




# Insulin Resistance in Gestational Diabetes Mellitus and Its Association With Anthropometric Fetal Indices

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## ABSTRACT

**BACKGROUND:** In pregnant women with gestational diabetes mellitus (GDM), insulin resistance (IR) increases the risk of developing manifest type 2 diabetes mellitus and is associated with complications in both mother and fetus.

**OBJECTIVES:** This research aimed to evaluate the associations between IR evaluated by 3 indices (namely updated homeostasis model assessment model (HOMA2), QUICKI, and McAuley's index) and the diabetes risk factors and the fetal growth indices in Vietnamese women with GDM.

**METHODS:** A cross-sectional descriptive study was conducted on 370 women with GDM and 40 healthy pregnant women from January 2015 to May 2019. IR was calculated by HOMA2 (HOMA2-IR), QUICKI, and McAuley's index. Fetal anthropometric measurements were assessed via ultrasound which was performed and interpreted by ultrasound experts.

**RESULTS:** In the simple regression analysis, McAuley's index illustrated had statistically significant correlations to the highest number of risk factors of diabetes mellitus compared with HOMA2-IR and QUICKI indices. Moreover, McAuley's index correlated statistically significantly to the highest number of fetal ultrasound measurements factors such as including biparietal diameter (BPD) ( $r = -0.271$ ,  $P < .001$ ), head circumference (HC) ( $r = -0.225$ ,  $P < .001$ ), abdominal circumference (AC) ( $r = -0.214$ ,  $P < .001$ ), femur length (FL) ( $r = -0.231$ ,  $P < .001$ ), estimated fetal weight (EFW) ( $r = -0.239$ ,  $P < .001$ ) and fetal estimated age ( $r = -0.299$ ,  $P < .001$ ). In the multivariable analysis, the McAuley's index contributed the greatest to AC (Standardized B of  $-0.656$ ,  $P < .001$ ).

**CONCLUSION:** The McAuley's index was significantly associated with a higher number of more risk factors for diabetes mellitus as well as fetal ultrasound sonography findings measurements than compared with HOMA2-IR and QUICKI indices.

**KEYWORDS:** Gestational diabetes mellitus, diabetes risk factors, insulin resistance index, fetal ultrasonography, McAuley's index

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## Introduction

Nearly 10% of pregnancies globally suffer from GDM.<sup>1,2</sup> Pregnancy during the last 2 trimesters is considered a somewhat reversible window of predisposing diabetes as pregnancy reduces the sensitivity of tissues to insulin, increases blood

insulin levels, and increases insulin dose in individuals who have previously had GDM.<sup>3,4</sup> A previous study using the glucose clamp technique showed a nearly 60% reduction in insulin sensitivity during normal pregnancy.<sup>5</sup> IR in pregnancy is caused by the placenta secreting hormones such as lactogen, cortisol, estrogen, and progesterone which stimulate both insulin secretion and insulin antagonism.<sup>6,7</sup> Production of hormones tends

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to increase during pregnancy and most of these hormones contribute to IR and pancreatic beta-cell dysfunction.<sup>5</sup> Apart from IR, beta-cell dysfunction makes pregnant women more likely to have increases the risk of developing type 2 diabetes mellitus and makes it difficult to control blood glucose in GDM cases, increasing the risk of complications in both the mother (future type 2 diabetes, hypertension, and preeclampsia) and the fetus (macrosomia, obesity, and type 2 diabetes mellitus later in life).<sup>6,8-10</sup> There have been many indices to assess IR in patients with diabetes such as original homeostasis model assessment (HOMA1), HOMA2, QUICKI, and the McAuley's index. All of them were built based on the non-pregnant diabetic population, which indicates that there could be some bias when used to gauge IR among GDM.<sup>11-13</sup>

