SPANDIDOS PUBLICATIONS

BIOMEDICAL REPORTS 6: 339-345, 2017

Association of blood glucose and lipid levels with complete blood count indices to establish a regression model

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Received October 10, 2016; Accepted November 23, 2016

DOI: 10.3892/br.2017.852

Abstract. Hyperglycemia and hyperlipidemia, which are usually diagnosed by analysis of blood glucose (GLU) and lipid levels, are two of the most common diseases in modern society. The purpose of the current study was to investigate the potential association between blood GLU and lipid levels with complete blood count (CBC) indices in overweight and healthy individuals and establish a regression model. There were 456 healthy and 421 overweight participants in the study. Data were collected on triglyceride (TG), total cholesterol (CHO), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), blood GLU and CBC. The distribution characteristics and differences between healthy and overweight subjects were analyzed. Subsequently, the associations between TG, CHO, HDL, LDL and GLU with CBC were analyzed using correlation analysis and multiple linear regression (MLR). Significant differences were identified between the healthy and overweight individuals in TG, CHO, HDL, LDL, GLU and in the majority of the CBC indices. The correlation analysis indicated that there were strong correlations between TG, LDL, HDL, CHO and GLU with CBC indices in the healthy and overweight subjects. The MLR demonstrated that the regression models of TG, LDL, HDL and CHO, but no GLU, were statistically significant in the two groups ($P<0.001$). The HDL regression model exhibited the best regression parameters; the multiple correlation coefficients (R) were 0.351 and 0.308 in the healthy and overweight subjects, respectively. In the overweight and healthy subjects, there were strong correlations between TG, LDL, HDL and CHO with CBC indices, with HDL being the most relevant to the CBC indices. The CBC demonstrated statistical significance in the diagnosis of hyperlipidemia.

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Key words: blood glucose, blood lipid, complete blood count, overweight

Introduction

Hyperglycemia and hyperlipidemia, characterized by elevated blood glucose (GLU) and lipid levels, are two of the most common public health issues worldwide in modern society (1). Hyperglycemia is the main symptom of type I and type II diabetes, and the incidence of diabetes has been rapidly increasing in recent years worldwide. It has been estimated that there was 382 million people with type II diabetes mellitus in 2013, while the prevalence of diabetes is estimated to increase by 55% in 2035, reaching a total number of 592 million (1). Dyslipidemia, which is defined by elevated total cholesterol (CHO), triglyceride (TG) and/or low-density lipoprotein cholesterol (LDL-C) levels, and non-optimal levels of high-density lipoprotein cholesterol (HDL-C), is particularly prevalent worldwide (2-4).

Persistent hyperglycemia and hyperlipidemia damages the eyes, kidneys, feet and heart and causes a series of cardiovascular diseases, such as stroke, coronary heart disease and peripheral arterial disease (5-8). According to an estimated 4 million mortalities each year, dyslipidemia is considered to be a major modifiable risk factor for cardiovascular disease worldwide (9). Therefore, hyperglycemia and hyperlipidemia have presented a serious social problem.

The examination of blood GLU and lipid levels is routinely performed for early diagnosis of hyperglycemia and hyperlipidemia. When compared with healthy weight individuals, overweight individuals exhibit a greater risk for hyperglycemia, hyperlipidemia, and other diseases, such as high blood pressure, diabetes mellitus and coronary heart disease (10-12). Thus, monitoring blood GLU and lipid levels is popular and necessary, particularly in overweight individuals.

Blood routine examination also termed complete blood count (CBC) is an analysis of three major types of cells: Red blood cells (RBCs), white blood cells (WBCs) and platelets. It is a common blood test used in clinical and routine health examinations, which is beneficial for early diagnoses of serial diseases, such as anemia and infections. Furthermore, there are benefits of identifying the association between these indices,

not only experienced by overweight people, but also in healthy individuals (13). However, there are critical knowledge gaps on the correlation of blood GLU and lipid levels with CBC test results. In the current study, the association between these indices in healthy and overweight individuals was investigated.

