The Relationship Between Hypertriglyceridemic Waist Circumference Phenotype and Gestational Diabetes Mellitus

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Abstract

Background: To investigate the correlation between hypertriglyceridemic waist circumference (HTWC) phenotype and gestational diabetes mellitus (GDM).

Methods: A total of 1083 patients with gestational age ≤8 weeks were divided into four groups: normal triglyceride and waist circumference group (group A, n=575), simple abdominal obesity group (group B, n=317), simple high triglyceride group (group C, n=125), and HTWC group (group D, n=66). General information and serum biochemical indicators were measured and recorded. Analysis of variance (ANOVA) and logistic regression analysis were used to evaluate the relationship between HTWC with GDM.

Results: The prevalence of GDM in the HTWC group was significantly greater than in the other three groups. After adjustment by multivariate logistic regression analysis, the proportion of GDM in the HTWC group was 1.753 times higher than in group A.

Conclusion: These findings suggest that there is a significant correlation between HTWC phenotype and GDM, indicating that the HTWC phenotype could be applied as a simple marker for identifying GDM risk factors.

Introduction

Hypertriglyceridemic waist circumference (HTWC) is a simple and useful screening phenotype test for diabetes mellitus (DM) and cardiovascular diseases [1][2]. It was first proposed by Isabelle Lemieux et al. [3], and has attracted much attention in recent years worldwide. Many studies in China and other countries have shown that HTWC can identify patients with early risk factors for DM and predict the occurrence and development of DM [1][4]. This study primarily aimed to explore the relationship between the clinical phenotype and GDM, in order to better prevent and control the occurrence and development of GDM.

Subjects And Methods

1. Subjects

From August 2015 to March 2018, a total of 1083 pregnant women undergoing a regular antenatal examination and oral glucose tolerance test (OGTT) in the Qinhuangdao Maternal and Child Health Hospital and the First hospital of Qinhuangdao were selected. Their ages ranged from 20 to 44 years, with an average of 29.52 ±4.62 years. All the subjects were followed up for 24-28 weeks. Inclusion criteria were as follows: (1) pregnant women aged ≥20 years who had undergone their first antenatal examination. (2) women with gestational age ≤8 weeks, (3) women who intended to undergo regular antenatal examinations and deliver in the First hospital of Qinhuangdao and Qinhuangdao Maternal and Child Health Hospital. Exclusion criteria were as follows: (1) pregnant women with pregestational diabetes mellitus, (2) women with multiple pregnancies, (3) women who did not complete OGTT (75g), (4) women who had thyroid or connective tissue disease.

2. Methods

(1) Height and body weight before pregnancy, and body weight and blood pressure at 24-28 weeks of gestation were measured. The waistline was accurately measured, midway between the lowest rib and the top of the iliac crest. Body mass index (BMI) was calculated (by using the formula body weight (kg) / height (m^2)) in the first trimester of pregnancy. (2) Total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL-c), low density lipoprotein (LDL-c) and serum uric acid (UA) were measured at fasting state in the first trimester of pregnancy. (3) OGTT and insulin release tests were performed at 24-28 weeks of gestation; plasma glucose and fasting insulin were measured at 60 and 120 minutes respectively, after 75g of oral glucose. Intravenous blood glucose, blood lipids and renal function were measured using an AU2700 automatic biochemical analyser, and serum insulin was determined using the Roche electro chemiluminescence system. AUCG = FPG/2 + 1 h blood glucose + 2 h blood glucose, HOMA-β = 20×FINS (fasting insulin) / (fasting blood glucose-3.5), and HOMA-IR = FPG ×FINS/22.5. These methods have been extensively employed in a number of studies.
Once the eligibility criteria had been confirmed, written informed consent was obtained from all patients. The study was approved by the Institute Ethics Committee. All methods were carried out in accordance with the relevant guidelines and regulations. The diagnostic criteria for GDM were ascertained by referring to the guidelines of the International Association of Diabetic Pregnancy Study Group (IADPSG), i.e. OGTT 0 h blood glucose $\geq 5.1$ mmol/L, 1 h blood glucose $\geq 10.0$ mmol/L, and 2 h blood glucose $\geq 8.5$ mmol/L. A diagnosis can be made if any of these criteria are met.

