDM and non-GDM groups regarding maternal anthropometric indices, lipid profiles, and insulin resistance markers, aligning with existing pathophysiological models of glucose dysregulation during gestation.[27,28]

The pathophysiology of GDM is centered on the exacerbation of pregnancy-induced IR and inadequate compensatory function of pancreatic β-cells. This study is the first to systematically validate the predictive value of the METS-IR index—a composite metric derived from metabolic syndrome-related parameters—for GDM in a Chinese pregnant population during early gestation. Our findings highlight that METS-IR shows promise for early GDM screening but is outperformed by TyG and HOMA-IR.

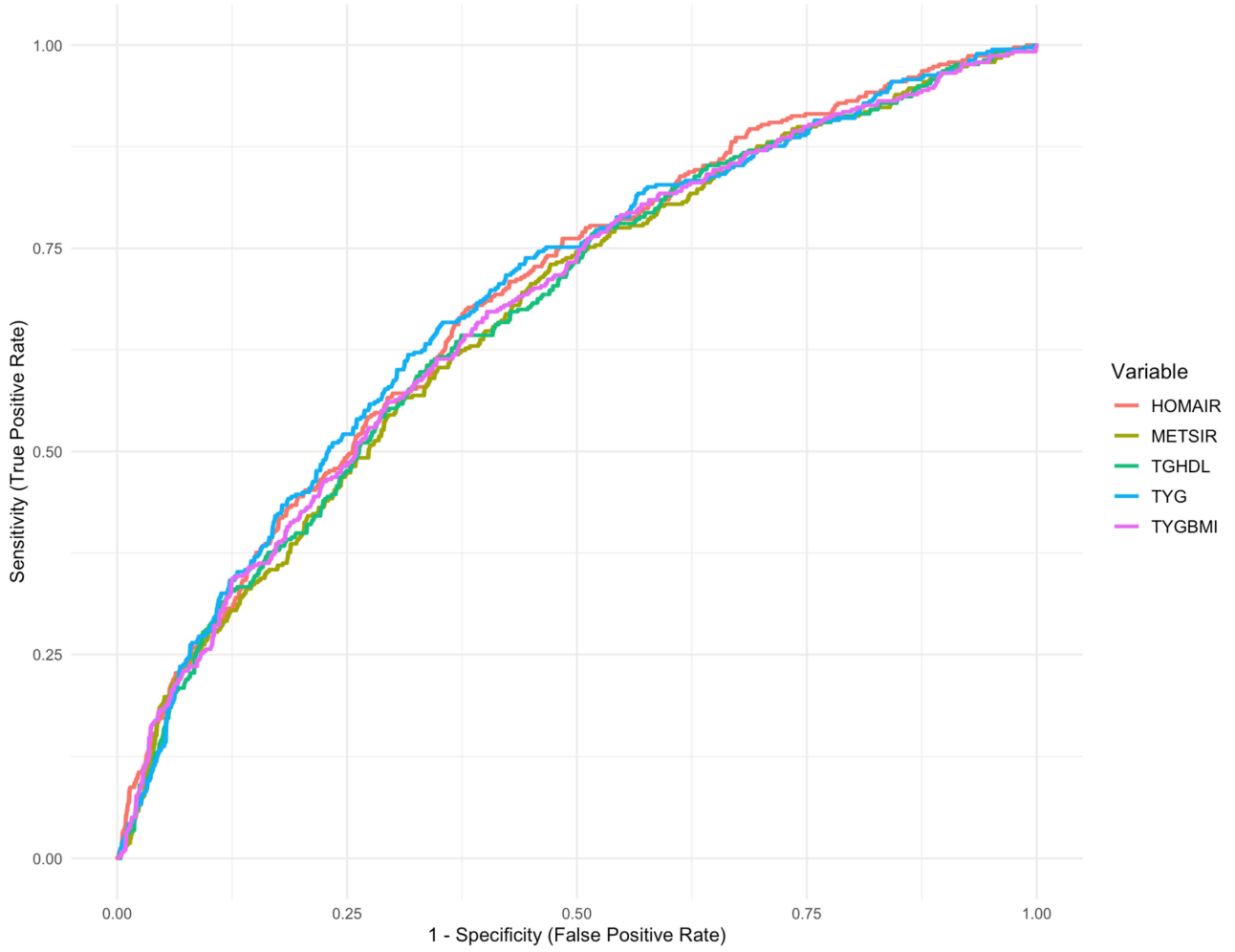

Figure 3 Multivariable-adjusted1 ROC curve of insulin resistance index for predicting GDM risk, Adjusted for age and prepregnant weight gain rate.

Biological Rationale of METS-IR and Its Relevance to GDM

This study demonstrated a significant dose-response relationship between METS-IR in early pregnancy and GDM risk. The strong unadjusted association between METS-IR and GDM risk (OR=3.33, Q4 vs Q1) aligns with its design as a composite metabolic marker incorporating BMI, lipid profiles, and glucose metabolism. Physiological fat accumulation and hyperlipidemia occur in early pregnancy,[29] which are associated with adverse pregnancy outcomes.[30] The absence of significant family history effects may reflect the cohort's metabolic risk profile, where adiposity-driven insulin resistance overshadowed genetic factors. While unmeasured variables (eg, Subject's ethnic information, lifestyle, prior GDM) may contribute residual confounding, their exclusion aligns with our hypothesis-driven focus on metabolic markers. Future work should integrate genetic and behavioral data. METS-IR can sensitively capture the early IR signal mediated by adipose tissue inflammation by incorporating BMI. The attenuation of this association after adjusting for LDL-C, fasting insulin, and blood pressure (adjusted OR=1.56) suggests that METS-IR primarily serves as an aggregator of established metabolic risk factors rather than an independent predictor. The stepwise attenuation of METS-IR's odds ratio (from OR=3.33 unadjusted to OR=1.56 fully adjusted), contrasted with the stable or improving discriminative capacity (AUC from 0.629 unadjusted to 0.677 fully adjusted), indicates that while METS-IR reflects metabolic dysregulation relevant to GDM risk and contributes to discriminative models, its apparent strong predictive association in unadjusted analyses is largely mediated by lipid abnormalities and insulin resistance.[31,32]