Materials and methods

Subjects and ethics. Individuals with a history of disease, such as hematopathy, angiocardiopathy, hepatopathy, nephrosis or pulmonary disease were not recruited for the present study. A total of 877 subjects were recruited between September and December 2015, comprising 456 healthy subjects (147 male and 308 female) and 421 overweight subjects (305 male and 116 female), with mean ages of 39.70±10.89 and 45.74±11.19 years, respectively. Their heights and weights were measured using a stadiometer and electronic weighing scale, respectively. Body mass index (BMI) was then calculated as follows: BMI=weight/height^2 to divide the subjects into the healthy (BMI=18-25.0 kg/m^2) and overweight (BMI=25.0-30 kg/m^2) groups according to the criterion recommended by the World Health Organization (14). The data (anonymous) for this study was provided by the First Affiliated Hospital of Wenzhou Medical University (Wenzhou, China). The study was approved by the hospital ethics committee and conducted in accordance with the Declaration of Helsinki. All participants provided informed consent for the analysis of their clinical data.

Blood examination. To determine the blood GLU and lipid levels, a total of 3 ml fasting venous blood was collected from the subjects into separation gel tubes and separated at 3,466 x *g* for 10 min. The plasma was analyzed in a Hitachi 705/717 biochemical instrument (Hitachi, Ltd., Tokyo, Japan) at 20˚C. The fasting blood GLU, TG, CHO, HDL and LDL levels were then determined (Table I). To establish the CBC indices, 2 ml venous blood was collected into heparinized tubes and determined using a BC-5500 Automatic Blood Cell Analyzer (Mindray Bio-Medical Electronics Co., Ltd., Shenzhen, China). A total of 18 CBC indices were included in the current study; their detailed descriptions are presented in Table I.

Statistical analysis. Prior to correlation analysis, the distribution characteristics of the blood indices data were analyzed using the Shapiro-Wilk and homogeneity of variances tests. The differences between healthy and overweight subjects were analyzed by nonparametric test when the indices were abnormally distributed, and the correlations between TG, CHO HDL, LDL and GLU, and CBC indices were analyzed by bivariate correlation.

When a correlation between blood GLU and lipid levels and CBC indices was identified, multiple linear regression (MLR) analysis was then conducted using a stepwise method. All CBC indices were subjected to MLR analyses to identify the relationship between TG, CHO and GLU. One-way ANOVA was used to analyze the difference and P<0.05 was considered to indicate a statistically significant difference. The correlation of the regression residual was determined by the Durbin-Watson value. All statistical analyses were conducted using SPSS software (version 17.0; SPSS, Inc., Chicago, IL, USA).

Results

Characteristics of healthy and overweight individuals. A total of 456 healthy subjects (147 male and 308 female) and 421 overweight subjects (305 male and 116 female) were included in the current study (mean age, 39.70±10.89 and 45.74±11.19 years, respectively). The BMIs were 19.66±5.59 and 26.39±1.92 for the healthy and overweight groups, respectively. As the results of the Shapiro-Wilk test showed that the indices were abnormally distributed in the two different groups, the blood GLU, blood lipid and CBC indices data from the two groups were analyzed using a nonparametric test. The variance analysis indicated that there were significant differences between the healthy and overweight subjects; the TG, CHO, HDL, LDL, GLU and the majority of the CBC indices were altered. The level of TG, CHO, LDL, and GLU increased (P<0.01), while the HDL level decreased (P<0.01) in the overweight subjects (Table I).

Correlation analysis of glucose and lipid levels in healthy and overweight subjects. The results indicated that TG, LDL and HDL were strongly correlated with the CBC indices of the healthy subjects (Table II). There were 9 indices of CBC correlated with TG, 6 indices of CBC correlated with LDL, and 11 indices of CBC correlated with HDL. Compared with TG (the most important index for hyperlipidemia), GLU and CHO only demonstrated three and two relevant CBC indices, respectively.

This correlation almost did not change in the overweight subjects (Table III). There were 8 indices of CBC correlated with TG, 5 indices of CBC correlated with LDL, and 11 indices of CBC correlated with HDL. In addition, the relevant CBC indices in the overweight subjects were almost the same as in the healthy subjects. These findings indicated that the correlation of TG, HDL, LDL, CHO and GLU with the CBC indices did not change according to weight.

MLR analysis. According to the results of correlation analysis, there was strong correlation of TG, LDL, HDL, CHO and GLU with the CBC indices, and scatter diagrams demonstrated their linear correlation, which indicated that MLR could be used in the study. As there were various indices associated with each other, in order to evaluate independent CBC indices correlated with TG, LDL, HDL, CHO and GLU, MLR analysis was conducted using a stepwise method.

