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# Assessing the diagnostic value of the metabolic score for insulin resistance in gestational diabetes mellitus

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ABSTRACT

The aim of this study is to evaluate the diagnostic accuracy of the Metabolic Score for Insulin Resistance (METS-IR), Body Mass Index (BMI), insulin levels, homeostatic model assessment of insulin resistance (HOMA-IR), Waist-TG Index (WTI), and Lipid Accumulation Product (LAP), among Saudi women, determining gestational diabetes mellitus (GDM). This multi-center case-control study included 495 pregnant women from Saudi, comprising 145 with GDM, considering a mean age of 30.1±5.6 years, including 350 without GDM, with a mean age of 28.6±5.2 years. Anthropometric measurements and fasting blood samples were taken to assess glycemic and lipid profiles. The METS-IR and additional indices were computed. Diagnostic validity was assessed through the area under the curve (AUC) analysis. METS-IR showed the highest AUC of 0.66, signifying its superior predictive capability for GDM, with a sensitivity of 51.3% and specificity of 73.1%. BMI and LAP exhibited moderate predictive power, evidenced by AUC values of 0.63. Insulin and HOMA-IR demonstrated high sensitivity and lower specificity, indicating their effectiveness in early screening while also revealing their limitations as independent diagnostic instruments. WTI exhibited a moderate level of predictive capability, evidenced by an AUC of 0.61. In conclusion, METS-IR demonstrates promise as a tool for predicting GDM, exhibiting a favorable balance of sensitivity and specificity, which indicates its potential for incorporation into clinical screening protocols. The diagnostic accuracy of BMI, insulin, and other indices is enhanced when integrated with METS-IR. The research highlights the necessity for a thorough assessment strategy that integrates the clustering of metabolic indices to improve risk stratification and management of GDM, thereby minimizing negative outcomes for both mothers and infants. Subsequent investigations should focus on validating these results across varied populations and examining the long-term impacts on the health of the mother and fetus.

## 1. Introduction

Gestational diabetes mellitus (GDM) is a predominant metabolic condition that presents considerable dangers to both the mother and fetus, including heightened likelihood of developing type 2 diabetes mellitus (T2DM), preeclampsia, and fetal macrosomia (American Diabetes 2019; Choudhury and Devi Rajeswari 2021). The prevalence of GDM exhibits significant variation among diverse populations, shaped by genetic, environmental, and lifestyle determinants (Buchanan *et al.*, 2012; Chakraborty and Yadav 2024).

Insulin resistance characterizes GDM, wherein the body's cells exhibit reduced responsiveness to insulin, resulting in increased blood glucose levels (Shamsad *et al.*, 2025). Identifying and quantifying insulin resistance in pregnant women is essential for the early diagnosis and management of GDM. Conventional approaches for evaluating insulin resistance, including the hyperinsulinemic-euglycemic clamp and the homeostasis model assessment of insulin resistance (HOMA-IR), while precise, frequently prove impractical in clinical environments due to their complexity and expense (Bello-Chavolla *et al.*, 2018). Other fasting insulin-based indices, such as the quantitative insulin sensitivity check index, commonly used in routine examinations, also suffer from limitations related to cost, complexity, and variability in measurement.

The Metabolic Score for Insulin Resistance (METS-IR) represents a new and effective method for evaluating insulin resistance. METS-IR is a composite index that integrates waist circumference, triglyceride levels, and fasting glucose levels, providing a more straightforward and accessible assessment of insulin resistance than conventional methods (Azizi *et al.*, 2013). The association between METS-IR and GDM may be explained by the fact that its components—waist circumference, triglyceride levels, and fasting glucose—reflect key aspects of visceral adiposity and dyslipidemia. Increased visceral fat accumulation promotes insulin resistance through the secretion of inflammatory cytokines and free fatty acids, which in turn predisposes pregnant women to GDM (Reaven, 2011).

Research indicates that METS-IR demonstrates a strong correlation with recognized indicators of insulin resistance and serves as an effective predictor of metabolic syndrome and cardiovascular risk across diverse populations (Jang *et al.*, 2021).

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There is a paucity of research regarding the application of METS-IR in Arab women, especially in those with and without GDM. Considering the significant prevalence of GDM among the Arab population and the related long-term health risks, it is crucial to assess the effectiveness of METS-IR in this demographic (Al-Daghri *et al.*, 2011). Examining the association between METS-IR and GDM offers important insights into the metabolic health of Arab women, aiding in the formulation of targeted strategies for the management and prevention of GDM.