https://doi.org/10.2147/DMSO.S538992

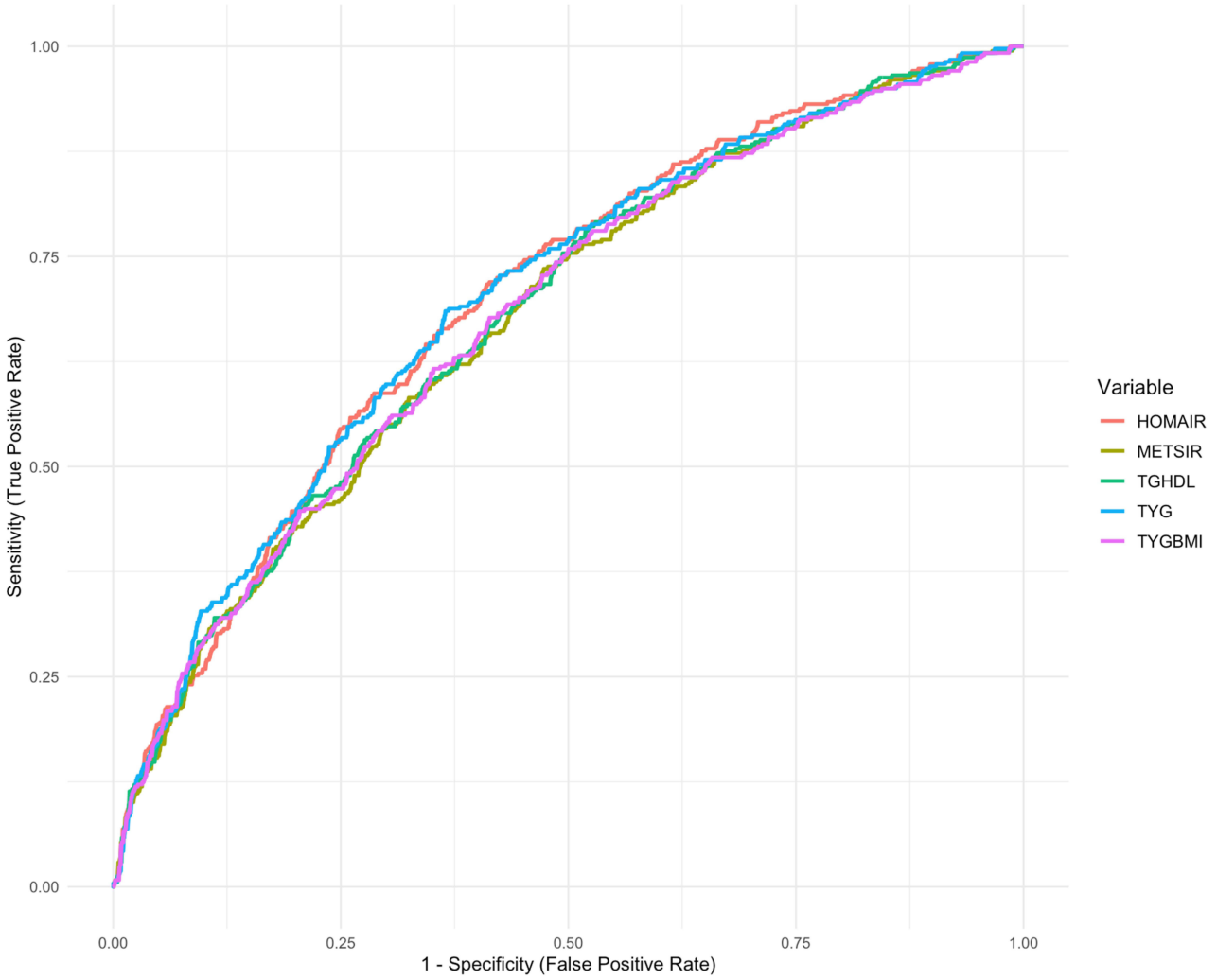

Figure 4 Multivariable-adjusted2 ROC curve of insulin resistance index for predicting GDM risk, Adjusted for age, prepregnant weight gain rate, diastolic blood pressure, fasting insulin and Low-density lipoprotein cholesterol.

Comparative Advantages Over Conventional IR Indices

Insulin resistance, characterized by diminished tissue responsiveness to physiological insulin concentrations, constitutes a fundamental pathophysiological mechanism in type 2 diabetes mellitus (T2DM) and shares molecular pathways with GDM.[33] Chronic insulin resistance during pregnancy leads to beta cell dysfunction and tissue insulin resistance, which are key elements in the pathophysiology of GDM.[34] While EHC remains the reference standard for quantifying insulin sensitivity, its clinical applicability is constrained by technical complexity and resource requirements.[35] Alternative insulin resistance indices such as HOMA-IR and METS-IR have consequently gained traction as clinically viable assessment tools. In recent years, the role of triglycerid-based metabolic parameters (TG/HDL-C)[36] and derived metabolic evaluation parameters (TyG, TyGBMI) in the occurrence and development of diabetes has also been confirmed.[37] For instance, the HOMA-IR, as a classical marker, demonstrates strong predictive value for GDM, with studies reporting AUC values up to 0.70 in early pregnancy cohorts.[9] Similarly, the TyG index (based on triglycerides and glucose) has shown superior performance in identifying GDM risk, particularly in high-risk populations, with Harding et al highlighting its correlation to T2DM pathogenesis.[8] Recent evidence also supports the TG/HDL-C ratio as a biomarker for GDM, reflecting lipid metabolism dysregulation.[11,38] The transient dietary sensitivity of TG levels suggests that isolated first-trimester measurements demonstrate substantial biological variability, thereby compromising their reliability as consistent biomarkers.[39] However, the need for fasting insulin and lipid level testing limits the application of HOMA-IR, the TyG index, and TG/HDL-C in primary care institutions. The