Grouping was done by taking serum triglyceride $\geq 1.7$ mmol/L and waist circumference $\geq 85$cm in the first trimester of pregnancy as a reference point [1]. The subjects were divided into four groups: normal waist circumference group (group A), simple high triglyceride group (group B), simple abdominal obesity group (group C) and HTWC group (group D).

### 3. Statistical analysis

SPSS 13.0 software was used for statistical analysis. Measurement data were expressed as $\pm s$, and were compared using variance analysis. Enumeration data were expressed by percentage and were compared using the Chi-square test. Logistic regression analysis was used to evaluate the correlation between HTWC and GDM. Multivariate logistic regression was used to adjust for age, BMI and family history of DM. P $< 0.05$ was considered to be a statistically significant difference. The size of the study was based on an earlier pilot study of 30 participants with GDM.

### Results

#### 1. Clinical data of the subjects

There were no significant differences in age, systolic blood pressure (SBP), diastolic blood pressure (DBP) and family history of DM among the four groups (P $> 0.05$). See Table 1.
Table 1
Characteristics of subjects by phenotypes of serum TG concentrations and WC (± s, %)

<table>
<thead>
<tr>
<th>Group</th>
<th>A (n = 575)</th>
<th>B (n = 317)</th>
<th>C (n = 125)</th>
<th>D (n = 66)</th>
<th>F/χ²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>29.85 ± 4.47</td>
<td>30.57 ± 4.91</td>
<td>29.39 ± 4.33</td>
<td>30.47 ± 4.08</td>
<td>1.786</td>
<td>0.076</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>72.08 ± 5.30</td>
<td>73.64 ± 5.81a</td>
<td>93.28 ± 7.07ab</td>
<td>92.73 ± 7.36ab</td>
<td>645.072</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Body weight 1 (kg)</td>
<td>55.02 ± 7.69</td>
<td>58.68 ± 9.13a</td>
<td>66.82 ± 11.31ab</td>
<td>69.01 ± 11.07abc</td>
<td>97.732</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Body weight 2 (kg)</td>
<td>62.48 ± 8.10</td>
<td>65.68 ± 9.12a</td>
<td>73.46 ± 11.00ab</td>
<td>75.26 ± 10.87ab</td>
<td>97.044</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BMI 1 (kg/m²)</td>
<td>20.84 ± 2.82</td>
<td>22.22 ± 3.25a</td>
<td>24.95 ± 3.93ab</td>
<td>26.53 ± 3abc</td>
<td>97.551</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BMI 2 (kg/m²)</td>
<td>23.67 ± 2.91</td>
<td>25.08 ± 3.38a</td>
<td>27.61 ± 3.66ab</td>
<td>28.73 ± 3.87.56abc</td>
<td>79.37</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Family history of DM (%)</td>
<td>10.17</td>
<td>8.87</td>
<td>9.61</td>
<td>12.28</td>
<td>0.714</td>
<td>0.87</td>
</tr>
<tr>
<td>GDM (%)</td>
<td>3.65</td>
<td>6.31a</td>
<td>5.60a</td>
<td>9.09abc</td>
<td>23.542</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>115.07 ± 10.68</td>
<td>115.86 ± 10.31</td>
<td>115.56 ± 11.28</td>
<td>115.32 ± 10.19</td>
<td>0.388</td>
<td>0.762</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>70.72 ± 7.71</td>
<td>71.05 ± 8.18</td>
<td>71.71 ± 7.63</td>
<td>71.08 ± 8.06</td>
<td>2.408</td>
<td>0.057</td>
</tr>
<tr>
<td>UA (umol/L)</td>
<td>193.56 ± 42.28</td>
<td>216.00 ± 55.25a</td>
<td>208.33 ± 60.53a</td>
<td>214.96 ± 55.45a</td>
<td>15.714</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TG (mmol/L)</td>
<td>1.27 ± 0.25</td>
<td>2.26 ± 0.73a</td>
<td>1.26 ± 0.26b</td>
<td>2.30 ± 0.48ac</td>
