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ORIGINAL ARTICLE

The study of soluble intercellular adhesion molecule-1 and ghrelin in adolescents with family history of type 2 diabetes

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Abstract The purpose of this study was to observe both the changes of soluble intercellular adhesion molecule-1 (sICAM-1) and ghrelin in adolescents with family history of type 2 diabetes (FHD) and the relationship between sICAM-1 and ghrelin. This case–control study included 63 adolescents (boys/girls 29/34, age 14.1 ± 0.7 years) without FHD (FHD−) and 67 adolescents (boys/girls 33/34, age 14.0 ± 0.8 years) with FHD (FHD+). Anthropometric measurements, including height, weight, waist circumference (WC), and blood pressure, were obtained. Blood samples were collected, and fasting plasma glucose (FPG), serum lipids, true insulin, sICAM-1, and ghrelin were assayed. The results showed that the age and gender were similar in two groups ($P > 0.05$). Body mass index (BMI), WC, FPG, fasting insulin, HOMA-IR, and sICAM-1 were all significantly higher in the FHD+ group than in the FHD− group ($P < 0.05$). Ghrelin was significantly lower in the FHD+ group than in the FHD− group ($P < 0.05$). sICAM-1 was positively correlated with WC ($r = 0.178$, $P = 0.043$), fasting insulin ($r = 0.195$, $P = 0.026$), HOMA-IR ($r = 0.197$, $P = 0.024$), and ghrelin ($r = 0.290$, $P = 0.001$). After multivariate analysis, the ghrelin ($\beta = 0.788$, 95 % CI: 0.416–1.159, $P = 0.000$) and HOMA-IR ($\beta = 0.106$, 95 % CI: 0.045–0.167, $P = 0.001$) maintained an independent association with sICAM-1. These findings led to the conclusion that endothelial dysfunction and decline of ghrelin were found in adolescents with family history of diabetes. The decline of ghrelin maybe a protection mechanism for endothelial function in adolescents with family history of diabetes and should be examined in future studies.

Keywords Type 2 diabetes · Family history · Soluble intercellular adhesion molecule-1 · Ghrelin

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Introduction

The prevalence of type 2 diabetes mellitus (T2DM) among adolescents has increased from 5- to 10-fold over the past few decades [1]. A family history of type 2 diabetes (FHD) is a major risk factor for this disease. Adolescents with T2DM had a significant FHD [2]. Adolescents with a positive FHD presented signs of insulin resistance [3]. It is paramount to identify young people with glucose regulation alterations for early, intensive intervention to prevent or at least postpone the onset of type 2 diabetes [4]. Genetic factors are important in determining which adolescents are affected.

Genetic predisposition to type 2 diabetes also accelerates the development of atherosclerosis and potentially increases the risk of coronary heart disease. Endothelial dysfunction is regarded as an early step in the development of atherosclerosis. Normoglycemic first-degree relatives of diabetic subjects have blunted endothelial function and increased stiffness of the large arteries. These alterations are already present at a very young age, before any alteration in glycemic control or blood pressure values can be detected [5]. Reduced nitric oxide synthesis and eNOS mRNA expression were found in endothelial cells from newborns with a strong family history of type 2 diabetes [6].

Ghrelin is a new 28 amino acid acylated peptide hormone identified as the endogenous ligand for the growth hormone secretagogue receptor [7]. Ghrelin is the first

circulating hormone demonstrated to stimulate food intake in man. Endogenous ghrelin is a potentially important new regulator of the complex systems controlling food intake and body weight [8]. These findings together with potential effects on glucose homeostasis make ghrelin play a potentially important role in the pathophysiology of Type 2 diabetes. Circulating ghrelin concentrations are reduced in healthy offspring of Type 2 diabetes [3]. Increasing evidence has demonstrated that ghrelin has a close relationship with cardiovascular system [9]. There is limited information on whether decreased circulating ghrelin concentrations are independently associated with endothelial dysfunction in adolescents with FHD.