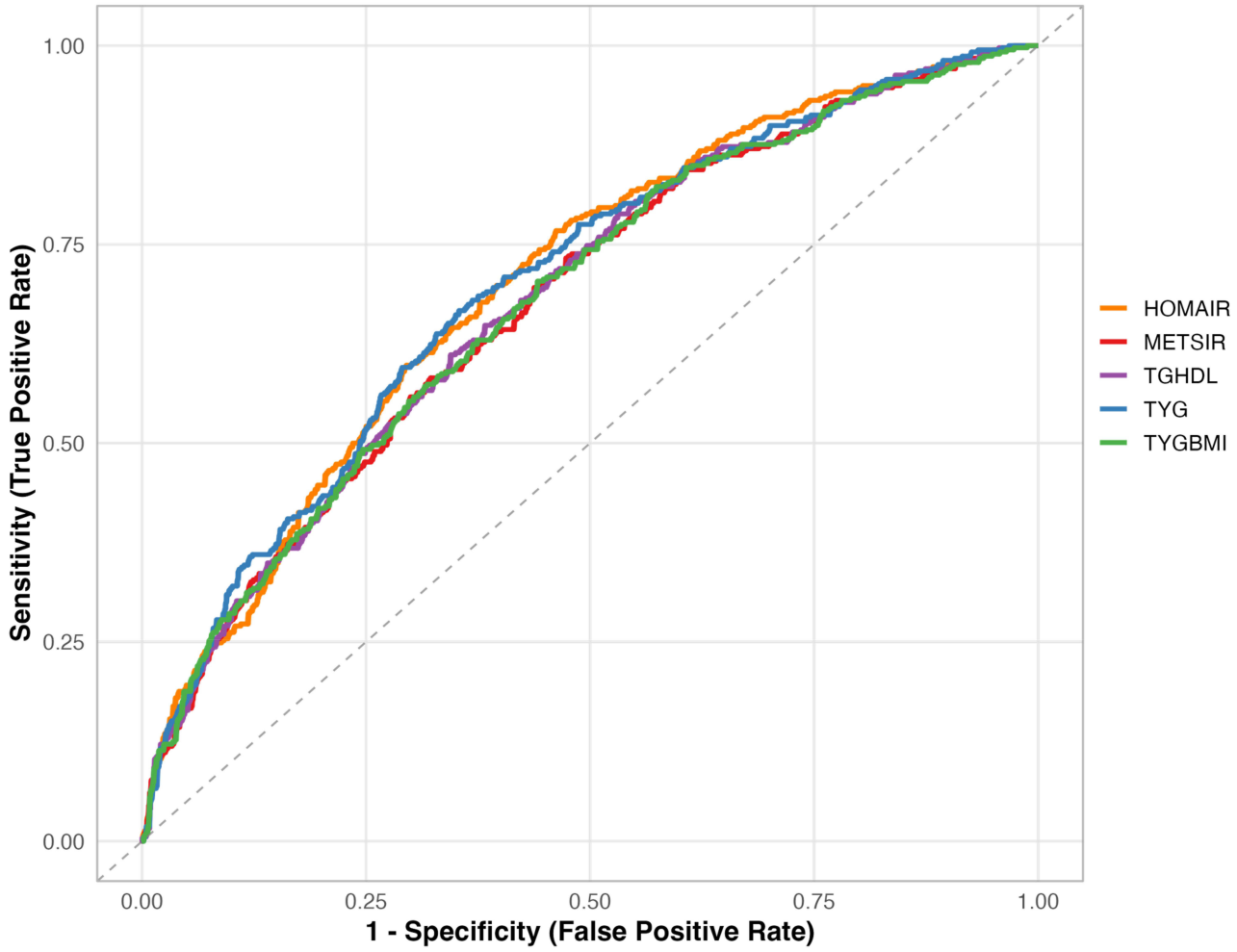

Figure 5 Multivariable-adjusted3 ROC curve of insulin resistance index for predicting GDM risk, Adjusted for age, prepregnant weight gain rate, diastolic blood pressure, fasting insulin, Low-density lipoprotein cholesterol and Family history of diabetes mellitus.

dependence of METS-IR on traditional indicators (BMI, blood lipids, and blood glucose) provides practical advantages for primary care screening, improving cost-effectiveness and scalability. In addition, METS-IR is in line with the comprehensiveness of pathophysiology. Although the TyG index reflects IR related to lipid toxicity, it ignores body fat distribution due to the pathogenic role of visceral fat ectopic deposition during pregnancy, and body fat distribution is a key driving factor for GDM.[40] This enhanced discriminatory ability may stem from its multi-dimensional integration of metabolic abnormalities. Our study demonstrates that METS-IR in early pregnancy correlates with GDM risk but is less predictive than TyG or HOMA-IR after adjustment for metabolic confounders. The dependence of METS-IR on metabolic covariates limits its utility in individualized risk stratification. It is necessary to formulate a stratified screening plan based on resource availability and the patient's metabolic status.

Clinical Implications and Translational Potential

Validated by our findings, METS-IR may serve as a high-efficiency tool for early GDM risk stratification. For women with METS-IR ≥38.5 (the optimal cutoff identified here), preemptive lifestyle interventions or intensified monitoring could improve the timeliness of secondary prevention. Future studies could integrate METS-IR into multimodal prediction models combining fetal ultrasound parameters (eg, abdominal circumference) or emerging biomarkers (eg, sex hormone-binding globulin). Additionally, longitudinal tracking of METS-IR dynamics may guide personalized glycemic management, with high-risk populations potentially benefiting from targeted lipid regulation and weight gain control.

