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Original Research Paper

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GLUCOSE EFFECTIVENESS AND LIVER FUNCTION ENZYME LEVEL IN ELDERLY PEOPLE

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ABSTRACT

Taiwan is a hyperendemic area of hepatitis. The liver is one of the major organs involved in glucose homeostasis, and abnormal liver function may trigger a vicious cascade of glucose intolerance that eventually leads to type 2 diabetes (T2D). Patients with hepatitis are 4 times more likely to have T2D than the general population. Deterioration of glucose effectiveness (GE) was proposed to be responsible for this relationship. In this study, our goal was to determine the relationship of glutamic pyruvic transaminase (GPT) level with GE in elderly residents of Taiwan.

Methods

In 2013 and 2015, from private clinics, we enrolled 19 067 men and 20 798 women (age > 60 years) randomly. Participants were grouped according to GPT level. Scatter plots were constructed and slopes were determined by simple correlation.

Results

For both sexes, significant differences were discovered between the patients with and without metabolic syndrome regarding various parameters. Four groups were subsequently defined on the basis of the quartiles of GPT level. The participants with higher GPT level were older and had higher GE. A scatter plot of the correlation between GE and GPT level indicated positive correlation. We further obtained the slopes of the GE in men and women.

Conclusion

We identified the negative relationship of GPT level with GE in elderly people of both sexes. No sex difference was discovered. The underlying causal relationship can be determined through longitudinal studies.

KEYWORDS : glutamic pyruvic transaminase, glucose effectiveness, diabetes, elderly patients

INTRODUCTION

Type 2 diabetes (T2D) has become considerably more prevalent recently in Taiwan as well as numerous other countries, and has been among the five commonest causes of mortality in Taiwan for several years. There are many comorbidities of T2D and, among these, it is well-known that liver fat is increased in T2D. Interestingly, on the other hand, Gray et al. discovered a positive relationship between higher liver function and the occurrence of diabetes in 1946, and various researchers have confirmed their results. This is not surprising that liver is one of the major organs involved in glucose homeostasis, and abnormal liver function may trigger a vicious cascade of glucose intolerance that eventually leads to T2D.

Abnormal liver function is observed frequently in clinical practice. The prevalence of abnormal liver function was estimated to be approximately 10% to 21%. The most common cause of abnormal glutamic pyruvic transaminase (GPT) level is nonalcoholic fatty liver disease, which accounts for 50% to 90% of instances. In addition, Taiwan is an endemic area for viral hepatitis. The prevalence of hepatitis B virus infection is 15% to 20%,, and individuals with this infection have abnormal liver function. Thus, understanding the relationship between abnormal liver function and T2D is crucial.

Three major perturbations are generally agreed to cause glucose intolerance: decreased insulin secretion, insulin action (insulin resistance; IR), and glucose effectiveness (GE). Of these, GE—the capability of the body to improve its uptake of glucose and suppress gluconeogenesis in the liver—is often overlooked. According to Best et al., GE is responsible for 60% of glucose clearance in normal subjects and 99% in those with diabetes. This is unsurprising because in patients with diabetes, both IR and decreased insulin secretion are relatively severe and the body is unable to maintain normal glucose tolerance. The role of GE has been the focus of only a few studies. To the best of our knowledge, the relationship between GE and GPT level has not yet been explored.

Because of a decreasing birth rate, Taiwan has been an aging society since March 2018. Of every 7 persons, one is more than 65 years old. Scholars have estimated that Taiwan will formally be an aged society within 8 years. Diabetes is one of the most common diseases in the elderly population, and its prevalence is clearly related to age. Understanding the underlying pathophysiology of T2D is thus a major concern for health providers and government.

In this study, we enrolled 39 865 patients who had no history of diabetes and who were not taking any medications for diabetes, hypertension, or dyslipidemia. Our objective was to determine how GPT level and GE are related in elderly people.

Methods

Private clinics located in Taiwan, MJ Health Screening Centers offer their members regular health examinations. We randomly enrolled 19 067 men and 20 798 women who were aged over 60 years and who attended the private clinics in 2013 and 2015. All participants provided informed consent and were assured anonymity. The protocol in this study was approved by MJ Health Screening Centers' Institutional Review Board. The company provided data solely for research purposes. We excluded any participants who were taking medications that affect blood pressure and glucose and lipid levels. Two participant groups were defined—those with and without metabolic syndrome, per the definition of the World Health Organization. The metabolic syndrome group comprised 6269 men and 8251 women, whereas the group without metabolic syndrome comprised 12 798 men and 12 547 women. To observe the effect of liver function, the groups were further subdivided into quartiles according to their GPT level.