As is well known, soluble intercellular adhesion molecule-1(sICAM-1) is related to the development of diabetes and diabetic complication. sICAM-1 is also a well-recognized marker of endothelial dysfunction in adolescents [10]. In our study, we attempted to explore the relationship between ghrelin and soluble intercellular adhesion molecule-1(sICAM-1) in adolescents with FHD.

Methods

Subjects

The subjects were recruited from middle school students (aged 13–15 years) in Qinhuangdao, Hebei province during 2006. The study subjects were evaluated using a self-administered questionnaire to determine FHD. The self-administered questionnaires were evaluated by adolescents and their parents together. The offspring were defined with FHD if either one or both of the parents had diabetes and the parents all were type 2 diabetes. The sample was divided into two groups according FHD. The control group consisted of 63 subjects (boys/girls 29/34, age 14.1 ± 0.7 years) without FHD (FHD−).The case group consisted of 67 subjects (boys/girls 33/34, age 14.0 ± 0.8 years) with FHD (FHD+).

In addition, all the participants were required to be in good health, which was corroborated by medical history, physical examination, and laboratory tests. To avoid the interference of other confounding factors on the possible relation between FHD, ghrelin, and sICAM-1, smokers and those who consume alcohol were excluded. Moreover, acute and chronic inflammations were excluded. This study was approved by the ethics committee of the First Hospital of Qinhuangdao. All subjects and their parents provided written informed consent before study initiation.

Anthropometric measurements

Anthropometric measurements, including height, weight, waist circumference (WC), and blood pressure, were obtained while the subjects were in light clothing and not wearing shoes. Body mass index (BMI) was calculated by dividing weight (kg) by height squared (m^2). Blood pressure was measured twice with a mercury sphygmomanometer after 10 min of rest while the subjects were seated, and the average of the two measurements was used for analysis.

Laboratory examinations

After an overnight fast of 10–12 h, blood samples were drawn from an antecubital vein in each subject and collected into vacutainer tubes. Fasting plasma glucose (FPG) levels were measured using the glucose oxidase method, and serum lipid levels were measured using enzymatic assays with an autoanalyzer (Hitachi, Tokyo, Japan). Plasma concentrations of insulin, ghrelin, and sICAM-1 were measured by enzyme-linked immunosorbent assay (ELISA) with model 680 microplate reader (BIO-RAD, USA).The ELISA kits were purchased from USCNLIFE company, USA. The following equation was used to calculate the homeostasis model assessment (HOMA)-IR index: (fasting insulin level x fasting glucose level)/22.5, while the intra- and inter-coefficient variations were 2.6 and 2.9 %, respectively.

Statistical analyses

All analyses were performed using the SPSS 11.5 statistical software (SPSS 11.5 for Windows; SPSS, Inc, Chicago, IL). The sample size was calculated to reach enough power statistics. Power = 0.95, $\beta = 0.05$, $u_\beta = 1.64$, $\alpha = 0.05$, $u_\alpha = 1.96$, $\delta = 0.47$, $\sigma = 0.72$, and $N = [2(u_\alpha + u_\beta)\ \sigma/\delta]^2 = 121.65 \approx 122$. Values are expressed as mean with standard deviation. When not normally distributed, the data were ln-transformed for analysis and are expressed as medians with interquartile ranges. The two groups were compared using the Student t test, and Pearson correlation coefficient was used to measure the strength of association between variables. Multiple linear regression analyses were performed to examine the relationships between ghrelin, HOMA-IR, sICAM-1, and other variables. $P < 0.05$ was considered as statistically significant.