Fetal ultrasound is not only a relatively easy-to-do imaging scan but also a safe method for the assessment of fetal growth. In Vietnam, it is recommended that all pregnant women have a pregnancy ultrasound scan at least 3 times during pregnancy at the end of each quarter to manage pregnancy and help the prognosis of delivery. By scanning fetal ultrasound images to help and evaluate many important indicators of the fetus such as BPD, HC, AC, FL, amniotic fluid index (AFI), and fetal heart rate (HR), and EFW, physicians can detect pathological status and monitor fetal development in the womb.<sup>14</sup> Measurement of fetal AC, BPD, and EFW are useful in screening for GDM at weeks 24 to 28. This procedure is performed with high repeatability and efficiency.<sup>15</sup> Some studies have shown that the lower maternal insulin sensitivity, the less responsive the fetal brain is, suggesting that maternal metabolic changes affect fetal brain activity and central IR may be observed during fetal development.<sup>16</sup> Although IR in pregnant women is the physiological adaptation required to supply glucose for the rapid development of the fetus, disturbances in maternal metabolism can induce structural and functional abnormalities for fetal development.<sup>9,17</sup>

This research aimed to evaluate the associations between IR evaluated by 3 indices (namely HOMA2, QUICKI, and McAuley's index) and the diabetes risk factors and the fetal growth indices in Vietnamese women with GDM.

## Methods

### *Study design and participant characteristics*

A cross-sectional descriptive study was conducted in 370 with GDM and 40 normal pregnancies, at the National Endocrinology Hospital, Hanoi, Vietnam during the period January 2015 to May 2019. Women aged  $\geq 20$  years from their second trimester of gestation without a history of diabetes mellitus before pregnancy and hereditary disorders visiting the Outpatient Department of the National Endocrine Hospital were enrolled.

GDM diagnosis was established based on the results of blood glucose at any of 3 time points (namely, before or 1-hour or 2-hours after a 75-g glucose load) of one-step approach with

the oral glucose tolerance test (OGTT) according to the International Association of Diabetes and Pregnancy Study Groups (IADPSG) (2010).<sup>18</sup> We excluded individuals with diabetes other than GDM or those who had conditions that affected blood glucose levels including severe chronic liver failure, heart failure or kidney failure, hemodynamic diseases (such as moderate-to-severe anemia, aplastic anemia, and hemolytic anemia), systemic diseases (systemic lupus erythematosus and peripheral arterial occlusive diseases), infections (tuberculosis, foot ulcer, and severe infections).

### *Clinical and biochemical assessments*

All study participants were examined for anthropometric indicators (height, weight, and body mass index was derived), systolic and diastolic blood pressure, clinical signs and symptoms of diabetes, and complete records of pregnancy history, comorbidity, current medications as well as family and personal history of diabetes.

The study participants were instructed to fast from 10 p.m. the night before. On the day of clinical examination, approximately 2.5 mL fasting blood was drawn at 7 a.m, and the study participant was given a 200 mL solution of water containing 75-g of glucose and instructed to drink the solution within 5 minutes for the OGTT. Venous blood samples were collected at 60 and 120 minutes. Fasting plasma glucose (FPG), blood glucose at 1 hour and 2 hours post-load were analyzed by hexokinase methods (Beckman AU680, USA). Serum insulin and C-peptide were measured by electrode chemiluminescence (COBAS E411, USA). Glycated hemoglobin (HbA<sub>1c</sub>) was measured as NGSP results by the high-performance liquid chromatography method (Adams A1C, Japan). Serum lipid profiles (ie, total cholesterol, triglycerides, LDL-C, and HDL-C), aspartate transaminase, alanine transaminase, and creatinine were measured by the enzyme colorimetric method (Beckman AU680, USA). The whole blood cell was counted by K-4500, Japan.

We employed 3 independent IR indices, that is, HOMA2-IR, QUICKI, and McAuley's index. As the HOMA2-IR model accounts for variations in hepatic and peripheral glucose resistance.<sup>19</sup> Regarding HOMA2-IR, increasing values corresponded to increased IR. For both QUICKI and McAuley's index, increased values corresponded to decreased IR.