GDM in Saudi women poses distinct challenges attributed to the elevated prevalence of obesity, sedentary behavior, and particular genetic factors (Wani *et al.*, 2020; Al-Musharaf *et al.*, 2021). Research indicates that the incidence of GDM in Saudi Arabia markedly exceeds global averages. Mahha *et al.* (2024) indicated the GDM prevalence among Saudi women at approximately 23.9%%, significantly exceeding the global prevalence (14.1%) estimated by the International Diabetes Federation (International Diabetes Federation 2021; Mahha *et al.*, 2024). The high prevalence is attributable to multiple factors, such as the swift transition from traditional to Westernized diets, reduced physical activity, and an elevated baseline prevalence of obesity (Mabry *et al.*, 2010; Mahha *et al.*, 2024).

Additionally, GDM presents considerable long-term health risks for women in Saudi Arabia (Alsaedi *et al.*, 2020). Women who have already had GDM exhibit an increased risk of developing T2DM and cardiovascular diseases in later stages of life (Sun *et al.*, 2021). Furthermore, offspring of moms who have GDM exhibit a heightened risk of obesity, glucose intolerance, and metabolic syndrome in childhood and adolescence (Li *et al.*, 2017). The significant prevalence of GDM and its associated complications requires the implementation of effective screening and management strategies that are specifically tailored to the needs of the Saudi population.

Studies demonstrate that Arab populations possess distinct genetic and lifestyle characteristics that influence the incidence of metabolic disorders (Al-Homedi *et al.*, 2021; Alshehri 2023; AlAnazi *et al.*, 2024). A study conducted in Saudi Arabia demonstrated a significant correlation between GDM and development of T2DM, emphasizing the necessity for effective diagnostic tools and preventive strategies. Recent findings suggest that lifestyle modifications, including increased physical activity and dietary interventions, play a crucial role in reducing the incidence of GDM among high-risk populations. (Tsironikos *et al.*, 2023). The METS-IR score has been validated across diverse ethnic groups, confirming its utility in identifying insulin resistance and predicting metabolic syndrome. Bello-Chavolla and colleagues (2018) discovered a strong association between METS-IR and metabolic syndrome as well as cardiovascular risk factors in the Mexican population (Azizi *et al.*, 2013). Studies conducted in Asian and European cohorts have corroborated the efficacy of METS-IR as a dependable indicator of insulin resistance (Badran and Laher 2012; Jang *et al.*, 2021).

This study evaluates the efficacy of METS-IR in detecting insulin resistance in Arab women, both with and without GDM. This study aims to compare METS-IR values between two groups to assess its efficacy as a diagnostic tool for insulin resistance in pregnant women and to investigate the effects of this disorder on the health of the mother and fetus. The findings may enhance screening practices and management strategies, thereby decreasing the burden of diabetes mellitus during pregnancy and its related complications in Arab women.

## 2. Materials and method

### *2.1 Subjects*

In all, 495 Saudi pregnant women aged 27-35 years were recruited and split into two groups: the GDM group (n= 145) and the control group (n= 350). Participants were thought to be at high risk of GDM due to variables such as GDM personal history or polycystic ovarian syndrome, glycosuria, T2DM familial history, great obesity, and macrosomia. The grouping of participants was based on the results of the standard 75 g oral glucose tolerance test (OGTT) performed at 27.1 ± 4.1 weeks of gestation. According to the International Association for Diabetes in Pregnancy Study Group criteria, women with a fasting glucose value of ≥5.1 mmol/L and/or a 2-hour OGTT value of ≥8.5 mmol/L were classified as GDM, while those with values below these thresholds were assigned to the control group (Metzger *et al.*, 2010; Gupta *et al.*, 2015). Although a history of GDM is generally regarded as a high-risk factor, it was deliberately excluded in this study to evaluate the predictive capability of metabolic indices in a cohort without prior GDM, thereby reducing potential confounding associated with recurrent GDM. They were selected from a variety of hospitals in Riyadh, Saudi Arabia. The inclusion criteria were pregnant Saudi women carrying a singleton pregnancy. To keep a very homogenous population, women with known multiple pregnancies, history of GDM, or those with chronic conditions like T2DM and renal or hepatic problems were eliminated. Additional criteria for inclusion and exclusion were previously stated. (Al-Ajlan *et al.*, 2015). All participants consented prior to inclusion. The study was approved by the Institutional Review Board (IRB) of the College of Medicine, King Saud University (KSU) (IRB no: E-13-1013).