<td>384.982</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TC (mmol/L)</td>
<td>4.23 ± 0.72</td>
<td>4.75 ± 0.92a</td>
<td>4.37 ± 0.70b</td>
<td>4.77 ± 0.83ac</td>
<td>33.556</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HDL-c (mmol/L)</td>
<td>2.04 ± 0.42</td>
<td>1.92 ± 0.47</td>
<td>1.98 ± 0.44</td>
<td>1.88 ± 0.44a</td>
<td>6.414</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LDL-c (mmol/L)</td>
<td>1.61 ± 0.58</td>
<td>1.84 ± 0.72a</td>
<td>1.80 ± 0.59a</td>
<td>1.85 ± 0.66a</td>
<td>11.385</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>4.80 ± 0.29</td>
<td>4.99 ± 0.41a</td>
<td>4.96 ± 0.36a</td>
<td>5.50 ± 0.32ac</td>
<td>27.956</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>FBG (mmol/L)</td>
<td>4.72 ± 0.38</td>
<td>4.85 ± 0.48a</td>
<td>4.84 ± 0.53a</td>
<td>4.99 ± 0.50abc</td>
<td>11.224</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>1 h blood glucose (mmol/L)</td>
<td>7.61 ± 1.48</td>
<td>8.22 ± 1.74a</td>
<td>7.74 ± 1.58b</td>
<td>8.75 ± 1.84abc</td>
<td>15.465</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>2 h blood glucose (mmol/L)</td>
<td>6.49 ± 1.20</td>
<td>7.05 ± 1.46a</td>
<td>6.80 ± 1.58b</td>
<td>7.39 ± 1.55abc</td>
<td>15.792</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>FINS (mIU/L)</td>
<td>9.15 ± 6.08</td>
<td>12.22 ± 6.21a</td>
<td>12.40 ± 6.69a</td>
<td>15.02 ± 6.51abc</td>
<td>26.739</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Note: Group A, normal TG levels and normal WC; group B, elevated TG levels and normal WC; group C, normal TG levels and elevated WC; group D, elevated TG levels and elevated WC. Body weight 1, body weight in the first trimester of pregnancy; BMI 1, BMI in the first trimester of pregnancy; body weight 2, body weight at 28 weeks of gestation; BMI 2, BMI at 28 weeks of gestation. BMI, body mass index; WC, waist circumference; GDM, gestational diabetes mellitus; SBP, systolic blood pressure; DBP, diastolic blood pressure; UA, uric acid; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; HbA1c, glycosylated hemoglobin A1c; FPG, fasting plasma glucose; FINS, fasting insulin; AUCG, area under curve of glucose; HOMA, homeostasis model assessment; IR, insulin resistance. a, compared with group A, P < 0.05; b, compared with group B, P < 0.05; c, compared with group C, P < 0.05.
2. Comparison of anthropometric and biochemical indices among the four groups

The body weight 1, body weight 2, BMI 1, BMI 2, WC, FBG, 1 h blood glucose, 2 h blood glucose, HbA1c, FINS, AUCG, HOMA-IR, HOMA-β, TG, TC, HDL-c, HDL-c and BUA levels in the HTWC group were significantly different from those in the other groups (P<0.05). See Table 1.

3. Proportion of GDM in each group

The proportion of GDM in the HTWC group was 9.09%, and was significantly higher than those in group C (5.60%), group B (6.31%) and group A (3.65%) (P<0.001). See Table 1.

4. Univariate logistic regression analysis

The prevalence of GDM in the HTWC group was 3.779 times higher than in group A (both TG and waist circumference were normal) (95% CI 2.163–6.602), while those in the normal and HTWC groups were 3.65% and 9.09%, respectively. After adjusting for age, BMI and family history of DM by multivariate logistic regression, the prevalence of GDM in the HTWC group was still 1.753 times higher than in the normal group (95% CI 1.238–2.483). See Table 2.

