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Correlation between serum lipids and 1-hour postload plasma glucose levels in normoglycemic individuals

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BACKGROUND: One-hour plasma glucose (1-h PG) level of ≥ 155 mg/dL during an oral glucose tolerance test (OGTT) predicts the development of type 2 diabetes mellitus among individuals with normal glucose tolerance (NGT). In addition, high triglyceride (TG) and low high-density lipoprotein-cholesterol (HDL-C) levels are risks factors for development of diabetes mellitus in the future.

OBJECTIVE: To examine the association between 1-h PG levels and serum lipid profiles in individuals with NGT.

METHODS: We enrolled 736 individuals with NGT who underwent a 75-g OGTT. They were divided into 2 groups, those with 1-h PG levels < 155 mg/dL (n = 543) and those with 1-h PG levels ≥ 155 mg/dL (n = 193). Multivariate linear regression analyses were performed to assess correlations between 1-h PG levels and lipid profiles.

RESULTS: The multiple linear regression analyses showed that 1-h PG levels negatively correlated with HDL-C in individuals with NGT who had 1-h PG levels ≥ 155 mg/dL as well as those with 1-h PG levels < 155 mg/dL ($\beta = -0.137$, $P = .001$ and $\beta = -0.214$, $P = .003$, respectively). In addition, 1-h PG levels positively correlated with log-transformed TG/HDL-C ratio in both groups ($\beta = 0.098$, $P = .032$ and $\beta = 0.152$, $P = .035$, respectively). Moreover, even after adjusting for confounding parameters, TG was higher and HDL-C was lower in individuals with NGT who had 1-h PG levels ≥ 155 mg/dL compared with those who had 1-h PG levels < 155 mg/dL.

CONCLUSION: HDL-C levels and TG/HDL-C ratios closely correlate with 1-h PG levels in individuals with NGT.

Type 2 diabetes mellitus (T2DM) is a chronic disease that causes serious morbidity and mortality because of vascular complications and also imposes a heavy economic burden.[1] Therefore, it is essential that high-risk individuals are identified in order to establish a successful primary prevention program for T2DM. Moreover, it is necessary to investigate the category of individuals with normal glucose tolerance (NGT) who are at a high risk of developing T2DM.

T2DM is closely associated with dyslipidemia. Recently, some studies have shown that dysfunction of pancreatic β

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cells caused by dyslipidemia precedes the manifestation of T2DM, and it is an independent risk factor for the development of T2DM.[2,3] However the principal differences between bezafibrate and other fibrates are related to their effects on glucose levels[4] because bezafibrate increased high-density lipoprotein cholesterol (HDL-C) levels by 16% and decreased triglyceride (TG) levels by 24%, which reduced the incidence and delayed the onset of T2DM in individuals with impaired fasting glucose levels.[5] Because high TG and low HDL-C levels are 2 key metabolic abnormalities associated with insulin resistance, the TG to HDL-C ratio (TG/HDL-C) has been advocated as a simple clinical indicator of insulin resistance.[6,7]

Evaluation of the 1-h plasma glucose (1-h PG) level during the 75-g oral glucose tolerance test (OGTT) can predict the progression to diabetes mellitus as well as prediabetes among individuals with NGT. A cutoff 1-h PG level of 155 mg/dL is considered as identifying individuals with NGT who are at a high risk for developing T2DM.[8,9] Those with 1-h PG levels $\geq$ 155 mg/dL have an 8.5% to 15.3% risk for developing diabetes mellitus in the future, which is significantly higher than the 1.3% to 2.9% risk among individuals with 1-h PG levels $<$ 155 mg/dL.[8,9] Moreover, the presence of metabolic syndrome among individuals with 1-h PG levels $\geq$ 155 mg/dL further increases the risk of developing T2DM.[8,9]

Despite numerous studies having demonstrated a strong association between 1-h PG levels or lipid profiles and the development of T2DM, to the best of our knowledge, none has investigated the association between 1-h PG levels during the OGTT as well as lipid profile tests. Therefore, using a large representative sample of Japanese adults with NGT who participated in an OGTT at the time of their annual health examination, we evaluated the association among TG, HDL-C, and 1-h PG levels during the 75-g OGTT.