HOMA2-IR were calculated from the automatic calculator from <https://www.dtu.ox.ac.uk/homacalculator/> (Diabetes Trial Unit, University of Oxford, United Kingdom) as the previous studies.<sup>11,20,21</sup>

QUICKI was calculated using the equation

$$\text{QUICKI} = \frac{1}{\log \left[ \text{fasting serum insulin (IU / mL)} \right] + \log \left[ \text{fasting serum glucose (mg / dL)} \right]}$$

The McAuley's index was calculated using the equation

$$\text{McAuley} = e^{2.63 - 0.28 \ln[\text{fasting serum insulin (IU/mL)}] - 0.31 \ln[\text{serum triglycerides (mmol/L)}]}$$

Following completion of the OGTT, the study participants were instructed to eat as usual and to go for a pregnancy ultrasound assessment test. Ultrasound of the fetus was performed by an ultrasound specialist with a transducer of 3 to 5 MHz. The procedure for fetal ultrasound, measuring and calculating BPD, HC, AC, FL, AFI, HR, EFW indices was performed according to the recommendations by the American College of Radiology guidelines.<sup>22</sup>

### Data analysis and statistical analysis

All results are presented as mean  $\pm$  standard deviation or if skewed, as median (interquartile range, Q1-Q3) for the continuous variables, and as a percentage for categorical variables. Differences between groups were examined with Student's *t*-test or Mann-Whitney's test. The relationships between indicators of IR and other factors were determined using univariable linear regression and multivariable linear regression. Pearson's *r* and standardized B were calculated for the correlation between IR indices and quantitative variables (such as developmental features of the fetus from ultrasound findings, blood pressure, maternal weight, total cholesterol, triglycerides, HDL-C, LDL-C, and hemoglobin) and dichotomous variables (family history of diabetes, acanthosis nigricans, and lipid disorders). A *P*-value  $< .05$  was considered statistically significant. Data were processed using SPSS software version 26 (64-bit) for Window (SPSS Inc, Chicago, IL).

### Results

There were disparities among the mean blood glucose levels that showed significantly higher values at FPG, 1 hour, and 2 hours after a 75-g glucose load in the GDM group. Particularly, whilst only 32.4% of GDM had high FPG, approximately 70% of GDM accounted for high blood glucose either at 1 hour or 2 hours after a 75-g glucose load. In addition, women with GDM had higher BMI at the time of OGTT and before pregnancy, systolic blood pressure, serum levels of insulin, C-peptide, cholesterol, LDL-C, triglycerides, and HbA<sub>1c</sub> compared with pregnant women with NGT. There were significant differences in IR based on HOMA2-IR, QUICKI, and McAuley's indices between the 2 groups. Specifically, in the women with GDM group, the HOMA2-IR index was significantly higher, and QUICKI and McAuley's index were statistically significantly lower compared with the NGT pregnant women group (Table 1).

In the simple regression analysis, there was a significantly positive correlation between McAuley's index and maternal family history of diabetes mellitus, acanthosis nigricans (standardized B of 0.133, *P* = .021 and .141, *P* = .015, respectively), total cholesterol, triglycerides, and LDL-C (*r* of -0.155,

*P* = .004; - 0.631, *P* < .001; and .154, *P* = .007, respectively). Maternal BMI at the time of OGTT, systolic blood pressure, and diastolic blood pressure were inversely correlated with QUICKI index (*r* of -0.432; -0.253; and -0.209, respectively, all *P* values < .001) and McAuley's index (*r* of -0.499, -0.272, and -0.256, respectively, all *P* values < .001). They also had significantly positive correlation with HOMA2-IR index by C-peptide (*r* of 0.228, *P* < .001; .212, *P* < .001; and 0.118, *P* = 0.025, respectively) and HOMA2-IR by insulin (*r* of 0.318; 0.218; and 0.193, respectively, all *P* values < .001). McAuley's index was correlated with the highest number of diabetes risk factors of all used IR indicators (Table 2).

