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Associations of body mass index with glycated albumin and glycated albumin/glycated hemoglobin A_{1c} ratio in Chinese diabetic and non-diabetic populations

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ABSTRACT

Background: Recent studies have discussed the relationship between body mass index (BMI) and glycated albumin (GA) level. However, the extent of the influence of BMI on GA remains uncertain. We investigated the associations between BMI and GA, glycated hemoglobin A_{1c} (HbA_{1c}) and GA/HbA_{1c}, and to analyze the influence of obesity on GA, HbA_{1c}, and GA/HbA_{1c} in both Chinese diabetic and non-diabetic populations.

Methods: A total of 2562 participants, including 1177 men and 1385 women (age 20–80 y), were enrolled. Each subject underwent a 75-g oral glucose tolerance test. Serum GA was detected using a liquid enzyme method, and HbA_{1c} was assayed using high-performance liquid chromatography.

Results: In the diabetic patients (n = 1223), the GA, $HbA_{1c,}$ and GA/HbA_{1c} levels were 16.7 ± 3.0%, 6.6 ± .9% (49 ± 9 mmol/mol), and 2.51 ± .33, respectively. In the non-diabetic subjects (n = 1339), the GA, $HbA_{1c,}$ and GA/HbA_{1c} concentrations were 13.8 ± 1.7%, 5.6 ± .4% (38 ± 4 mmol/mol), and 2.47 ± .31, respectively. Decreasing trends in the GA and GA/HbA_{1c} concentrations and an increasing trend in the HbA_{1c} concentration (all P for trend < .05) were found to accompany with the increase in BMI, regardless of diabetes status. Multiple regression analysis revealed that BMI was independently related to HbA_{1c} in the non-diabetic population (standardized β = .158, P < .001); however, the relationship disappeared in the diabetic population (P > .05). Moreover, in the diabetic and non-diabetic populations, BMI was negatively correlated with GA (standardized β = −.167 and − .231, both P < .001) and GA/HbA_{1c} (standardized β = −.273 and − .310, both P < .001). Further analysis showed that a 1 kg/m^2 increment in BMI was associated with a .13% decrease in the absolute value of GA.

Conclusions: In both diabetic and non-diabetic populations, GA and GA/HbA_{1c} levels are independently and negatively associated with BMI. For every 1 kg/m^2 increment in BMI, the absolute value of GA decreases approximately .13%.

1. Introduction

Obesity is caused by an energy imbalance between energy intake and energy consumption. In recent years, the prevalence of obesity and diabetes has increased significantly due to changes in dietary structures and the lack of physical activity [1]. According to the China Chronic Disease and Risk Factors Surveillance study conducted in 2013, the proportion of overweight/obese in diabetic patients had increased dramatically to 36.5% [2]. Compared with non-obese diabetic patients, obese diabetic patients tend to have worse glucose control, leading to more rapid progression of chronic complications and worse prognoses [3]. Therefore, comprehensive management of blood glucose for obese diabetic patients is of great value to prevent diabetes-related complications and to improve patients' quality of life.

Glycated albumin (GA), an indicator reflecting the mean glycemia over 2 to 3 weeks, has advantages when evaluating glycemic excursion,

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as well as postprandial hyperglycemia; thus, it has become an important indicator of glucose monitoring and evaluating therapeutic efficacy in patients with diabetes [4,5]. Recent studies have discussed the relationship between body mass index (BMI) and GA concentraiton. Our previous study noted that fat mass and visceral adipose tissue were negatively associated with GA in Chinese with normal glucose tolerance [6]. Other studies have also demonstrated that when compared with non-obese subjects, obese subjects usually have relatively lower GA concentration, regardless of diabetes status [7–10]. Therefore, studying the influence extent of BMI on GA concentration is of great significance to the optimal application of GA in the clinical setting.

However, previous studies of the relationship between BMI and GA usually had small sample sizes, and few studies have simultaneously discussed the above relationship in diabetic and non-diabetic populations. In addition, the extent to which BMI influences GA remains uncertain.

2. Materials and methods

2.1. Study population

Subjects in this study were recruited from the outpatient clinic of the Department of Endocrinology and Metabolism of Shanghai Jiao Tong University Affiliated Sixth People's Hospital from July 2014 to October 2017. All subjects underwent a 75-g oral glucose tolerance test (OGTT). Individuals with a medical history of diabetes or impaired glucose tolerance were excluded based on the 2010 American Diabetes Association standards. And we have also excluded subjects with a history of diet control, current use of hypoglycemic agents, hepatic or renal dysfunction, acute infection, pregnancy, tumors, abnormal albumin metabolism, hyperthyroidism or hypothyroidism, and severe cardiovascular diseases. In addition, those who with any medical history or conditions that could interfere with HbA_{1c} testing results, including but not limited to hemoglobinopathies, or receiving high-dose vitamin C intake and erythropoietin treatment, et al., were also excluded. Finally, a total of 2562 participants, including 1177 men and 1385 women (age 20–80 y), were enrolled. The study was approved by the Ethics Committee of Shanghai Jiao Tong University Affiliated Sixth People's Hospital, and all subjects provided written informed consent prior to study participation.