On the day of a participant's involvement, a senior member of nursing staff recorded the medical history of the participant (e.g., their current medications), and a physical examination was conducted. Body mass index (BMI) was determined as weight/height^2, where weight and height are in kilograms and meters, respectively. Waist circumference (WC) was measured horizontally at the level of the natural waist. Systolic and diastolic blood pressure (SBP and DBP, respectively) were measured using a standard mercury sphygmomanometer, worn by a seated participant on their right arm.

Blood samples were obtained from the participants for biochemical analyses after they had fasted for 10 hours. Within 1 hour, the plasma was extracted from the blood and stored at 30°C before being analyzed for fasting plasma glucose (FPG) and lipid profiles using the glucose oxidase method (YSI 203 glucose analyzer, Yellow Springs Instruments, Yellow Springs, USA). We determined total cholesterol and triglyceride (TG) levels using the dry, multilayer analytical slide method, implemented with the Fuji Dri-Chem 3000 analyzer (Fuji Photo Film, Tokyo, Japan). Dextran sulfate precipitation followed by an enzymatic cholesterol assay were used to measure serum high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) concentrations.

The equation used to calculate GE is listed below. All units are in international units. To demonstrate the reliability of our equations, a short statement is given here. When performing the studies, 70% of the participants were used to build the equation and the remaining 30% were used as external validation. Thus, the accuracy of the equations could be tested.

GE: Totally there were 227 participants. The GE was measured by frequently sampled intravenous glucose tolerance test. The r value between the measured and calculated GE was 0.43 (p = 0.001). It was published in 'Metabolic Syndrome and Related Disorders' in 2016.

GE = (29.196 - 0.103 age - 2.722 TG - 0.592 FPG) 10 -3 (PredictingGlucoseEffectivenessinChineseParticipants Using Routine Measurements.

We employed SPSS 19.0 (IBM Inc., Armonk, NY, USA) for statistical analysis. Data are expressed as means ± standard deviations. Normal distribution of the data was verified using the Kolmogorov–Smirnov test, and data homogeneity of variance was determined using Levene's test. If the data were not normally distributed, they were log-transformed before being analyzed. We employed a *t* test to evaluate the differences between the groups with and without metabolic syndrome. Differences between the means of the 4 groups were determined using ANOVA. Intergroup comparisons were realized through Bonferroni post hoc analysis. We evaluated the relationship between 2 independent variables using simple correlation. To compare the slopes of 2 lines and thus determine whether they were significantly separated, Chris's calculator was used (https://www.surrey.ac.uk/search?query=calculator&op=Search).

RESULTS

Table 1 presents the participants' demographic data. Significant differences were discovered between the groups with and without metabolic syndrome in both sexes. GPT level was higher and GE lower in the participants with metabolic syndrome. We then divided the GPT levels of the participants into quartiles (Table 2). The GE was significantly lower in the group with higher GPT levels. This was observed in both sexes. To further analyze this relationship, we performed simple linear regression (Table 3). A significant negative correlation was discovered between GPT level and GE, with a *P* value of <.001. The correspondent simple dot plot is displayed in Figure 1. Most of the data are clustered in the left upper quadrant, which indicates high GE and low GPT level. This is logical because most of our participants were healthy. Comparing the sexes, no difference was noted (Figure 2).

DISCUSSION

A negative relationship was determined between GPT level and GE in an elderly ethnic Chinese population. Per the best of the authors' knowledge, the present study is the first to obtain these results for a group of relatively healthy subjects with elimination of any possible confounding effects caused by drugs for treating hypertension, dyslipidemia, or diabetes.

Glucose level is dependent on 3 factors: (1) hepatic glucose production; (2) insulin-dependent glucose uptake (INGU), which represents insulin action and sensitivity; and (3) non-insulin-dependent glucose uptake, which is the GE. In those without diabetes, both insulin secretion and INGU are relatively normal, and because the insulin concentration is sufficient and insulin action is intact, blood glucose can be easily maintained at a stable level. However, in those with glucose intolerance, insulin secretion is insufficient and insulin action is damaged, leading to the development of diabetes. Under this circumstance, 2 notable things occur. First, the body's ability to clear glucose becomes solely reflected by the GE. Second, higher plasma glucose results in more glucose being taken up through GE compared with the situation in those who have normal glucose level. Best et al. proved this hypothesis by demonstrating that GE accounts for 66% of glucose utilization in healthy people but 99% in individuals with T2D because of IR and impaired insulin secretion.