### *2.2 Anthropometry and blood collection*

Baseline examinations, including fasting blood withdrawal and anthropometric measurements, were performed at the time of recruitment (in the first trimester, between 8 and 14 weeks of gestation) as previously reported (Al-Ajlan *et al.*, 2015). Anthropometric measurements comprised height (cm), weight (kg), waist and hip circumferences (cm), and systolic and diastolic blood pressure (mmHg) taken using conventional protocols. The fasting blood samples collected during this visit were immediately transferred to the Chair for Biomarkers in Chronic Diseases at KSU, where they were processed, aliquoted, and kept at the proper temperature for subsequent analysis. Later on in pregnancy (age of gestation 27.1 ± 4.1 weeks), participants were contacted for a follow-up hospital visit for standard GDM screening as previously described (Metzger *et al.*, 2010; Gupta *et al.*, 2015)

### *2.3 Laboratory measurements*

Glucose, HbA1c%, total cholesterol, HDL cholesterol, triglycerides, and insulin (μU/mL) were the biochemical parameters examined for fasting blood samples taken at the first visit. Routine biochemical testing in an automated biochemistry analyzer (Konelab 20, Thermo-Fischer Scientific, Espoo, Finland) measured these parameters. For glucose, the computed total CV was ≤5%; for HbA1c, ≤3.5%; for total cholesterol, ≤4%; for HDL cholesterol, ≤4%; for triglycerides, ≤4%; for insulin, ≤4%. KSU's Quality Assurance Department constantly assessed the standards and controls used for these biochemical tests to guarantee very repeatable study results.

### *2.4 Follow-up visit for GDM screening:*

Later in pregnancy (age of gestation 27.1 ± 4.1 weeks), participants were contacted for a follow-up hospital visit for standard GDM screening. Blood samples were taken two hours after prandial and before eating (fasting).

*2.4.1* The “Insulin resistance index” used was “Homeostasis Model Assessment for Insulin Resistance” (HOMA-IR) calculated as: (Tang *et al.*, 2015)

$$\text{HOMA} - \text{IR} = \frac{\text{fasting insulin(uU/mL)} \times \text{fasting glucose(mmol/L)}}{22.5}$$

*2.4.2* WTI consisting of WC (cm) and TG (mg/dL) was calculated as follows (Liu *et al.*, 2020)

$$\text{WTI} = \ln\left(\text{triglycerides(mg/dL)} \times \frac{\text{waist circumference(cm)}}{2}\right)$$

*2.4.3* The LAP index in females was computed based on the following equation:(Kahn 2005)

$$\text{LAP} = (\text{waist circumference(cm)} - 58) \times \text{triglycerides}(mmol/L)$$

*2.4.4* METS-IR was calculated as follow: (Bello-Chavolla *et al.*, 2018)

$$METS - IR = \frac{ln[2 \times FPG\ (mg/dL) + TG(mg/dL)] \times BMI(kg/m^2)}{ln[HDL(mg/dL)]}$$

Given that the accuracy of our study relies on the precise application of the METS-IR score in detecting insulin resistance in pregnant women with and without GDM, any inaccuracy in the formula would compromise the validity of our findings.

### *2.5 Statistical analysis*

SPSS program version 21 (SPSS Inc., Chicago, IL) was used to analyze data. Participants' demographic and clinical traits were compiled using descriptive statistics. Mean ± standard deviation (SD) showed continuous data; categorical variables were stated as frequencies and percentages. The chi-square test for categorical variables and the independent t-test for continuous variables let one compare women with and without GDM. Pearson correlation analysis was used to evaluate METS-IR's association with other clinical criteria. In addition, multivariate logistic regression analysis—adjusted for potential confounders such as age, BMI, and family history of diabetes—was conducted to examine the relationship between METS-IR and GDM. A p-value < 0.05 was considered statistically significant.

## 3. Results

The study analyzed clinical characteristics of participants, divided into a control group and a group with GDM, as presented in Table 1. The research included 495 pregnant women from Saudi Arabia, with 350 in the control group and 145 in the GDM group. Data collected encompassed demographic details, physical measurements, and metabolic parameters. The average age was 28.6 years in the control group and 30.1 years in the GDM group, a statistically significant difference (p=0.004). Both groups showed similar mean ages at menarche, with no significant variation (p=0.33). The mean age at first pregnancy was 24.1 years in the control group versus 24.8 years in the GDM group, which was not statistically significant (p=0.12). Parity, however, differed significantly, with averages of 2.3 and 2.8 for the control and GDM groups, respectively (p=0.016).

The GDM group had notably more weight (P < 0.001). With a p-value of <0.001, the BMI in the GDM group—29.6 kg/m$^2$—was noticeably greater than that in the control group—26.9 kg/m$^2$. The waist-hip ratio (WHR) was also larger in the GDM group (p=0.016), and both waist and hip circumferences were noticeably higher in this group as well (p<0.001 and p=0.003, respectively). Blood pressure readings in the two groups showed no appreciable variations (p-values 0.45 and 0.47, respectively).

The GDM group had much higher fasting glucose and the HbA1c values (P < 0.001 for both). With P-values of 0.01, 0.13, and 0.001, respectively, the GDM group had total cholesterol, HDL cholesterol, and triglyceride levels all higher. In the GDM group, insulin levels and HOMA-IR were significantly higher, p-values of 0.008 and 0.002, respectively. The Waist-TG Index (WTI) (p < 0.001), Lipid Accumulation Product (LAP) (p < 0.001), and METS-IR (p < 0.001) demonstrated statistically significant differences between the groups. In particular, the differences in LAP and METS-IR indicate that these indices were markedly higher in the GDM group compared to the control group.