Results

Age, gender, as well as anthropometric and biochemical data, are presented in Table 1. The age and gender were similar in two groups ($P > 0.05$). BMI, WC, FPG, fasting insulin, HOMA-IR, and sICAM-1 were all significantly higher in the FHD+ group than in the FHD− group ($P < 0.05$). Ghrelin was significantly lower in the FHD+

Table 1 Clinical and laboratory characteristics of the subjects in each group

Variable	FHD− group ($n = 63$)	FHD+ group ($n = 67$)	t	P
Age (year) mean (SD)	14.1 (0.7)	14.0 (0.8)	0.462	0.645
BMI (kg/m^2) mean (SD)	21.5 (4.0)	23.0 (4.2)	1.980	0.049
WC (cm) mean (SD)	69.4 (8.9)	73.4 (10.6)	2.318	0.022
SBP (mmHg) mean (SD)	103.6 (12.9)	107.1 (16.1)	1.352	0.179
DBP (mmHg) mean (SD)	66.7 (9.6)	68.8 (9.0)	1.311	0.192
TG (mmol/L) mean (SD)	1.18 (0.73)	1.05 (0.62)	1.070	0.287
TC (mmol/L) mean (SD)	3.76 (0.59)	3.92 (0.64)	1.431	0.155
HDL-C (mmol/L) mean (SD)	1.36 (0.24)	1.39 (0.32)	0.463	0.644
LDL-C (mmol/L) mean (SD)	1.88 (0.52)	2.04 (0.53)	1.663	0.099
FPG (mmol/L) mean (SD)	4.94 (0.38)	5.23 (0.38)	4.277	0.000
Fasting insulin (μU/ml) median (IQR)	12.0 (7.0)	19.0 (14.6)	5.678	0.000
HOMA-IR median (IQR)	2.53 (1.35)	4.32 (3.68)	6.027	0.000
Ghrelin (ng/ml) mean (SD)	1.3 (0.4)	0.9 (0.3)	5.403	0.000
sICAM-1 (ng/ml) mean (SD)	1.83 (0.56)	2.52 (1.11)	2.523	0.013

Values are expressed as mean (SD), and when not normally distributed, they were ln-transformed for analysis and are expressed as medians (IQR)

FHD family history of type 2 diabetes, *SD* standard deviation, *IQR* interquartile range, *BMI* body mass index, *WC* waist circumference, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *TG* triglyceride, *TC* total cholesterol, *HDL-C* high density lipoprotein cholesterol, *LDL-C* low density lipoprotein cholesterol, *FPG* fasting plasma glucose, *HOMA* homeostasis model assessment, *sICAM-1* soluble intercellular adhesion molecule-1

Table 2 Simple correlations between the ghrelin and other variables in the study subjects

Variable	FHD− group ($n = 63$)		FHD+ group ($n = 67$)		Two group ($n = 130$)	
	r	P	r	P	r	P
Age (year)	0.044	0.732	−0.026	0.837	0.140	0.113
BMI (kg/m^2)	0.016	0.900	0.118	0.342	−0.020	0.820
WC (cm)	0.124	0.332	0.107	0.387	0.012	0.889
SBP (mmHg)	0.116	0.364	0.084	0.499	0.035	0.691
DBP (mmHg)	0.204	0.109	0.043	0.728	0.071	0.424
TG (mmol/L)	0.047	0.714	0.192	0.120	0.135	0.125
TC (mmol/L)	−0.060	0.643	−0.093	0.455	−0.120	0.173
HDL-C (mmol/L)	0.193	0.130	−0.128	0.308	0.007	0.938
LDL-C (mmol/L)	−0.172	0.178	−0.132	0.288	−0.199	0.023
FPG (mmol/L)	−0.288	0.022	−0.276	0.024	−0.345	0.000
Fasting insulin (μU/ml)	−0.160	0.211	0.099	0.425	−0.206	0.019
HOMA-IR	−0.192	0.132	0.086	0.489	−0.229	0.009
sICAM-1 (ng/ml)	0.538	0.000	0.457	0.000	0.290	0.001

FHD family history of type 2 diabetes, *BMI* body mass index, *WC* waist circumference, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *TG* triglyceride, *TC* total cholesterol, *HDL-C* high density lipoprotein cholesterol, *LDL-C* low density lipoprotein cholesterol, *FPG* fasting plasma glucose, *HOMA* homeostasis model assessment, *sICAM-1* soluble intercellular adhesion molecule-1

group than in the FHD− group ($P < 0.05$). No significant differences between the two groups in any of the other variables investigated, including blood pressure and serum lipid levels, were observed ($P > 0.05$).