Table 2

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>GDM</th>
<th>OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>575</td>
<td>21(3.65)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>B</td>
<td>317</td>
<td>20(6.31)</td>
<td>2.153 (1.547–2.996) b</td>
<td>1.292 (1.036–1.612) b</td>
</tr>
<tr>
<td>C</td>
<td>125</td>
<td>7(5.60)</td>
<td>1.901 (1.203–3.004) a</td>
<td>1.204 (0.923–1.570) a</td>
</tr>
<tr>
<td>D</td>
<td>66</td>
<td>5(9.09)</td>
<td>3.779 (2.163–6.602) b</td>
<td>1.753 (1.238–2.483) b</td>
</tr>
</tbody>
</table>

Note: a, P < 0.05; b, P < 0.01. Group A, normal TG levels and normal WC; group B, elevated TG levels and normal WC; group C, normal TG levels and elevated WC; group D, elevated TG levels and elevated WC; GDM, gestational diabetes mellitus; TG, triglyceride; WC, waist circumference; OR, odds ratio; CI, confidence interval.
Discussion

Gestational diabetes mellitus (GDM) seriously threatens the health of mothers as well as infants, and its occurrence is increasing year by year [5]. Identifying groups at high risk of GDM in the early stages of pregnancy, and taking active measures to reduce its occurrence and associated complications is a current concern. The HTWC phenotype is a clinical phenotype that combines biochemical and anthropometric indices. Previous results have shown that the risk of DM significantly increases in those with the HTWC phenotype, and that this information can be used to predict the likelihood of DM occurring [6, 7, 8]. Therefore, in this study, the relationship between HTWC and GDM was explored, and the risk factors for GDM were analysed to find a theoretical basis for its early prevention and treatment.

This study found several indices for metabolic abnormalities in pregnant women with the HTWC phenotype, and these were significantly higher than in other groups. These include indices for abnormal glucose metabolism (e.g. OGTT 0 h, 1 h and 2 h blood glucose, AUCG, increased glycated haemoglobin and HOMA-B changes), and indices for abnormal lipid metabolism (e.g. lower HDL-C and higher LDL-C, TG, and TC levels). Insulin resistance related indices showed increased levels of HOMA-IR and UA. This suggested that pregnant women with the HTWC phenotype had multiple risk factors for DM, and their risk of GDM was also significantly increased. This study found that the occurrence of GDM in the HTWC phenotype group was significantly higher than in the other three groups (P < 0.001). Multivariate logistic regression showed that the prevalence of GDM in the HTWC group was 3.779 times higher than in group A (both TG and waist circumference were normal) with 95% CI 2.163–6.602. After adjusting many risk factors by multivariate logistic regression analysis, the prevalence of GDM in the HTWC phenotype group was still 1.753 times higher than in the normal group (95% CI 1.238–2.483). Previous studies have shown that the HTWC phenotype represents an aggregation of multiple metabolic abnormalities. This can be used to screen the population who are at high risk of GDM, and has a significant ability to predict the onset of GDM [9].

GDM leads to adverse pregnancy outcomes [10], and the long-term prognosis for women and children affected by it is poor. The risk of developing Type 2 diabetes mellitus in future is more than 7 times higher than that of the general population [11]. GDM has attracted a lot of attention from endocrinologists and obstetricians, and there are also an increasing number of studies regarding its pathogenesis. At present, it is generally believed that the occurrence of GDM is related to increased insulin resistance. During pregnancy, the secretion of a variety of hormones with insulin antagonism increases, resulting in decreased sensitivity of the surrounding tissues to insulin, producing insulin resistance (IR). IR has a significant effect on the glucose metabolism of pregnant women and is characterised by decreased glucose uptake and utilisation, as well as a gradual increase in blood glucose. Wang et al. [12], have shown that untreated GDM patients had more severe IR than normal pregnant women during the first, second and third trimesters. Waist circumference was considered as a predictor of abdominal obesity [12], and elevated TG was an early manifestation of IR [13]. Therefore, HTWC leads to IR [14], and increases the risk of GDM. However, the prevalence of simple abdominal obesity and simple hypertriglyceridemia in GDM patients is lower than in HTWC patients. In this study, the prevalence of GDM in groups A, B and C was significantly lower than in group D. Therefore, combining waist circumference and TG improved the ability to detect early GDM. The occurrence of GDM in women in the early stages of pregnancy, with the HTWC phenotype, was more prevalent than in the other groups. Early detection of the HTWC phenotype and active intervention in the development of obesity and abnormal lipid metabolism could effectively reduce the risk of GDM.