The characteristics of fetal growth indices were presented in Supplemental Table S1. The correlation between fetal ultrasound measurements and the IR indices were shown in Table 3. HR and EFW were positively correlated with the HOMA2-IR index by insulin (*r* of 0.106, *P* = .041 and .114, *P* = .027, respectively). EFW and fetal age were positively correlated with the HOMA2-IR index by C-peptide (*r* of 0.156, *P* = .002 and .141, *P* = .005, respectively). There were negative correlations between McAuley's index and fetal ultrasound findings (with BPD: *r* of -0.271; with HC: *r* of -0.225; with AC: *r* of -0.214; with FL: *r* of -0.231; with EFW: *r* of -0.239, and with fetal age: *r* of -0.299; all *P* values < .001). The fetal growth indices did not correlate with the QUICKI index (*P* > .05) (Table 3).

When conducting in the multivariable analysis that included AC and other dependent factors (IR index, maternal weight, blood glucose after taking OGTT, and acanthosis nigricans status) as variables, only maternal BMI at the time of OGTT, the McAuley's index, and QUICKI scores were statistically significantly associated with AC. Of those, the McAuley's index contributed the greatest to AC (Standardized B of -0.656, *P* < .001) (Table 4).

### Discussion

#### *The associations between insulin resistance indices and the diabetes risk factors in gestational diabetes mellitus*

There have been some risk factors for GDM and diabetes including gene, age, height, BMI, and previous history of GDM.<sup>23-26</sup> Changes in triglyceride could contribute to fetal growth and postnatal development.<sup>27</sup> Furthermore, in addition to metabolic changes during pregnancy, lipid metabolism and serum lipid profile also changed,<sup>28</sup> which is thought to be due to a variety of causes, including IR.<sup>29</sup> Given these theories, to assess IR we employed HOMA2 indices, QUICKI, and McAuley's index. The results of our study showed that in women with GDM, whilst HOMA2-IR was higher but,

**Table 1.** Characteristics of the study population.

| VARIABLES, UNIT                            | GESTATIONAL DIABETES MELLITUS (n=370) | NORMAL PREGNANCY (n=40) | P-VALUE |
|--|---------------------------------------|-------------------------|---------|
| Age, year                                  | 30.00 (27.00-34.00)                   | 29.50 (26.00-34.00)     | .688    |
| Age ≥ 35 years                             | 86 (23.3)                             | 11 (27.5)               | .554    |
| BMI at the time of OGTT, kg/m <sup>2</sup> | 25.24 (23.26-27.34)                   | 23.43 (21.89-25.15)     | <.001   |
| BMI before pregnancy, kg/m <sup>2</sup>    | 21.33 (19.64-23.23)                   | 19.82 (18.52-20.93)     | <.001   |
| Family of history diabetes mellitus (n, %) | 55 (14.9)                             | 0 (0)                   | N.A     |
| Acanthosis nigricans (n, %)                | 87 (23.5)                             | 0 (0)                   | N.A     |
| Systolic blood pressure, mmHg              | 110.00 (100.00-120.00)                | 110.00 (110.00-120.00)  | .044    |
| Diastolic blood pressure, mmHg             | 70.00 (60.00-70.00)                   | 70.00 (70.00-70.00)     | .150    |
| Red Blood Cell, T/L                        | 4.10 (3.85-4.37)                      | 4.15 (3.87-4.32)        | .959    |
| Hemoglobin, g/L                            | 119.58 ± 9.99                         | 121.30 ± 10.00          | .245    |
| Alanine transferase, U/L                   | 14.00 (11.00-19.00)                   | 13.00 (9.75-17.00)      | .001    |
| Aspartate transferase, U/L                 | 18.00 (15.00-21.00)                   | 15.00 (12.00-17.00)     | .042    |
| Creatinine, μmol/L                         | 54.00 (50.00-58.00)                   | 55.50 (51.00-60.75)     | .237    |
| Insulin, pmol/L                            | 79.60 (49.66-123.80)                  | 61.00 (42.91-90.75)     | .027    |
| C-peptide, nmol/L                          | 0.97 (0.66-1.35)                      | 0.73 (0.52-1.02)        | <.001   |
| Lipid profiles, mmol/L                     |                                       |                         |         |
| Total cholesterol, mmol/L                  | 5.71 (5.02-6.51)                      | 5.28 (4.48-6.04)        | .008    |
| HDL-C, mmol/L                              | 1.77 (1.55-2.00)                      | 1.29 (1.17-2.14)        | <.001   |
| LDL-C, mmol/L                              | 3.00 (2.00-3.00)                      | 2.40 (1.85-3.68)        | .967    |
| Triglycerides, mmol/L                      | 2.75 (2.13-3.69)                      | 2.30 (1.50-2.98)        | .005    |
| OGTT with a 75-g glucose load, mmo/L       |                                       |                         |         |
| FPG, mmol/L<br>(% increase)                | 4.89 (4.47-5.37)<br>(32.4%)           | 4.10 (3.90-4.50)        | <.001   |
| 1 h-PPG, mmol/L<br>(% increase)            | 10.47 (9.82-11.32)<br>(68.9%)         | 7.60 (6.45-8.58)        | <.001   |
| 2h-PPG, mmol/L<br>(% increase)             | 9.30 (8.61-10.10)<br>(70.8%)          | 6.40 (5.40-7.18)        | <.001   |
| HbA1c, %                                   | 5.30 (5.10-5.60)                      | 4.90 (4.50-5.20)        | <.001   |
| Trimester                                  |                                       |                         |         |
| Second Trimester, %                        | 14.25                                 | 27.50                   |         |
| Third Trimester, %                         | 85.75                                 | 72.50                   |         |
| Time of OGTT, weeks                        | 30.0 (26.0-33.0)                      | 29.5 (24.0-34.0)        | .083    |
| HOMA2-IR (C-peptide)                       | 2.13 (1.38-2.87)                      | 1.43 (1.10-1.88)        | .001    |
| HOMA2-IR (Insulin)                         | 1.44 (0.91-2.29)                      | 1.15 (0.88-1.67)        | .006    |
| QUICKI index                               | 0.34 ± 0.037                          | 0.35 ± 0.026            | .001    |
| McAuley's index                            | 5.10 (4.26-6.10)                      | 5.89 (5.01-6.67)        | .002    |