The gestational week did not show any significant variation across the groups (p=0.81.). Results of all glucose tolerance tests revealed notably higher values in the GDM group (p<0.001 for fasting, 1-hour, and 2-hour glucose levels).

It is important to note that although METS-IR is proposed as a predictive tool for GDM, the standard 75-gram OGTT was performed later in pregnancy (at 27.1 ± 4.1 weeks of gestation). Baseline measurements—including fasting blood glucose, triglyceride levels, BMI, and HDL cholesterol—were obtained during the first trimester (between 8 and 14 weeks of gestation). This early assessment allowed for the calculation of METS-IR before the conventional GDM diagnosis, and its first-trimester values were subsequently correlated with the later GDM diagnosis. This approach evaluates whether early metabolic profiling using METS-IR can provide additional predictive value over standard diagnostic methods, potentially enabling earlier intervention and improved risk stratification.

**Table 1.**
Clinical characteristic of the subjects.

| Parameters | Non-GDM | GDM | P-value |
|---|---|---|---|
| N | 350 | 145 | |
| Age (year) | 28.6 ± 5.2 | 30.1 ± 5.6 | 0.004 |
| Menarche age | 12.4 ± 1.4 | 12.5 ± 1.5 | 0.33 |
| Age at first pregnancy | 24.1 ± 4.4 | 24.8 ± 4.6 | 0.12 |
| Gestational week | 26.4 ± 2.4 | 26.34 ± 2.4 | 0.81 |
| Parity | 2.3 ± 1.9 | 2.8 ± 2.1 | 0.016 |
| ***Anthropometrics*** | | | |
| Weight (kg) | 64.6 ± 14.7 | 70.6 ± 16.4 | <0.001 |
| BMI (kg/m$^2$) | 26.9 ± 6.2 | 29.6 ± 6.7 | <0.001 |
| Waist (cm) | 90.2 ± 12.6 | 95.4 ± 13.4 | <0.001 |
| Hips (cm) | 106.7 ± 11.7 | 110.3 ± 11.1 | 0.003 |
| WHR | 0.85 ± 0.07 | 0.86 ± 0.08 | 0.016 |
| Systolic BP (mmHg) | 114.1 ± 13.6 | 113.0 ± 12.4 | 0.45 |
| Diastolic BP (mmHg) | 67.3 ± 9.4 | 67.4 ± 9.5 | 0.47 |
| ***Glycemic Profile*** | | | |
| Fasting glucose (mmol/L) | 4.25 ± 0.5 | 5.23 ± 0.9 | <0.001 |
| Glucose 1-hour | 6.78 ± 1.5 | 9.09 ± 2.3 | <0.001 |
| Glucose 2-hour | 5.94 ± 1.2 | 7.89 ± 2.1 | <0.001 |
| HbA1c (%) | 5.03 ± 0.5 | 5.27 ± 0.5 | <0.001 |
| Insulin (uU/mL) | 8.56 (4.46-19.46) | 11.54 (6.28-21.10) | 0.008 |
| HOMA-IR | 1.82 (0.9-4.0) | 2.66 (1.37-5.28) | 0.002 |
| ***Lipid profile*** | | | |
| Total cholesterol (mmol/L) | 4.93 ± 1.0 | 5.16 ± 1.1 | 0.01 |
| HDL cholesterol (mmol/L) | 1.32 ± 0.3 | 1.28 ± 0.4 | 0.13 |
| Triglycerides (mmol/L) | 1.35 ± 0.6 | 1.52 ± 0.6 | 0.001 |
| ***Indices*** | | | |
| WTI | 8.52 ± 0.5 | 8.69 ± 0.5 | <0.001 |
| LAP | 45.9 ± 29.1 | 58.8 ± 31.9 | <0.001 |
| METS-IR | 7.57 ± 0.34 | 7.78 ± 0.36 | <0.001 |

**Note**: Data presented mean ± SD. SBP: systolic blood pressure, DBP: diastolic blood pressure, FPG: fasting plasma METS-IR metabolic score for insulin resistance, HOMR-IR: homeostatic model assessment for insulin resistance, MET: (metabolic equivalent) of task P-value for the comparison of baseline characteristics between participants who developed GDM and those who did not develop GDM at the baseline survey. Significance was set at a p < 0.05

These findings highlight the significant metabolic differences between the control and GDM groups, emphasizing the need for careful monitoring and management of metabolic parameters in pregnant women at risk for GDM. The relative risk for GDM-associated with various metabolic parameters has been presented in Table 2. The odds ratios (OR) and 95% confidence intervals (CI) were calculated using two models: Model 1 (unadjusted) and Model 2 (adjusted for age, parity, previous GDM, menarche age, family history of GDM, and first relative DM). P-values indicate the statistical significance of the associations, with significance levels at 0.05 and 0.01.