2.2. Anthropometric and biochemical assessments

Anthropometric assessments, including height, weight, and blood pressure levels, were recorded. BMI was calculated as weight (kg)/height (m) ^{2}. Blood samples were collected after the patients had fasted overnight for at least 10-h to examine fasting plasma glucose (FPG), GA, and HbA_{1c} concentrations. Each subject underwent a 75-g OGTT to assay the 2-h postload plasma glucose (2hPG). FPG and 2 hPG concentrations were immediately determined by the glucose oxidase method (Kehua Biological Engineering Co., Ltd) using the Hitachi 7600 autoanalyzer. Serum GA was detected using the enzyme method (Lucica GA-L, Asahi Kasei Pharma) on a 7600 analyzer (Hitachi). The inter- and intra-assay CVs were < 5.0% and < 3.5%, respectively. HbA_{1c} was assayed using HPLC (Variant II hemoglobin analyzer, Bio-Rad), with inter- and intra-assay CVs of < 3.5% and < 3.0%, respectively.

2.3. Diagnostic criteria

Diabetes was defined according to the 2010 American Diabetes Association classification standards [11]. Overweight/obese was diagnosed as participants with BMI ≥ 25.0 kg/m^2, based on the 1998 World Health Organization criteria [12].

Table 1
Characteristics of the study participants.

Variable	Total	BMI < 25 kg/m^2	BMI ≥ 25 kg/m^2
Gender (men/women)	2562 (1177/1385)	1498 (600/898)	1064 (577/487)**
Diagnosed diabetes mellitus, *n* (%)	1223 (47.74%)	645 (43.06%)	578 (54.32%) **
Age (y)	51 ± 13	51 ± 13	50 ± 13**
BMI (kg/m^2)	24.59 ± 3.59	22.22 ± 1.95	27.91 ± 2.61**
Systolic blood pressure (mmHg)	131 ± 18	128 ± 17	136 ± 17**
Diastolic blood pressure (mmHg)	80 ± 11	78 ± 10	83 ± 11**
FPG (mmol/l)	6.29 ± 1.35	6.15 ± 1.31	6.49 ± 1.37**
2hPG (mmol/l)	10.73 ± 4.25	10.19 ± 4.23	11.48 ± 4.17**
GA (%)	15.2 ± 2.8	15.3 ± 2.7	14.9 ± 2.9**
HbA_{1c} (%)	6.1 ± .8	6.0 ± .8	6.2 ± .9**
HbA_{1c} (mmol/mol)	43 ± 9	42 ± 9	44 ± 10**
GA/HbA_{1c}	2.49 ± .32	2.55 ± .31	2.40 ± .31**

Data were expressed as mean ± SD or *n* (%).
FPG = fasting plasma glucose; 2hPG = 2-h postload plasma glucose; GA = glycated albumin.
** $P < .01$ versus BMI < 25 kg/m^2.

2.4. Statistical analysis

SPSS ver 21.0 was used for all statistical analyses. All continuous variables are presented as the mean ± standard deviation. Categorical variables are expressed as percentages (%). Inter-group comparisons of variables were performed using an unpaired Student's *t*-test, and one-way ANOVA was used for trend analyses. The chi-squared test was used for inter-group comparisons of categorical variables. Multiple regression analysis was conducted to explore the relationship between BMI and GA, HbA_{1c}, and GA/HbA_{1c}. All *P* values were two-tailed, and $P < .05$ was considered to be statistically significant.

3. Results

3.1. Clinical characteristics of the study participants

In total, 2562 participants were enrolled in the present study (average, 51 ± 13 y), including 1498 subjects with a BMI < 25 kg/m^2 and 1064 subjects with a BMI ≥ 25 kg/m^2. As shown in Table 1, subjects in the BMI ≥ 25 kg/m^2 group were younger and had significantly higher levels of systolic blood pressure, diastolic blood pressure, FPG, 2hPG, and HbA_{1c} (all $P < .01$), compared to those with BMI < 25 kg/m^2. In addition, overweight/obese participants presented with higher rates of diagnosed diabetes, as well as lower concentrations of GA and GA/HbA_{1c} (all $P < .01$) than subjects with BMI < 25 kg/m^2.

3.2. The concentrations of GA, HbA_{1c}, and GA/HbA_{1c} in diabetic and non-diabetic populations with different BMI levels

In diabetic patients ($n = 1223$), the GA, $HbA_{1c,}$ and GA/HbA_{1c} concentrations were 16.7 ± 3.0%, 6.6 ± .9% (49 ± 9 mmol/mol), and 2.51 ± .33, respectively. In non-diabetic subjects ($n = 1339$), the GA, $HbA_{1c,}$ and GA/HbA_{1c} concentrations were 13.8 ± 1.7%, 5.6 ± .4% (38 ± 4 mmol/mol), and 2.47 ± .31, respectively.

All subjects were divided into 9 groups based on BMI ranges: < 18.5 kg/m^2 ($n = 77$), 18.5–20.4 kg/m^2 ($n = 214$), 20.5–21.9 kg/m^2 ($n = 297$), 22.0–23.4 kg/m^2 ($n = 424$), 23.5–24.9 kg/m^2 ($n = 472$), 25.0–26.4 kg/m^2 ($n = 397$), 26.5–27.9 kg/m^2 ($n = 281$), 28.0–29.9 kg/m^2 ($n = 200$) and ≥ 30.0 kg/m^2 ($n = 200$). The analysis showed that decreasing trends in the GA and GA/HbA_{1c} concentrations (both *P* for