Abbreviations: OGTT, oral glucose tolerance test; FPG, fasting plasma glucose; PPG, postprandial glucose. Data were shown as either Mean ± standard deviation or percentage or Median (Interquartile range, Q1-Q3).

**Table 2.** The correlation between insulin indices and diabetic risk factors in pregnancies with gestational diabetes mellitus.

| VARIABLES, UNIT                            | HOMA2-IR C-PEPTIDE | HOMA2-IR INSULIN   | QUICKI              | MCAULEY             |
|--|--------------------|--------------------|---------------------|---------------------|
| Family history of diabetes, positive       | -0.052             | -0.028             | 0.107               | 0.133 <sup>†</sup>  |
| BMI at the time of OGTT, kg/m <sup>2</sup> | 0.228 <sup>¶</sup> | 0.318 <sup>†</sup> | -0.432 <sup>¶</sup> | -0.499 <sup>¶</sup> |
| Systolic blood pressure, mmHg              | 0.212 <sup>¶</sup> | 0.218 <sup>¶</sup> | -0.253 <sup>¶</sup> | -0.272 <sup>¶</sup> |
| Diastolic blood pressure, mmHg             | 0.118 <sup>†</sup> | 0.193 <sup>¶</sup> | -0.209 <sup>¶</sup> | -0.256 <sup>¶</sup> |
| Acanthosis nigricans, positive             | -0.018             | 0.016              | 0.074               | 0.141 <sup>†</sup>  |
| Lipid profiles                             |                    |                    |                     |                     |
| Total cholesterol, mmol/L                  | 0.16 <sup>†</sup>  | 0.030              | -0.001              | -0.155 <sup>†</sup> |
| Triglyceride, mmol/L                       | 0.273 <sup>¶</sup> | 0.177 <sup>†</sup> | -0.262 <sup>¶</sup> | -0.631 <sup>¶</sup> |
| HDL-C, mmol/L                              | -0.053             | -0.051             | 0.046               | 0.097               |
| LDL-C, mmol/L                              | -0.038             | -0.094             | 0.153 <sup>†</sup>  | 0.154 <sup>†</sup>  |
| Lipid disorders, positive                  | -0.010             | 0.048              | -0.096              | -0.048              |
| Hemoglobin, g/L                            | 0.088              | 0.061              | -0.089              | -0.102              |

Abbreviations: OGTT, oral glucose tolerance test.