For BMI, in Model 1, the odds of developing GDM were 1.42 times higher for those with a BMI of 25-30 and 2.48 times higher for those with a BMI greater than 30 compared to those with a BMI < 25. The p-value was significant at <0.001 for the >30 BMI category. In Model 2, the odds increased to 1.49 for the 25-30 BMI range and 2.92 for the >30 category (p=0.003).

Regarding insulin levels, in Model 1, participants in the second tertile (6.31-14.38) had a 1.74 times higher risk, and those in the third tertile (>14.38) had a 1.77 times higher risk of GDM, with P-values of 0.033 and 0.023, respectively. In Model 2, the odds ratios were not significant, indicating that adjustment for confounders reduced the association. For HOMA-IR, Model 1 showed a 1.98 times higher risk

**Table 2.**
Relative risk for GDM.

| Parameters | Model 1 | | Model 2 | |
|---|---|---|---|---|
| | Odd ratio (95%) | P- value | Odd ratio (95%) | P-value |
| **BMI** | | | | |
| <25 | 1 | | 1 | |
| 25-30 | 1.42 (0.86-2.33) | 0.17 | 1.49 (0.7-3.16) | 0.29 |
| >30 | 2.48 (1.55-3.96) | <0.001 | 2.92 (1.43-5.98) | 0.003 |
| **Insulin** | | | | |
| T1 (<6.31) | 1 | | 1 | |
| T2 (6.31-14.38) | 1.74 (1.05-2.89) | 0.03 | 0.94 (0.45-1.94) | 0.88 |
| T3 (>14.38) | 1.77 (1.08-2.90) | 0.02 | 0.96 (0.46-1.98) | 0.91 |
| **HOMA-IR** | | | | |
| T1 (<1.30) | 1 | | 1 | |
| T2 (1.30-3.29) | 1.98 (1.19-3.31) | 0.009 | 1.67 (0.82-3.38) | 0.16 |
| T3 (>3.29) | 1.86 (1.13-3.10) | 0.02 | 1.07 (0.50-2.30) | 0.85 |
| **WTI** | | | | |
| T1(<8.34) | 1 | | 1 | |
| T2 (8.35-8.80) | 1.58 (0.89-2.81) | 0.12 | 1.74 (0.85-3.58) | 0.13 |
| T3 (>8.8) | 2.58 (1.48-4.51) | <0.001 | 2.25 (1.06-4.78) | 0.03 |
| **LAP** | | | | |
| T1 (<30) | 1 | | 1 | |
| T2 (30.99-56.84) | 1.48 (0.82-2.67) | 0.19 | 1.42 (0.67-3.01) | 0.35 |
| T3 (>56.84) | 2.86 (1.63-5.0) | <0.001 | 2.45 (1.16-5.15) | 0.02 |
| **METS-IR** | | | | |
| T1 (<7.44) | 1 | | 1 | |
| T2 (7.44-7.77) | 1.47 (0.85-2.53) | 0.17 | 1.03 (0.49-2.12) | 0.94 |
| T3 (>7.77) | 3.45 (2.1-5.79) | <0.001 | 2.37 (1.13-4.97) | 0.02 |

Note: Data presented Odd ratio (95% CI), Model 1 unadjusted and model 2 to adjusted for age, parity, Previous GDM, Menarche age, Family GDM and first relative DM, P-value significant at 0.05 and 0.01 level.

for the second tertile and a 1.86 times higher risk for the third tertile, both significant with p-values of 0.009 and 0.015, respectively. Model 2 showed reduced odds ratios, and no significance was observed for the third tertile. The WTI in Model 1 showed a 2.58 times higher risk for those in the third tertile (>8.8) with a P-value of <0.001. In Model 2, the odds ratio for the third tertile was 2.25, significant at 0.034. For LAP, Model 1 indicated a 2.86 times higher risk for the third tertile, with a P-value of <0.001. In Model 2, the risk was 2.45 times higher for the third tertile, with a P-value of 0.018. Lastly, METS-IR in Model 1 showed a 3.45 times higher risk in the third tertile, with a significant p<0.001. In Model 2, the odds ratio for the third tertile was 2.37, significant at p=0.022. These results underscore the strong associations between elevated BMI, insulin, HOMA-IR, WTI, LAP, and METS-IR with the increased risk of developing GDM, highlighting the importance of monitoring these parameters in pregnant women. The adjustments in Model 2 demonstrate the impact of confounding factors on these associations, emphasizing the need for comprehensive risk assessments in clinical settings.

Table 3 evaluates the accuracy of the Receiver Operating Characteristic (ROC) analysis for many metabolic markers to project GDM. Among the measures measured are BMI, insulin, HOMA-IR, WTI, LAP, and METS-IR. Every parameter—optimal cut-off value, sensitivity, specificity, accuracy, and Youden index (J)—is shown along with its Area Under the Curve (AUC) and 95% confidence interval (CI).