Obesity may be crucial to explaining the relationship between GPT level and GE. As mentioned earlier, no studies focusing on GE and GPT level have been conducted. However, that obesity is related to GPT level is well established., This association was first reported in 1967. After several years of extensive research, researchers lost interest in this topic, and fewer articles have been published in the past 20 years. The direct underlying mechanism is that individuals with obesity have greater cell mass than those without obesity.

Our findings in the present study would be explained if obesity has a negative relationship with GE. Several studies have reported the effect of BMI on GE, but the results have been inconsistent. We discovered negative correlation between GE and BMI ($r = -0.082$ for men and −0.069 for women); this finding is in agreement with those of Kautzky-Willer et al.[21] and Lopes et al. but in disagreement with that of Healy et al. Measuring GE using frequently sampled intravenous glucose tolerance tests in a population of white and African Americans, Healy et al. demonstrated that the correlation was absent in individuals with prediabetes.[23] The inconsistency of the findings may be due to the studies' different GE estimation methods, inclusion criteria, and ethnic populations, as well as the BMI (37.8 ± 6.3 kg/m^2 in Healy et al.) and age (46.5 ± 11.2 years in Healy et al.) of the study participants. In particular, very few individuals of Chinese ethnicity have a BMI similar to 37.8 kg/m^2.

The present study was limited in some respects, the first of which is its cross-sectional nature, meaning that causal relationships could not be determined. Compared with a longitudinal study, a cross-sectional study obtains less information. In the future, a well-designed longitudinal study might be conducted to further investigate the causal relationships. Second, the equation that was used to measure SPIS is less accurate than use of the hyperglycemic clamp test. However, this test would have required considerable staff time and money if it was used in a cohort as large as ours. Thus, even though the method employed is less satisfactory, our results should be reliable because of the large cohort used.

In conclusion, our data suggest a negative relationship between GPT level and GE in elderly Chinese people. Whether this relationship is a cause or effect remains to be determined.

Tables and Figures:

Table 1. The demographic data of the participants with and without metabolic syndrome

	MetS (–)	MetS (+)	P
Male			
n	12 798	6269	
Age	66±5.8	66±5.9	<.001
BMI (kg/m2)	23.0±2.7	25.9±2.8	<.001
WC (cm)	82.0±7.7	91.4±7.7	<.001
SBP (mmHg)	129±19	142±18	<.001
DBP (mmHg)	75±11	81±11	<.001
FPG (mg/dL)	104.2±26.1	120.1±36.9	<.001
TG (mg/dL)	104.1±47.5	179.5±75.5	<.001
Log TG (mg/dL)	1.980±0.178	2.215±0.189	<.001
HDL-C (mg/dL)	53.41±13.50	42.08±10.72	<.001
LDL-C (mg/dL)	124.8±32.1	125.4±33.5	<.001
GPT (U/L)	26.55±21.10	32.04±24.89	<.001
GE (10−2 dL/min/kg)	0.016±0.002	0.013±0.003	<.001
Female			
n	12 547	8251	
Age	64±5.0	66±5.8	<.001
BMI (kg/m2)	23.0±3.0	26.0±3.3	<.001

WC (cm)	75.3±7.2	83.9±7.9	<.001
SBP (mmHg)	130.2±20.0	144.1±18.6	<.001
DBP (mmHg)	73.4±11.3	79.6±11.1	<.001
FPG (mg/dL)	100.8±21.6	119.1±37.8	<.001
TG (mg/dL)	104.5±45.1	172.6±71.6	<.001
Log TG (mg/dL)	1.985±0.170	2.200±0.184	<.001
HDL-C (mg/dL)	63.9±14.7	49.8±12.0	<.001
LDL-C (mg/dL)	128.7±33.2	131.2±35.0	<.001
GPT(U/L)	24.34±21.74	28.55±22.98	<.001
GE (10−^{2} dL/min/kg)	0.016±0.002	0.013±0.003	<.001

MetS (−) = without metabolic syndrome; MetS (+) = with metabolic syndrome; BMI = body mass index; WC = waist circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure; FPG = fasting plasma glucose; TG = triglyceride; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; GPT = glutamic pyruvic transaminase; GE = glucose effectiveness.
Data shown are mean ± SD

Table 2. The parameters of quartiles divided by the levels of glutamic pyruvic transaminase