Methods

Study population

This study included 736 participants aged 35 years and older who underwent a 75-g OGTT between January 2008 and December 2012 at Iida Municipal Hospital during a routine health checkup. Patients who were on antidiabetic agents or were taking drugs that interfered with lipid metabolism were excluded from the investigation. In the morning, after a fasting period ($>$ 12 h), a standard 75-g OGTT was conducted for each subject. Blood samples were collected at 0, 1, and 2 hours after the OGTT. NGT was defined using the following criteria of the American Diabetes Association (2011): fasting plasma glucose (FPG) $<$ 100 mg/dL and 2-hour postload plasma glucose level (2-h PG) $<$ 140 mg/dL.[10] Individuals with NGT were further divided into 2 groups according to the 1-h PG cutoff point of 155 mg/dL, those with NGT and a 1-h PG level $<$ 155 mg/dL (n = 543) and those with NGT and a 1-h PG level $\geq$ 155 mg/dL (n = 193). Informed consent was obtained from all individuals.

Blood samples were mixed with dipotassium ethylenediaminetetraacetic acid and tested within 30 minutes of collection to minimize variations resulting from sample aging. Systolic blood pressure, diastolic blood pressure, plasma glucose levels, serum total cholesterol (TC), TG, HDL-C, low-density lipoprotein cholesterol (LDL-C) levels, uric acid (UA), creatinine, and high-sensitivity C-reactive protein (hs-CRP) levels were determined using standard methods. The estimated glomerular filtration rate (eGFR) was calculated using the formula eGFR (mL/min/1.73 m^2) = 194 $\times$ (serum creatinine) $^{-1.094}$ $\times$ age$^{-0.287}$ ($\times$ 0.739 if female).[11] The body mass index (BMI) was calculated as (weight)/(height)^2 (kg/m^2). The HbA1c level (%) was estimated according to the National Glycohemoglobin Standardization Program (NGSP)-equivalent value (%) calculated using the formula, NGSP (%) = 1.02 $\times$ Japan Diabetes Society (%) + 0.25%, considering the relationship between HbA1c (Japan Diabetes Society) (%) measured using the previous Japanese standard substance and HbA1c (NGSP).[12]

A questionnaire was used to obtain information about familial medical history and the subjects' lifestyle, such as smoking habits and alcohol ingestion. Familial history of diabetes was defined as having 1 or more relatives (parent or sibling) with diabetes. Individuals who had smoked $<$ 100 cigarettes during their lifetime were considered nonsmokers, those who had smoked $\geq$ 100 cigarettes and were currently not smoking were considered former smokers, and those who had smoked $\geq$ 100 cigarettes and were currently smoking were considered current smokers. The following criteria were defined for alcohol consumption groups: drinking never or rarely (less than 1 time/month), occasionally (1–3 times/month), and regularly (1–7 times/week).

Statistical analysis

The sample size was estimated using G*Power 3.0.10 software (Franz Faul, University of Kiel, Kiel, Germany), considering the effect size 0.75, the minimum power 0.80, and α = 0.05, resulting in 14 subjects.[13] However, it was possible to evaluate 736 total subjects in the present investigation. Statistical analyses were performed using SPSS software version 21.0 (SPSS Inc., Chicago, IL). The clinical characteristics of subjects with 1-h PG $<$ 155 mg/dL and those with 1-h PG $\geq$ 155 mg/dL were compared using the unpaired t test for continuous variables and the chi-square test was used to compare categorical parameters.

Pearson's correlation coefficients were calculated to evaluate the relationships between 1-h PG and several clinical variables (sex, age, systolic blood pressure, diastolic blood pressure, BMI, FPG, TC, HDL-C, LDL-C, UA, hs-CRP, eGFR, smoking status, and alcohol consumption). Distributions of TG levels and TG/HDL-C ratio were skewed; therefore, Pearson's linear correlation was