BMI showed an AUC of 0.63 (95% CI: 0.56-0.69) with an optimal cut-off value of 26.11. It had a sensitivity of 64.1% and specificity of 56.3%, resulting in a J of 0.204, indicating moderate discriminatory ability. Insulin had an AUC of 0.59 (95% CI: 0.53-0.65) with a cut-off value of 5.86, demonstrating high sensitivity (77.8%) but lower

**Table 3.**
ROC, optimal cut-off values, sensitivity, specificity and Youden index for GDM.

| Parameters | AUC (95% CI) | Cutoff | P-value | Sensitivity (%) | Specificity (%) | Younden Index J |
|---|---|---|---|---|---|---|
| BMI | 0.63 (0.56-0.69) | 26.1 | <0.001 | 64.1 | 56.3 | 0.204 |
| Insulin | 0.59 (0.53-0.65) | 5.9 | <0.001 | 77.8 | 40.8 | 0.186 |
| HOMA-IR | 0.60 (0.54-0.66) | 1.1 | <0.001 | 79.5 | 39.6 | 0.191 |
| WTI | 0.61 (0.55-0.67) | 8.7 | <0.001 | 54.7 | 66.8 | 0.215 |
| LAP | 0.63 (0.57-0.69) | 51.6 | <0.001 | 55.6 | 66.8 | 0.224 |
| METS-IR | 0.66 (0.60-0.72) | 7.8 | <0.001 | 51.3 | 73.1 | 0.244 |

Note: Data presented AUC (95%) CI, Sensitivity (%), Specificity (%) and Younden index J. P-value significant at 0.05 and 0.01 level.

specificity (40.8%), leading to a J of 0.186. HOMA-IR exhibited an AUC of 0.60 (95% CI: 0.54-0.66) with a cut-off of 1.14, achieving sensitivity and specificity values of 79.5% and 39.6%, respectively, and a J of 0.191.

The WTI had an AUC of 0.61 (95% CI: 0.55-0.67) with a cut-off value of 8.72. It showed balanced sensitivity and specificity (54.7% and 66.8%), resulting in a J of 0.215. The LAP index had an AUC of 0.63 (95% CI: 0.57-0.69) with a cut-off of 51.60, showing sensitivity and specificity of 55.6% and 66.8%, with a J of 0.224. The MET-IR demonstrated the highest predictive ability with an AUC of 0.66 (95% CI: 0.60-0.72) and a cut-off value of 7.75. It had a sensitivity of 51.3% and the highest specificity of 73.1%, resulting in the highest J of 0.244 among the indices evaluated.

These results indicate that while METS-IR has the highest AUC and specificity, insulin and HOMA-IR demonstrate higher sensitivity. The J value suggests that MET-IR provides the best balance between sensitivity and specificity, making it a potentially valuable tool for predicting GDM. The P-values for all parameters were significant at the 0.05 and 0.01 levels, indicating the robustness of the findings.

The ROC curves for many metabolic markers have been shown in Fig. 1 as predictors of GDM. Since the discriminating threshold of a binary classifier system varies, the ROC curve, a graphical depiction, showcases its diagnostic power. The AUC gauges a parameter's capacity to separate the two diagnostic groups—control from GDM. Better diagnosis performance is indicated by AUC values near to 1. Every metabolic indicator in the figure—including BMI, insulin, HOMA-IR, WTI, LAP, and METS-IR—is shown by its ROC curve along with matching AUC values. The ROC curve demonstrates that METS-IR and HOMA-IR have the highest AUC values, suggesting they are the most effective predictors of GDM among the indices tested. BMI, WTI, and LAP also show good predictive capabilities but are slightly less effective compared to MET-IR and HOMA-IR. The optimal cut-off points for each parameter can be identified by the point on the ROC curve closest to the top-left corner of the plot, representing the best balance between sensitivity and specificity.

Sensitivity (true positive rate) and specificity (true negative rate) values are derived from the ROC curve to evaluate the performance of each index. Higher sensitivity indicates the parameter is good at identifying true positive cases (women with GDM), while higher specificity reflects its ability to identify true negative cases (women without GDM). The results suggest that incorporating MET-IR and HOMA-IR into clinical assessments could enhance the early detection and management of GDM in pregnant women. This analysis emphasizes the importance of choosing appropriate indices for GDM screening to improve outcomes for both mothers and their infants. These findings highlight the value of ROC curve analysis in evaluating the diagnostic performance of various metabolic indices, providing insights into the most effective predictors for GDM.