The correlation coefficients between ghrelin and the other variables for all of the subjects are shown in Table 2. Ghrelin was negatively correlated with FPG ($r = -0.345$, $P = 0.000$), fasting insulin ($r = -0.206$, $P = 0.019$), HOMA-IR ($r = -0.229$, $P = 0.009$), LDL-C ($r = -0.199$, $P = 0.023$), and positively correlated with sICAM-1($r = 0.290$, $P = 0.001$). When we separately analyze FDH- vs FHD+ subjects, ghrelin still correlated with FPG in two groups (FHD− group: $r = -0.288$, $P = 0.022$ vs. FHD+ group: $r = -0.276$, $P = 0.024$). When ghrelin

Table 3 Multiple linear regression analyses for ghrelin (Stepwise Method)

Model	Unstandardized coefficients B	Std. error	Standardized coefficients B	*t*	*P*	95 % CI	r^2
Constant	2.857	0.416		6.873	0.000	2.035 to 3.680	
FPG	−0.337	0.081	−0.345	−4.138	0.000	−0.498 to −0.176	0.119

Dependent variable: ghrelin

FPG fasting plasma glucose

was considered as the dependent variable in a multiple regression analysis with age, gender, BMI, WC, SBP, DBP, TG, TC, HDL-C, LDL-C, FPG, fasting insulin, HOMA-IR, and sICAM-1 as independent variables, the FPG ($\beta = -0.337$, 95 % CI: −0.498 to −0.176, $P = 0.000$) maintained an independent association with ghrelin (Table 3).

The correlation coefficients between HOMA-IR and the other variables for all of the subjects are shown in Table 4. HOMA-IR was positively correlated with BMI ($r = 0.469$, $P = 0.000$), WC ($r = 0.486$, $P = 0.000$), SBP ($r = 0.177$, $P = 0.044$), TG ($r = 0.204$, $P = 0.020$), sICAM-1 ($r = 0.197$, $P = 0.024$) and negatively correlated with HDL-C ($r = -0.253$, $P = 0.004$), ghrelin ($r = -0.229$, $P = 0.009$). When we separately analyze FDH− versus FHD+ subjects, HOMA-IR still correlated with WC in two groups (FHD− group: $r = 0.411$, $P = 0.001$ versus FHD+ group: $r = 0.504$, $P = 0.000$). When HOMA-IR was considered as the dependent variable in a multiple regression analysis with age, gender, BMI, WC, SBP, DBP, TG, TC, HDL-C, LDL-C, ghrelin, and sICAM-1 as independent variables, the WC ($\beta = 0.116$, 95 % CI: 0.080–0.152, $P = 0.000$) and sICAM-1 ($\beta = 0.570$, 95 % CI: 0.159–0.982, $P = 0.007$) maintained an independent association with HOMA-IR (Table 5).

The correlation coefficients between sICAM-1 and the other variables for all of the subjects are shown in Table 6. sICAM-1 was positively correlated with WC ($r = 0.178$, $P = 0.043$), fasting insulin ($r = 0.195$, $P = 0.026$), HOMA-IR ($r = 0.197$, $P = 0.024$), and ghrelin ($r = 0.290$, $P = 0.001$). When we separately analyze FDH− versus

Table 4 Simple correlations between the HOMA-IR and other variables in the study subjects