Regression models were generated for TG, LDL, HDL and CHO (Table IV), but not GLU, where no regression model was generated in the healthy subjects according to the stepwise method. The regression models of TG, LDL, HDL, and CHO all demonstrated statistical significance in the two groups (P<0.001). The regression models of healthy subjects exhibited greater multiple correlation coefficient (R), determinate coefficient (R^2) and F values when compared with the overweight subjects with regard to TG, LDL, HDL and CHO. These results indicated that the regression models of the healthy subjects were better than those for the overweight subjects.

Table I. Characteristics and variance analysis of blood glucose, lipid and CBC indices in healthy (n=456) and overweight (n=421) subjects.

			Healthy		Overweight		
Blood index	Abbreviation	Unit	Mean	SD	Mean	SD	P-value
Triglyceride	TG	mmol/l	0.97	0.41	1.99	1.60	0.000
Low-density Lipoprotein	LDL	mmol/l	2.48	0.57	2.88	0.70	0.000
High-density lipoprotein	HDL	mmol/l	1.51	0.30	1.27	0.29	0.000
Total cholesterol	CHO	mmol/l	4.48	0.66	4.96	0.88	0.000
Glucose	GLU	mmol/l	5.34	0.41	5.90	1.14	0.000
Percentage of monocyte	PMC	%	0.07	0.02	0.07	0.02	0.573
Absolute value of monocyte	AVM	$x10^9$/l	0.42	0.14	0.49	0.17	0.000
Red blood cell	RBC	$x10^{12}$/l	4.66	0.47	4.98	0.47	0.000
Hematocrit	HCT	l/l	0.43	0.04	0.45	0.04	0.000
Percentage of leukomonocyte	PLC	%	0.37	0.08	0.37	0.08	0.766
Absolute value of leukomonocyte	AVLC	$x10^9$/l	2.13	0.60	2.41	0.66	0.000
Mean corpuscular volume	MCV	fl	91.61	5.81	91.42	5.62	0.248
Mean corpuscular hemoglobin	MCH	pg	29.79	2.32	30.20	2.30	0.001
Mean corpuscular hemoglobin concentration	MCHC	g/l	324.89	10.04	330.06	11.19	0.000
Mean platelet volume	MPL	fl	10.83	1.80	10.93	1.57	0.394
Absolute value of eosinophils	AVE	$x10^9$/l	0.13	0.10	0.17	0.12	0.000
Percentage of eosinophils	PE	%	0.02	0.02	0.02	0.02	0.023
Hemoglobin	HB	g/l	138.34	14.70	149.95	15.47	0.000
Blood platelet	PLT	$x10^9$/l	221.56	48.89	224.31	51.35	0.748
Thrombocytocrit	THR	l/l	0.24	0.06	0.24	0.06	0.261
Percentage of neutrophils	PN	%	0.53	0.08	0.54	0.08	0.969
Absolute value of neutrophils	AVN	$x10^9$/l	3.16	1.03	3.62	1.23	0.000
Red blood cell volume distribution width	RBCVD	%	12.81	0.94	12.79	0.92	0.642

CBC, complete blood count; SD, standard deviation.

In these four types of regression model, the multiple Rs of the HDL regression model were 0.351 and 0.308 in the healthy and overweight subjects, respectively, which were greater than those of the TG, LDL and CHO regression models. In addition, the R^2 and F values of HDL regression model were higher than TG, LDL and CHO regression models, and the regression standardized residual demonstrated a normal distribution (Fig. 1). However, the R of TG was 0.319 in the healthy subjects, and was decreased to 0.189 in the overweight subjects, and the regression standardized residual was similar to a skewed normal distribution (Fig. 2). Therefore, HDL was identified as the most suitable index for linear regression when CBC indices were selected as independent variables.

Discussion

CBC is the most ubiquitous diagnostic parameter in the clinical setting, and is routinely analyzed to evaluate the health of patients (15). Generally, the CBC test provides important information regarding three major types of cells in the blood, RBCs, WBCs and platelets. Other indices, such as absolute value of monocyte, hematocrit, absolute value of leukomonocyte, mean corpuscular hemoglobin concentration, hemoglobin, PLC and thrombocytocrit, are all obtained from these three types of cell. These measurements are usually performed to test for blood disease, infection and many other disorders, which are associated with RBCs, WBCs and platelets. For example, inflammation, leukemia, bone marrow failure and immunodeficiency are diagnosed by irregular WBC counts and their differentials (16).

In the current study, the association of CBC with blood GLU and lipid levels in overweight and healthy subjects was analyzed. In addition, the correlation of CBC indices with TG, LDL, HDL, CHO and GLU was analyzed (Tables II and III). However, a limitation regarding the CBC indices is that there were may be multiple co-linear associations between these CBC indices.