https://doi.org/10.2147/DMSO.S538992

Innovation and Limitations

This study innovatively establishes METS-IR as a novel predictor of GDM in early pregnancy and confirms its generalizability in Chinese women. The limitations include the lack of information on the sample ethnic groups, the omission of measurable lifestyle factors, and the absence of macrosomia data. Low asphyxia cases (n=10) limited power. The molecular mechanisms linking METS-IR to pathogenesis require elucidation through basic research. Future studies should include these variables.

Future Directions

Subsequent research should prioritize: 1) establishing ethnicity-specific METS-IR thresholds for pregnancy; 2) leveraging omics technologies to delineate molecular signatures in high METS-IR subgroups; and 3) evaluating whether METS-IR-guided interventions reduce GDM incidence and adverse outcomes. Longitudinal studies exploring METS-IR's association with postpartum metabolic disorders are also warranted.

Conclusion

As a noninvasive, multidimensional IR assessment tool, METS-IR demonstrates unique advantages in early GDM screening and mechanistic exploration. METS-IR offers practical screening utility in primary care, but TyG and HOMA-IR show superior independent predictive value for GDM risk stratification. This study provides robust evidence for optimizing metabolic management strategies during pregnancy and underscores the translational potential of metabolic syndrome-derived indices in perinatal medicine.

Data Sharing Statement

Research data supporting this investigation remain restricted to authorized academic use. Access to deidentified datasets requires formal justification submitted through institutional channels, with inquiries and material requests processed via the corresponding principal investigator's contact portal (Junxiang Gao: gjx9754@163.com). Data sharing adheres to institutional review board protocols governing participant confidentiality and ethical research conduct.