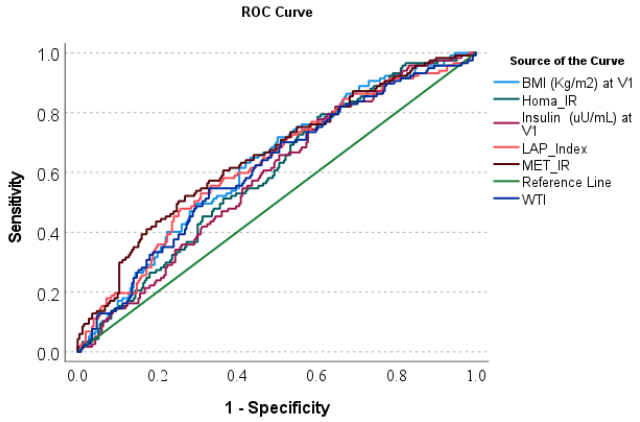


**Fig. 1.** AUC plots of METS-IR and other metabolic indices. METS-IR: Metabolic score for insulin resistance.

Supplementary Table S1 shows the correlations among BMI, insulin levels, HOMA-IR, WTI, LAP, and METS-IR.

## 4. Discussion

The present study evaluated the predictive capabilities of various metabolic indices, including BMI, insulin, HOMA-IR, WTI, LAP, and METS-IR, in diagnosing GDM. The analysis of these indices provides insights into their relative effectiveness and potential utility in clinical settings. Our findings offer valuable contributions to the growing body of research on the identification and management of GDM.

One potential mechanism underlying the association between METS-IR and GDM is that the components of METS-IR—waist circumference, triglyceride levels, and fasting glucose—are direct reflections of visceral adiposity and dyslipidemia. Increased visceral fat is known to secrete pro-inflammatory cytokines (such as TNF-α and IL-6) and free fatty acids, which impair insulin signaling and lead to systemic insulin resistance. This inflammatory state, combined with dysregulated lipid metabolism, contributes significantly to the development of GDM (Reaven, 2011). Moreover, these metabolic disturbances are captured by the METS-IR score, thereby explaining its strong predictive value for GDM.

The ROC analysis indicated that METS-IR had the highest AUC, suggesting it is the most effective predictor of GDM among the indices tested. With an AUC of 0.66 and a J of 0.244, METS-IR demonstrated the best balance between sensitivity (51.3%) and specificity (73.1%). This finding highlights the potential of METS-IR as a reliable tool for GDM screening, offering a practical alternative to traditional methods by integrating key metabolic parameters such as waist circumference, triglycerides, and fasting glucose. These results are consistent with previous studies that have shown the efficacy of METS-IR in predicting insulin resistance and related metabolic disorders (Bello-Chavolla *et al.*, 2018). Other studies have also found METS-IR to be useful in predicting metabolic syndrome and type 2 diabetes in non-pregnant populations, indicating its broader applicability (Qiu *et al.*, 2024).

BMI and LAP also showed moderate predictive capabilities, with AUC values of 0.63, but they had different sensitivity and specificity profiles. BMI exhibited a sensitivity of 64.1% and specificity of 56.3%, indicating its utility in identifying individuals at risk but with limited specificity. LAP, on the other hand, showed slightly better specificity (66.8%), which may be advantageous in specific clinical contexts where reducing false positives is critical. The findings suggest that while BMI is a widely used and easily accessible measure, its use in isolation may not be sufficient for accurate GDM prediction (Cho *et al.*, 2018).

The role of BMI in predicting GDM has been supported by some studies, which emphasize that higher BMI increases the risk of developing GDM due to increased insulin resistance and altered adipokine secretion (Nakshine and Jogdand 2023). However, other research has suggested that BMI should be used in combination with other metabolic indices to enhance predictive accuracy, as it does not fully capture the complex metabolic changes occurring during pregnancy (Teshome *et al.*, 2021).

Insulin and HOMA-IR showed high sensitivity, 77.8% and 79.5%, respectively, indicating their strength in identifying true positive cases of GDM. However, their lower specificity values (40.8% and 39.6%, respectively) suggest a higher rate of false positives, which may limit their utility as standalone screening tools. The high sensitivity of these indices suggests that they could be particularly useful in early screening to ensure high-risk individuals are not missed, but they should be complemented with other measures to improve specificity (Metzger *et al.*, 2010; Landon *et al.*, 2011).

HOMA-IR, in particular, has been extensively studied and validated as a measure of insulin resistance, with numerous studies supporting its use in predicting GDM risk (Buchanan *et al.*, 2012; Xiang *et al.*, 2013). It reflects the interaction between fasting glucose and insulin levels, providing insights into the insulin sensitivity of peripheral tissues (Reaven 2011). However, its lower specificity in this study suggests that relying solely on HOMA-IR may lead to overdiagnosis in clinical practice.