For further analysis, MLR was used to evaluate the correlation of TG, LDL, HDL, CHO and GLU with CBC indices. MLR models the association between two or more explanatory variables and a response variable by fitting a linear equation (17). This differs from an artificial intelligence algorithm, which commonly requires complicated programming (18). MLR more easily provides regression models, which are linearly associated with their parameters.

The model summary (Table IV) demonstrated that the strongest correlation with the CBC indices was HDL, followed by TG, LDL, CHO and GLU, which was consistent with the

Table II. Correlation of TG, LDL, HDL, CHO and GLU with CBC indices in 456 healthy subjects.

CBC index	TG coefficient	P-value	GLU coefficient	P-value	LDL coefficient	P-value	HDL coefficient	P-value	CHO coefficient	P-value
Percentage of monocyte	0.012	0.802	-0.039	0.401	0.000	0.988	-0.040	0.393	0.000	0.998
Absolute value of monocyte	0.173[a]	0.000	0.043	0.356	0.046	0.326	-0.219[a]	0.000	-0.019	0.688
Red blood cell	0.255[a]	0.000	0.104[b]	0.027	0.165[a]	0.000	-0.274[a]	0.000	0.049	0.299
Hematocrit	0.288[a]	0.000	0.096[b]	0.041	0.180[a]	0.000	-0.294[a]	0.000	0.078	0.098
Percentage of leukomonocyte	-0.011	0.822	-0.042	0.366	0.026	0.576	-0.019	0.682	0.010	0.824
Absolute value of leukomonocyte	0.127[a]	0.007	0.050	0.285	0.069	0.143	-0.172[a]	0.000	0.002	0.970
Mean corpuscular volume	0.005	0.915	-0.010	0.823	-0.031	0.511	-0.004	0.934	0.006	0.904
Mean corpuscular hemoglobin	0.067	0.156	-0.015	0.757	0.038	0.421	-0.119[b]	0.011	0.017	0.721
Mean corpuscular hemoglobin concentration	0.130[a]	0.005	-0.003	0.956	0.137[a]	0.003	-0.240[a]	0.000	0.024	0.609
Mean platelet volume	0.020	0.672	0.006	0.904	-0.028	0.554	0.013	0.784	0.009	0.856
Absolute value of eosinophils	0.092	0.050	0.079	0.093	0.112[b]	0.016	-0.156[a]	0.001	0.059	0.212
Percentage of eosinophils	0.069	0.144	0.092[b]	0.049	0.078	0.097	-0.127[a]	0.007	0.041	0.387
Hemoglobin	0.279[a]	0.000	0.085	0.070	0.191[a]	0.000	-0.311[a]	0.000	0.074	0.114
Blood platelet	0.103[b]	0.028	-0.001	0.979	0.095[b]	0.044	-0.010	0.835	0.085	0.071
Thrombocytocrit	0.129[a]	0.006	0.018	0.694	0.090	0.055	0.003	0.953	0.096[b]	0.040
Percentage of neutrophils	0.005	0.917	0.023	0.626	-0.029	0.533	0.038	0.416	-0.015	0.742
Absolute value of neutrophils	0.136[a]	0.004	0.090	0.054	0.037	0.431	-0.131[a]	0.005	-0.009	0.848
Red blood cell volume distribution width	0.030	0.525	0.068	0.149	0.089	0.058	0.164[a]	0.000	0.158[a]	0.001

[a]P<0.01 and [b]P<0.05 level (2-tailed). CBC, complete blood count; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CHO, total cholesterol; GLU, glucose.

Table III. Correlation of TG, LDL, HDL, CHO, GLU with CBC indices in 421 overweight subjects.