Ethical Approval

This investigation was conducted as a multicenter prospective cohort initiative involving two specialized maternal healthcare institutions in Beijing (Haidian and Chaoyang District Maternal and Child Health Hospitals), with ethical oversight maintained throughout the study period (2019 onward). All participants provided documented written consent prior to enrollment. The research protocol received formal ethical clearance from the National Center for Women and Children's Health Ethics Committee, Chinese CDC (Approval: FY2019-01; 03 April 2019) and was registered with ClinicalTrials.gov (Identifier: NCT03246295). Study implementation strictly adhered to the 2013 revision of the Helsinki Declaration's international standards for human subject research.

Acknowledgments

The authors thank all the participants in this study.

Funding

Funding disclosure: Research activities including experimental design, data interpretation, and manuscript preparation received financial backing from China's Thirteenth Five-Year Plan Initiative for Pharmaceutical Innovation (Grant ID: 2019ZX09734001), awarded to principal investigator WZ through the National New Drug Development Major Project framework.

Disclosure

The research team collectively confirms no financial conflicts of interest or competing affiliations requiring disclosure. All investigators involved in this study affirm the absence of personal, professional, or financial relationships that could influence research objectivity or data interpretation.

References

1. Sun H, Saeedi P, Karuranga S, et al. IDF diabetes atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract*. 2022;183(183):109119. doi:10.1016/j.diabres.2021.109119
2. Committee on Practice Bulletins—Obstetrics, American College of Obstetricians and Gynecologists. Practice bulletin No. 190 summary OBSTETRICS & GYNECOLOGY # gestational diabetes mellitus. *Obstetrics Gynecol*. 2018;(131):407. doi:10.1097/AOG.0000000000002501
3. Popova PV, Isakov AO, Rusanova AN, et al. Personalized prediction of glycemic responses to food in women with diet-treated gestational diabetes: the role of the gut microbiota. *Biofilms and Microbiomes*. 2025. doi:10.1038/s41522-025-00650-9
4. Gao C, Sun X, Lu L, et al. Prevalence of gestational diabetes mellitus in mainland China: a systematic review and meta-analysis. *J Diabetes Investig*. 2019;(10):154–162. doi:10.1111/jdi.12854
5. Zhang J, Fang X, Song Z, et al. Positive association of triglyceride glucose index and gestational diabetes mellitus: a retrospective cohort study. *Front Endocrinol*. 2025. doi:10.3389/fendo.2024.1475212
6. Bello-Chavolla OY, Almeda-Valdes P, Gomez-Velasco D, et al. METS-IR, a novel score to evaluate insulin sensitivity, is predictive of visceral adiposity and incident type 2 diabetes. *Eur J Endocrinol*. 2018;178(5):533–544. doi:10.1530/EJE-17-0883
7. Cheng H, Yu X, Li Y-T, et al. Association between METS-IR and prediabetes or type 2 diabetes mellitus among elderly subjects in China: a large-scale population-based study. *Int J Environ Res Public Health*. 2023. doi:10.3390/ijerph20021053
8. Harding JL, Pavkov ME, Magliano DJ, et al. Global trends in diabetes complications: a review of current evidence. *Diabetologia*. 2019;(62):3–16. doi:10.1007/s00125-018-4711-2
9. Lee CH, Shih AZ, Woo YC, et al. Optimal cut-offs of homeostasis model assessment of insulin resistance (HOMA-IR) to identify dysglycemia and type 2 diabetes mellitus: a 15-year prospective study in Chinese. *PLoS One*. 2016;11(9):e0163424. doi:10.1371/journal.pone.0163424
10. Poveda NE, Garcés MF, Darghan AE, et al. Triglycerides/glucose and triglyceride/high-density lipoprotein cholesterol indices in normal and preeclamptic pregnancies: a longitudinal study. *Int J Endocrinol*. 2018;2018:8956404. doi:10.1155/2018/8956404
11. Song S, Zhang Y, Qiao X, et al. ALT/AST as an independent risk factor of gestational diabetes mellitus compared with TG/HDL-C. *Int J Gen Med*. 2022;15:115–121. doi:10.2147/IJGM.S332946
12. Liang X, Lai K, Li X, et al. Association between triglyceride glucose-body mass index and gestational diabetes mellitus: a prospective cohort study. *BMC Pregnancy Childbirth*. 2025;25(1):170. doi:10.1186/s12884-025-07294-9