The WTI showed a moderate predictive capacity with an AUC of 0.61. Although it provided balanced sensitivity and specificity, its overall performance was less robust compared to MET-IR and other indices. This suggests that while WTI can be part of a comprehensive assessment strategy, it may not be suitable as a primary diagnostic tool for GDM. Previous research has highlighted the potential of WTI in assessing cardiovascular and metabolic risk, but its utility in GDM prediction remains less clear (Sweeting *et al.*, 2022). Waist circumference, a component of WTI, is an indicator of visceral fat, which is metabolically active and contributes to insulin resistance (Ramírez-Manent *et al.*, 2023).

The correlation analysis further supported these findings, revealing strong associations between MET-IR and other metabolic parameters. MET-IR's strong correlations with indices like HOMA-IR and LAP indicate its ability to capture multiple aspects of insulin resistance and lipid accumulation, which are critical factors in the pathophysiology of GDM. This aligns with previous studies that have emphasized the importance of comprehensive metabolic profiling in predicting GDM risk (Farrar *et al.*, 2017).

Overall, this study underscores the importance of utilizing a combination of metabolic indices to enhance the accuracy and reliability of GDM screening. The integration of METS-IR with other measures could optimize risk stratification and improve outcomes for pregnant women by enabling timely interventions. Future studies should focus on validating these findings in larger and more diverse populations to confirm the generalizability of these indices and refine their application in clinical practice. Additionally, longitudinal studies could elucidate how these indices predict long-term maternal and fetal outcomes, further enhancing their clinical utility (Morgan *et al.*, 2021, Chen *et al.*, 2023). The early detection and management of GDM are crucial in preventing adverse pregnancy outcomes such as macrosomia, pre-eclampsia, and the T2DM development later in life for both the mother and the child (Zhang *et al.*, 2016).

The main benefits of this work are its thorough evaluation of numerous metabolic indices, including METS-IR, BMI, insulin, HOMA-IR, WTI, and LAP. This multifarious strategy emphasizes each index's possible contribution to early identification and therapy and enables a complete knowledge of the metabolic alterations related to GDM. The research increases the knowledge of how a combination of metabolic indicators might enhance the prediction of GDM by concentrating on METS-IR, a very novel and integrative index. Clinicians might find METS-IR a useful tool as it can balance sensitivity and specificity, therefore providing a possible benefit over conventional indices. Furthermore, the computation of AUCs and the use of ROC curves provide a strong approach for evaluating the diagnostic performance of every index, thus enabling direct comparisons of their efficacy in controlling GDM. The results underline the need to include many metabolic indicators in GDM screening procedures, hence enhancing risk classification and intervention plans in clinical environments. The research has some restrictions. It was conducted on a particular population, so the generalizability might be limited. A greater sample size would help to verify the relevance of these indicators throughout several ethnic groups and geographical areas. As it limits the ability to show causal relationships between the metabolic indices and the

development of GDM, the cross-sectional aspect of the study underlines the need for longitudinal studies to monitor changes over time and generate causation. Though some confusing elements were considered, there might still be unmeasured variables affecting the correlations between the metabolic indices and GDM. The emphasis of the research on early pregnancy indicators did not fully reflect all the metabolic changes that develop later in pregnancy, thereby influencing the prediction capacity of the indices. Moreover, the research neglected to thoroughly assess lifestyle elements, including nutrition and physical exercise, which are known to affect the metabolic condition and can affect the indices' prognostic accuracy. Eventually, the dependence on biochemical measurements, which may be influenced by many elements like stress, disease, or laboratory variability, may impair the outcomes. Dealing with these constraints in future studies might help to improve the creation of efficient screening tools and provide a more complete knowledge of the use of these indices in forecasting GDM.

## 5. Conclusion

This research emphasizes how certain metabolic indices, including METS-IR, may be useful in predicting GDM. The findings suggest that METS-IR, which integrates key metabolic parameters, offers a more balanced approach in terms of sensitivity and specificity compared to traditional indices like BMI, insulin, and HOMA-IR. The comprehensive assessment of these indices emphasizes the importance of a multifaceted approach to screening, which can enhance the accuracy and reliability of GDM predictions. The results indicate that incorporating METS-IR alongside other indices could improve risk stratification and early identification of high-risk individuals, ultimately facilitating timely intervention and management of GDM. This approach can potentially reduce adverse maternal and fetal outcomes associated with GDM, such as macrosomia, pre-eclampsia, and the development of T2DM later in life

## CRediT authorship contribution statement

**Sobhy M Yakout, Malak N.K. Khattak, Amal Alenad, Nasser M. Al-Daghri:** Conceptualization, Investigation, Methodology, Resources, Formal analysis, Data curation, Validation, and Manuscript review and editing. **Sobhy M. Yakout:** Writing–original draft, Writing–review and editing, and software analysis. **Malak N.K. Khattak and Abdullah M. Alnaami:** Formal analysis, Data curation, Validation, and Manuscript review and editing.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Declaration of Generative AI and AI-assisted technologies in the writing process

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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## Supplementary data

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