<sup>†</sup>*P* < .05.<sup>¶</sup>*P* < .001.**Table 3.** The correlation between insulin indices and developmental features of the fetus.

| VARIABLES, UNIT      | HOMA2-IR C-PEPTIDE | HOMA2-IR INSULIN   | QUICKI | MCAULEY             |
|----------------------|--------------------|--------------------|--------|---------------------|
| BPD, mm              | 0.084              | 0.060              | -0.080 | -0.271 <sup>¶</sup> |
| HC, mm               | 0.088              | 0.025              | -0.036 | -0.225 <sup>¶</sup> |
| AC, mm               | 0.085              | -0.002             | -0.021 | -0.214 <sup>¶</sup> |
| FL, mm               | 0.071              | 0.071              | -0.082 | -0.231 <sup>¶</sup> |
| AFI, mm              | 0.061              | -0.133             | 0.155  | 0.092               |
| HR, beats per minute | 0.026              | 0.106 <sup>†</sup> | -0.100 | -0.024              |
| EFW, gram            | 0.156 <sup>‡</sup> | 0.114 <sup>†</sup> | -0.097 | -0.239 <sup>¶</sup> |
| Fetal age, week      | 0.141 <sup>‡</sup> | 0.086              | -0.092 | -0.299 <sup>¶</sup> |

Abbreviations: BPD, biparietal diameter; HC, head circumference; AC, abdominal circumference; FL, femur length; EFW, estimated fetal weight; HR, fetal heart rate; AFI, amniotic fluid index.

<sup>†</sup>*P* < .05.<sup>‡</sup>*P* < .01.<sup>¶</sup>*P* < .001.

QUICKI and McAuley's index were significantly lower compared to normal pregnant women. Regarding the correlation between the IR indices (HOMA2-IR by C-peptide, HOMA2-IR by insulin, QUICKI, and McAuley's index) and some maternal diabetes risk factors, we found that there was a statistically significant correlation between most indicators of IR with maternal weight and blood pressure. However, the results of regression analysis outlined that there was only a correlation between McAuley's index with a family history of diabetes and acanthosis nigricans. Studies have shown the role of a family history of diabetes and acanthosis nigricans in IR.<sup>30-33</sup>

Patients with concurrent acanthosis nigricans will have many risk factors for diabetes and will be at a greater risk of developing diabetes.<sup>34-36</sup> Similarly, a family history of having a father or a sibling with diabetes was also considered as a risk factor for diabetes.<sup>36-38</sup> Thus, among the indicators used to evaluate the current common IR, for patients with diabetes, McAuley's index achieved the most correlation with the risk factors of GDM. Besides, insulin concentrations and fasting blood triglyceride levels in GDM patients were both higher than in normal women, resulting in a disturbance in both excretion and metabolism. Blood glucose levels, IR associated with an

**Table 4.** The results of multivariable linear regression analysis: Standardized Beta Coefficients of Independent Variables and Fetal abdominal circumference.

| DETERMINANTS, UNIT                         | STANDARDIZED $\beta$ | VIF   | P-VALUE |
|--|----------------------|-------|---------|
| BMI at the time of OGTT, kg/m <sup>2</sup> | 0.299                | 1.310 | <.001   |
| Maternal blood glucose, mmol/L             |                      |       |         |
| After OGTT 1 hour                          | -0.060               | 1.051 | .274    |
| After OGTT 2 hours                         | -0.037               | 1.027 | .500    |
| HOMA2-IR Cpeptide                          | 0.006                | 1.255 | .915    |
| McAuley's index                            | -0.656               | 4.260 | <.001   |
| QUICKI                                     | 0.645                | 3.880 | <.001   |
| Acanthosis nigricans                       | 0.080                | 1.069 | .155    |

Abbreviations: OGTT, oral glucose tolerance test; VIF, the variance inflation factor.