13. Czech MP. Insulin action and resistance in obesity and type 2 diabetes. *Nat Med*. 2017;(23):804–814. doi:10.1038/nm.4350
14. Vardeny O, Gupta DK, Claggett B, et al. Insulin resistance and incident heart failure the ARIC study (Atherosclerosis risk in communities). *JACC Heart Fail*. 2013;1(6):531–536. doi:10.1016/j.jchf.2013.07.006
15. Matthews DR, Hosker JP, Rudenski AS, et al. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*. 1985;28(7):412–419. doi:10.1007/BF00280883
16. Poon AK, Meyer ML, Tanaka H, et al. Association of insulin resistance, from mid-life to late-life, with aortic stiffness in late-life: the atherosclerosis risk in communities study. *Cardiovasc Diabetol*. 2020;19(1):11. doi:10.1186/s12933-020-0986-y
17. Ding X, Wang X, Wu J, et al. Triglyceride-glucose index and the incidence of atherosclerotic cardiovascular diseases: a meta-analysis of cohort studies. *Cardiovasc Diabetol*. 2021;20(1):76. doi:10.1186/s12933-021-01268-9
18. Er LK, Wu S, Chou HH, et al. Triglyceride glucose-body mass index is a simple and clinically useful surrogate marker for insulin resistance in nondiabetic individuals. *PLoS One*. 2016;11(3):e0149731. doi:10.1371/journal.pone.0149731
19. Chiang JK, Lai NS, Chang JK, et al. Predicting insulin resistance using the triglyceride-to-high-density lipoprotein cholesterol ratio in Taiwanese adults. *Cardiovasc Diabetol*. 2011;10:93. doi:10.1186/1475-2840-10-93
20. Saravanan P. Diabetes in pregnancy working group; maternal medicine clinical study group; royal college of obstetricians and gynaecologists, UK. Gestational diabetes: opportunities for improving maternal and child health. *Lancet Diabetes Endocrinol*. 2020;8(9):793–800. doi:10.1016/S2213-8587(20)30161-3
21. Zhu Y, Zhang C. Prevalence of gestational diabetes and risk of progression to type 2 diabetes: a global perspective. *Curr Diab Rep*. 2016;16(1):7. doi:10.1007/s11892-015-0699-x
22. Maslova E, Hansen S, Grunnet LG, et al. Maternal glycemic index and glycemic load in pregnancy and offspring metabolic health in childhood and adolescence-a cohort study of 68,471 mother-offspring dyads from the Danish National Birth Cohort. *Eur J Clin Nutr*. 2019;73(7):1049–1062. doi:10.1038/s41430-018-0316-6
23. Hammoud NM, Visser GHA, van Rossem L, et al. Long-term BMI and growth profiles in offspring of women with gestational diabetes. *Diabetologia*. 2018;61(5):1037–1045. doi:10.1007/s00125-018-4584-4
24. Wang H, Li N, Chivese T, et al. IDF diabetes atlas: estimation of global and regional gestational diabetes mellitus prevalence for 2021 by international association of diabetes in pregnancy study group's criteria. *Diabet Res Clin Pract*. 2022;183:109050. doi:10.1016/j.diabres.2021.109050
25. Wang Y, Wu P, Huang Y, et al. BMI and lipidomic biomarkers with risk of gestational diabetes in pregnant women. *Obesity*. 2022;30(10):2044–2054. doi:10.1002/oby.23517
26. Zhang C, Rawal S, Chong YS. Risk factors for gestational diabetes: is prevention possible? *Diabetologia*. 2016;59(7):1385–1390. doi:10.1007/s00125-016-3979-3
27. Alsaedi SA, Altalhi AA, Nabrawi MF, et al. Prevalence and risk factors of gestational diabetes mellitus among pregnant patients visiting national guard primary health care centers in Saudi Arabia. *Saudi Med J*. 2020;41(2):144–150. doi:10.15537/smj.2020.2.24842
28. Lai M, Fang F, Ma Y, et al. Elevated midtrimester triglycerides as a biomarker for postpartum hyperglycemia in gestational diabetes. *J Diabetes Res*. 2020;2020:3950652. doi:10.1155/2020/3950652
29. Eppel D, Feichtinger M, Lindner T, et al. Association between maternal triglycerides and disturbed glucose metabolism in pregnancy. *Acta Diabetol*. 2021;58(4):459–465. doi:10.1007/s00592-020-01644-z
30. Lv Y, Xu L, He Z, et al. The association between pregnancy levels of blood lipids and the risk of preterm birth. *Sci Rep*. 2024;14(1):10800. doi:10.1038/s41598-024-61119-x
31. Qian T, Sheng X, Shen P, et al. Mets-IR as a predictor of cardiovascular events in the middle-aged and elderly population and mediator role of blood lipids. *Front Endocrinol*. 2023;14:1224967. doi:10.3389/fendo.2023.1224967