CBC index	TG coefficient	P-value	GLU coefficient	P-value	LDL coefficient	P-value	HDL coefficient	P-value	CHO coefficient	P-value
Percentage of monocyte	0.021	0.670	-0.014	0.773	-0.043	0.375	-0.054	0.271	-0.029	0.547
Absolute value of monocyte	0.147[a]	0.003	0.105[b]	0.031	-0.018	0.717	-0.150[a]	0.002	-0.029	0.550
Redblood cell	0.225[a]	0.000	-0.058	0.233	0.055	0.261	-0.244[a]	0.000	-0.007	0.883
Hematocrit	0.247[a]	0.000	0.008	0.876	0.110[b]	0.024	-0.202[a]	0.000	0.061	0.212
Percentage of leukomonocyte	0.020	0.688	-0.060	0.217	0.153[a]	0.002	0.053	0.275	0.154[a]	0.001
Absolute value of leukomonocyte	0.190[a]	0.000	0.042	0.392	0.103[b]	0.035	-0.118[b]	0.015	0.082	0.094
Mean corpuscular volume	0.003	0.956	0.119[b]	0.014	0.071	0.144	0.089	0.068	0.092	0.060
Mean corpuscular hemoglobin	0.125[b]	0.010	0.083	0.089	0.052	0.291	-0.047	0.335	0.066	0.175
Mean corpuscular hemoglobin concentration	0.205[a]	0.000	-0.041	0.403	0.015	0.761	-0.208[a]	0.000	0.011	0.818
Mean platelet volume	-0.003	0.954	0.027	0.583	-0.031	0.521	0.011	0.829	0.005	0.925
Absolute value of eosinophils	0.042	0.395	0.024	0.618	-0.022	0.657	-.100[b]	0.040	-0.049	0.318
Percentage of eosinophils	0.001	0.991	-0.059	0.224	-0.030	0.539	-0.074	0.127	-0.050	0.309
Hemoglobin	0.270[a]	0.000	-0.012	0.804	0.087	0.075	-0.224[a]	0.000	0.050	0.310
Blood platelet	0.036	0.461	0.067	0.167	0.049	0.315	0.025	0.606	0.044	0.370
Thrombocytocrit	0.034	0.487	0.065	0.183	0.043	0.373	0.021	0.666	0.052	0.285
Percentage of neutrophils	-0.013	0.796	0.079	0.107	-0.144[a]	0.003	-0.026	0.598	-0.138[a]	0.005
Absolute value of neutrophils	0.123[b]	0.011	0.114[b]	0.019	-0.076	0.122	-0.138[a]	0.005	-0.093	0.057
Redblood cell volume distribution width	-0.027	0.577	0.002	0.972	0.053	0.278	0.136[a]	0.005	0.128[a]	0.009

[a]P<0.01 and [b]P<0.05 level (2-tailed). CBC, completeblood count; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CHO, total cholesterol; GLU, glucose.

Table IV. Model summary of TG, LDL, HDL and CHO in healthy (n=456) and overweight (n=421) subjects.

Model	Index	R	R^2	Durbin-Watson	Predictors (constant)	ANOVA	
						F-value	P-value
Healthy	TG	0.319	0.102	0.19	HCT, PLT	25.708	0.000
	LDL	0.249	0.062	1.93	HB, RBCVD, THR	9.93	0.000
	HDL	0.351	0.123	1.57	HB, MPL, AVM	21.18	0.000
	CHO	0.232	0.054	1.9	THR, RBCVD, MCH	8.55	0.000
Overweight	TG	0.189	0.036	1.93	HB	15.53	0.000
	LDL	0.189	0.036	2.07	PLC, HCT	7.78	0.000
	HDL	0.308	0.095	1.93	RBC, RBCVD, AVM	14.62	0.000
	CHO	0.150	0.022	2.03	PLC	9.59	0.002

TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CHO, total cholesterol; R, correlation coefficient; R^2, determinate coefficient; HCT, hematocrit; PLT, blood platelet; HB, hemoglobin; RBCVD, red blood cell volume distribution; THR, thrombocytocrit; MPL, mean platelet volume; AVM, absolute value of monocyte; MCH, mean corpuscular hemoglobin; PLC, percentage of leukomonocyte.