inadequate insulin secretion response are the main mechanisms of GDM.<sup>1</sup> On the other hand, our study showed that only 32.4% of GDM had high FPG, approximately 70% of GDM accounted for high blood glucose either at 1 hour or 2 hours after a 75-g glucose load. So IR indices (QUICKI and HOMA2-IR) based on fasting values only might not provide the full picture of the observed magnitude of IR. Though it was documented that fasting IR indices correlate very well with each other, at least in not pregnant women, correlation with IR indices derived from OGTT (eg, Matsuda or Belfiore indices) is much weaker.<sup>39,40</sup> Therefore, McAuley's index was determined based on insulin concentration and fasting blood triglycerides concentration, which seems to reflect the true nature of the origin of IR in GDM rather than other indicators (QUICKI and HOMA2-IR).

#### *Insulin resistance and fetal ultrasound findings in pregnant women with gestational diabetes mellitus*

The results of our study showed that the IR index is related to some anthropometric indicators of the fetus in GDM mothers. In particular, McAuley's index is inversely correlated with most of the primary fetal growth indicators including BPD, HC, AC, FL, EFW, and fetal age. The growth rate of fetuses of pregnant women with GDM differs from that of the normal population. Growth acceleration persists until the late third trimester. Moreover, periconceptional glucose control appears to have a significant effect on the accelerated growth of the fetal abdominal area.<sup>41</sup> Numerous studies have demonstrated the role of IR in pregnancy and its relation to fetal development.<sup>42</sup> Decreased insulin sensitivity in GDM may increase nutrient availability to the fetus, possibly accounting for the higher risk of fetal overgrowth and adiposity.<sup>9</sup> The fetus of mothers with GDM had significantly higher anterior abdominal wall thickness at week 20 despite lower measures of HC, FL, BPD, and AC compared with a control group. Anterior abdominal wall thickness remained

higher in the fetuses of mothers with GDM at week 32 despite similar measures for HC, FL, BPD, and AC between groups.

Despite smaller body weight, an increase in fat pad mass proportion was observed in the fetuses of mothers with GDM, even after 20 weeks, thus pre-dating the biochemical diagnosis of GDM. Increased anterior abdominal wall thickness may serve as an early marker of GDM.<sup>43</sup> An abdominal fetal overgrowth often precedes the diagnosis of GDM in pregnant populations of non-Asian ethnicity.<sup>44,45</sup> Among fetal ultrasound indicators, the rise of AC based on either AC growth monitoring or any mid-range sample has been investigated as an implication for maternal IR and as a prognostic factor for GDM and fetal weight at birth.<sup>46,47</sup> When conducting multivariate analysis between AC and other dependent factors (IR index, maternal weight, blood glucose after taking OGTT and acanthosis nigricans status), only maternal weight, the McAuley's index, and QUICKI scores were statistically significantly associated with AC. Of those, McAuley's index contributed the greatest to AC (Standardized B of -0.656). The results of the study may reflect the role of IR in pregnancy on the development of the fetus, and suggest the role of McAuley's index in assessing IR status in type 2 diabetes patients as well as in pregnant women is more valuable than other methods.<sup>48</sup> Even so, further research is needed on the role of McAuley's index in the assessment of IR and its implications for fetal development.

There are some limitations in our research. The study did not evaluate the influence of the mother's obstetric history on these factors. The population of normal pregnancy group was relatively small. Furthermore, we did not assess postpartum outcomes for both mothers and fetuses in this population.

#### **Conclusion**

In pregnant women with GDM, the McAuley's index was significantly associated with a higher number of risk factors for GDM as well as fetal growth indices than compared with the HOMA2-IR and the QUICKI.

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## Author contribution(s)

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Ethical Approval

All participants provided written informed consent, and the protocol was approved by the Institutional Review Board of the Thai Binh University of Medicine and Pharmacy, Vietnam (decision No.1262/HĐĐĐ). The study was also conducted using good clinical practice following the Declaration of Helsinki.

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## Supplemental Material

Supplemental material for this article is available online.

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