32. Lv D, Liu Z, Wu X, et al. Novel metabolic indicators and the risk of cardiovascular disease in patients with hypertension: a primary-care cohort study. *Nutr, Metab Cardiovasc Dis*. 2025;35(3):103749. doi:10.1016/j.numecd.2024.09.019
33. Lee SH, Park SY, Choi CS. Insulin resistance: from mechanisms to therapeutic strategies. *Diabetes Metab J*. 2022;46:15–37. doi:10.4093/dmj.2021.0280
34. Plows JF, Stanley JL, Baker PN, et al. The pathophysiology of gestational diabetes mellitus. *Int J Mol Sci*. 2018;19:3342. doi:10.3390/ijms19113342
35. Kim JK. Hyperinsulinemic-euglycemic clamp to assess insulin sensitivity in vivo. *Methods Mol Biol*. 2009;560:221–238. doi:10.1007/978-1-59745-448-3_15
36. Zhou M, Zhu L, Cui X, et al. The triglyceride to high-density lipoprotein cholesterol (TG/HDL-C) ratio as a predictor of insulin resistance but not of β cell function in a Chinese population with different glucose tolerance status. *Lipids Health Dis*. 2016;15:104. doi:10.1186/s12944-016-0270-z
37. Zhao S, Wang Z, Qing P, et al. Comprehensive analysis of the association between triglyceride-glucose index and coronary artery disease severity across different glucose metabolism states: a large-scale cross-sectional study from an Asian cohort. *Cardiovasc Diabetol*. 2024;23(1):251. doi:10.1186/s12933-024-02355-3
38. Wang D, Xu S, Chen H, et al. The associations between triglyceride to high-density lipoprotein cholesterol ratios and the risks of gestational diabetes mellitus and large-for-gestational-age infant. *Clin Endocrinol*. 2015;83(4):490–497. doi:10.1111/cen.12742
39. Liu PJ, Liu Y, Ma L, et al. The predictive ability of two triglyceride-associated indices for gestational diabetes mellitus and large for gestational age infant among Chinese pregnancies: a preliminary cohort study. *Diabetes Metab Syndr Obes*. 2020;13:2025–2035. doi:10.2147/dmso.S251846
40. Brenes-Martín F, Melero-Jiménez V, López-Guerrero MÁ, et al. First trimester evaluation of maternal visceral fat and its relationship with adverse pregnancy outcomes. *Biology*. 2023;12(2):144. doi:10.3390/biology12020144