	GPT 1	GPT 2	GPT 3	GPT 4	P
Male					
n	4997	4479	4951	4631	
Age	68±6.5234	66±5.7134	65±5.412	65±5.312	<.001
BMI (kg/m2)	23±3234	24±3134	24±3124	25±3123	<.001
WC (cm)	82.2± 8.7234	84.3± 8.5134	86.0± 8.5124	87.8± 8.9123	<.001
SBP (mmHg)	132±214	133±204	134±19	134±1912	<.001
DBP (mmHg)	76±12234	77±12134	78±1112	79±1112	<.001
FPG (mg/dL)	106.9± 30.64	108.2± 30.74	109.2± 2914	113.4± 33.0123	<.001
TG (mg/dL)	113.4± 58.2234	122.2± 62.1124	133.8±69. 6134	146.8±76. 8123	<.001
Log TG (mg/dL)	2.007± 0.199234	2.039± 0.203124	2.074±0.2 13134	2.111±0.2 21123	<.001
HDL-C (mg/dL)	50.7±13.84	50.5±13.64	49.9± 13.54	47.5± 13.7123	<.001
LDL-C (mg/dL)	122.4± 31.423	122.7± 31.61	126.9± 33.014	124.0± 34.03	<.001
GPT(U/L)	14.2± 2.49234	20.0± 1.40134	26.4±2.49 124	53.9±33.8 123	<.001
GE (10−2 dL/min/kg)	0.0152± 0.002334	0.0151± 0.002334	0.0147±0. 0025124	0.0143±0. 0028123	<.001
Female					
n	5063	5713	4743	5268	
Age	66±6234	65±51	65±51	65±51	<.001
BMI (kg/m2)	23±3234	24±3134	25±3124	25±3123	<.001
WC (cm)	76.7± 8.2234	77.8± 8.2134	79.3± 8.5124	81.1± 8.7123	<.001
SBP (mmHg)	135±214	135±214	136±20	137±2012	<.001
DBP (mmHg)	75±1234	75±1234	76±1212	77±1112	<.001
FPG (mg/dL)	104± 2734	106±2734	109± 30124	114± 36123	<.001
TG (mg/dL)	121± 61234	126±63134	135± 67124	144± 71123	<.001
Log TG (mg/dL)	2.04± 0.20234	2.05± 0.20134	2.08± 0.21124	2.11± 0.21123	<.001
HDL-C (mg/dL)	59.1± 15.44	59.6±15.54	58.5± 15.44	56.0± 14.8123	<.001
LDL-C (mg/dL)	128.5± 33.6	130.5±32.9	130.9± 34.1	129.0± 35.4	.001
GPT(U/L)	12.8± 2.0234	17.9± 1.4134	23.5± 2.0124	49.7± 34.0123	<.001
GE (10−2 dL/min/kg)	0.0152± 0.002434	0.0151± 0.002434	0.0148±0. 0025124	0.0143±0. 0027123	<.001

MetS (−) = without metabolic syndrome; MetS (+) = with metabolic syndrome; BMI = body mass index; WC = waist circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure; FPG = fasting plasma glucose; TG = triglyceride; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; GPT = glutamic pyruvic transaminase; GE = glucose effectiveness.
Data shown are mean ± SD

Table 3. the P and r values of simple correlation between glucose effectiveness and levels of glutamic pyruvic transaminase

	r	P
Male		
GE	−0.082	<.001
Female		
GE	−0.069	<.001

Figure 1. The scatter plot of glucose effectiveness and glutamic pyruvic transaminase for men and wemen

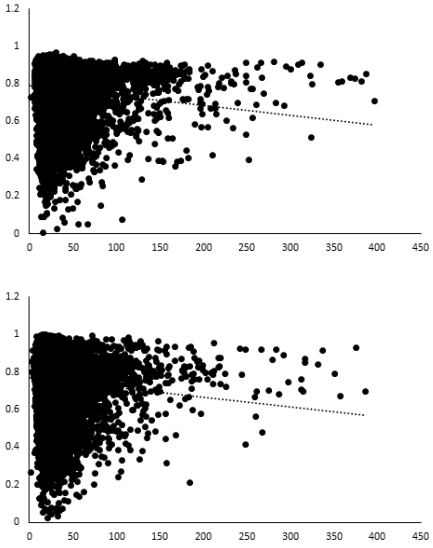

Figure 2. The comparison of the slopes between men and women by using Chris's calculator