This study found that FINS in the HTWC group was higher than in the other groups, and HOMA-β was higher than in group A. The reason for this might be that due to IR increasing during pregnancy, the function of islet β cells was enhanced to compensate. This enhancement is mainly due to increased basal insulin secretion, but is not enough to overcome the gradually increasing IR, and so results in increased blood glucose levels after fasting and glucose load during all stages. Paradisi et al. [15] also found that fasting insulin was increased by 37.5% in the third trimester of pregnancy when compared with the second trimester of pregnancy. Wang et al. [12] found that HOMA-β values during the first, second and third trimesters of pregnancy in the group with GDM were higher than in the corresponding control group, indicating that the function of islet β cells in GDM patients was slightly impaired but still had compensatory ability. Although the postpartum blood glucose levels in these groups can return to normal levels, the risk of postpartum Type 2 diabetes was increased due to IR and mild impairment of islet β cell function [16–18], indicating that IR in pregnant women gradually increased from the first trimester to the third trimester of
pregnancy, and insulin sensitivity gradually decreased. However, this study only observed the islet β cell function index and IR index during the second trimester of pregnancy. It would be more useful to comprehensively analyse the development of IR in GDM, and the relationship between insulin resistance and the onset of GDM, if the data for islet function in the first and third trimesters of pregnancy were available.

This study found that people with the HTWC phenotype had more abnormal indices of glycolipid metabolism, insulin secretion and IR than those in the normal group, simple high triglyceride group and simple abdominal obesity group. Also, the occurrence of GDM in women with the HTWC phenotype was higher than in the other three groups, indicating that the risk of GDM in this group was higher. This suggested that the occurrence and development of GDM might be affected by obesity, IR and other effects.

In conclusion, this is a preliminary study that explored the value of the HTWC phenotype in screening for GDM. The results showed that the HTWC phenotype significantly increased the risk of GDM and independently predicted the risk of GDM occurring. However, these findings need further clarification, so in future studies a larger sample size would be useful. The measurement of waist circumference and TG is simple and inexpensive. When screening for GDM, if the HTWC phenotype can be used for early detection and control, the risk can be effectively reduced and the health of mothers as well as infants can be protected.

However, there were certain limitations in the current study. First, this study used a cross-sectional design, limiting our ability to conclusively prove the results. Second, BMI 1 was self-reported by the subjects without being independently measured by professionals. Finally, although the results were adjusted for many variables, there may be others (such as dietary habits and physical exercise) that were not allowed for.

**Abbreviations**

HTWC: hypertriglyceridemic waist circumference

GDM: gestational diabetes mellitus

ANOVA: Analysis of variance

DM: diabetes mellitus

OGTT: oral glucose tolerance test

BMI: Body mass index

TC: Total cholesterol

TG: triglycerides

HDL-c: high density lipoprotein

LDL-c: low density lipoprotein

UA: uric acid

IADPSG: International Association of Diabetic Pregnancy Study Group

SBP: systolic blood pressure

DBP: diastolic blood pressure

IR: insulin resistance
Declarations

Ethical statement

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of First Hospital of Qinhuangdao.

Consent for publication

All authors final approval of the version to be published.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare no competing interests.

Funding

None.

Author Contributions

LQ designed the Project, Conceptualization and Supervision. HTS performed the experiments. JXJ, WJX performed the data analyses and wrote the manuscript. BLW, HTS, HZH and LQ helped perform the analysis with constructive discussions.

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References