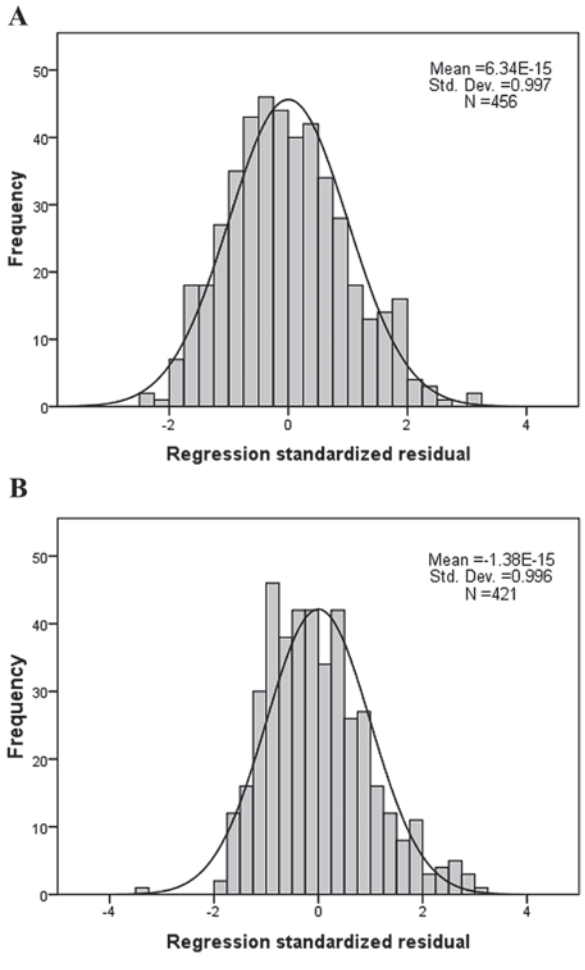

Figure 1. Histogram of regression standardized residuals (dependent variable, HDL) in (A) healthy and (B) overweight subjects. HDL, high-density lipoprotein.

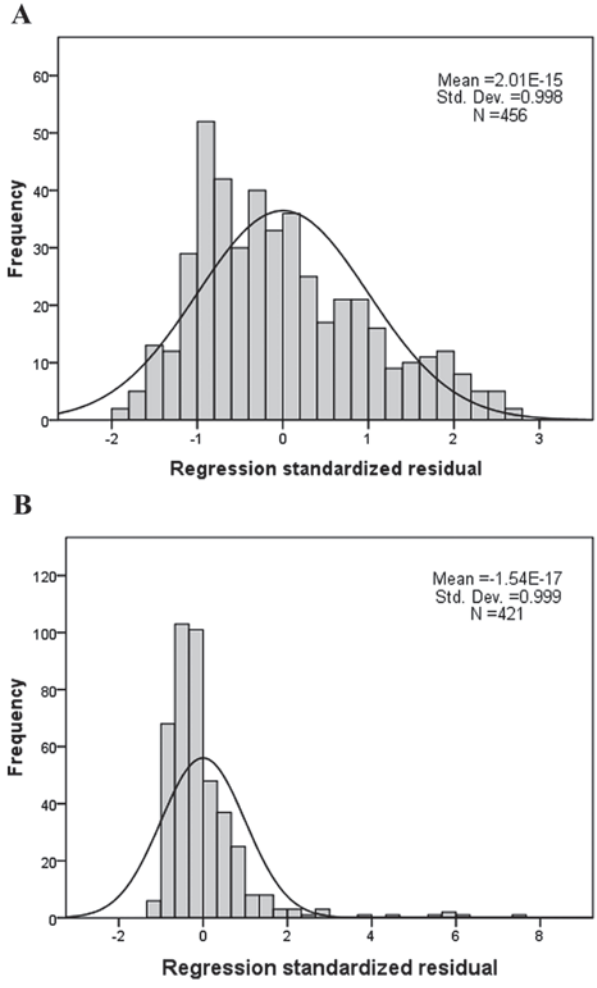

Figure 2. Histogram of regression standardized residuals (dependent variable, TG) in (A) healthy and (B) overweight subjects. TG, triglyceride.

results of the correlation analysis. However, almost the same associated CBC indices were identified between TG and HDL (Tables II and III). The multiple R and R^2 were decreased markedly (Table IV). In addition, the regression standardized residual was not normally distributed in TG, which indicates that TG is influenced by increasing weight, whereas HDL is not. Therefore, HDL is the most stable and correlated index within the CBC indices. According to the results of the present

study, this prediction model may be developed in further studies, such as back-propagation artificial neural network (19) and extreme learning machine (10) models, and support vector machine (20) to improved predictive capabilities.

In conclusion, significant differences in GLU, lipid and CBC indices were observed between healthy and overweight subjects. The correlation and MLR analyses indicated that there were strong correlations between TG, LDL, HDL and CHO, but not GLU, for which no linear regression model was generated. Among these indices, HDL was identified as the index that was most strongly correlated with the CBC indices. Thus, the CBC test is considered to be helpful in the diagnosis of hyperlipidemia.

Acknowledgements

The present study was supported by the National Science and Technology Major Project (grant no. 2012ZX10002004) and the Chinese High Tech Research & Development (863) Program (grant no. 2013AA020102).

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