Variable	FHD− group ($n = 63$)		FHD+ group ($n = 67$)		Two group ($n = 130$)	
	r	*P*	*r*	*P*	*r*	*P*
Age (year)	−0.192	0.132	0.046	0.712	−0.052	0.557
BMI (kg/m^2)	0.361	0.004	0.483	0.000	0.469	0.000
WC (cm)	0.411	0.001	0.504	0.000	0.486	0.000
SBP (mmHg)	0.106	0.408	0.154	0.213	0.177	0.044
DBP (mmHg)	0.034	0.789	0.121	0.329	0.129	0.144
TG (mmol/L)	0.223	0.079	0.348	0.004	0.204	0.020
TC (mmol/L)	−0.141	0.272	0.084	0.498	0.065	0.462
HDL-C (mmol/L)	−0.314	0.012	−0.307	0.012	−0.253	0.004
LDL-C (mmol/L)	−0.149	0.243	0.090	0.469	0.072	0.417
Ghrelin (pg/ml)	−0.192	0.132	0.086	0.489	−0.229	0.009
sICAM-1(ng/ml)	0.037	0.775	0.131	0.289	0.197	0.024

FHD family history of type 2 diabetes, *BMI* body mass index, *WC* waist circumference, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *TG* triglyceride, *TC* total cholesterol, *HDL-C* high density lipoprotein cholesterol, *LDL-C* low density lipoprotein cholesterol, *HOMA* homeostasis model assessment, *sICAM-1* soluble intercellular adhesion molecule-1

Table 5 Multiple linear regression analyses for HOMA-IR (Stepwise Method)

Model	Unstandardized coefficients B	Std. error	Standardized coefficients B	*t*	*P*	95 % CI	r^2
Constant	−3.509	1.378		−2.546	0.012	−6.237 to −0.781	
WC	0.116	0.018	0.472	6.422	0.000	0.080 to 0.152	0.256
sICAM-1	0.570	0.208	0.211	2.745	0.007	0.159 to 0.982	0.296

Dependent variable: HOMA-IR

HOMA homeostasis model assessment, *WC* waist circumference, *sICAM-1* soluble intercellular adhesion molecule-1

Table 6 Simple correlations between the soluble intercellular adhesion molecule-1 and other variables in the study subjects

Variable	FHD− group ($n = 63$)		FHD+ group ($n = 67$)		Two group ($n = 130$)	
	r	P	r	P	r	P
Age (year)	−0.036	0.778	−0.084	0.497	0.076	0.388
BMI (kg/m^2)	0.084	0.514	−0.014	0.911	0.053	0.552
WC (cm)	0.174	0.172	0.132	0.287	0.178	0.043
SBP (mmHg)	0.090	0.484	−0.018	0.883	0.037	0.678
DBP (mmHg)	0.119	0.353	−0.094	0.451	0.005	0.952
TG (mmol/L)	0.085	0.510	0.169	0.172	0.166	0.060
TC (mmol/L)	−0.037	0.774	−0.008	0.951	0.012	0.894
HDL-C (mmol/L)	0.094	0.463	−0.159	0.202	−0.079	0.373
LDL-C (mmol/L)	−0.102	0.427	−0.051	0.680	−0.031	0.730
FPG (mmol/L)	−0.171	0.181	0.035	0.780	0.050	0.573
Fasting insulin (μU/ml)	0.065	0.615	0.127	0.307	0.195	0.026
HOMA-IR	0.037	0.775	0.131	0.289	0.197	0.024
Ghrelin (pg/ml)	0.538	0.000	0.457	0.000	0.290	0.001

FHD family history of type 2 diabetes, *BMI* body mass index, *WC* waist circumference, *SBP* systolic blood pressure, *DBP*, diastolic blood pressure, *TG* triglyceride, *TC* total cholesterol, *HDL-C* high density lipoprotein cholesterol, *LDL-C* low density lipoprotein cholesterol, *FPG* fasting plasma glucose, *HOMA* homeostasis model assessment

Table 7 Multiple linear regression analyses for soluble intercellular adhesion molecule-1 (Stepwise Method)

Model	Unstandardized coefficients B	Std. error	Standardized coefficients B	t	P	95 % CI	r^2
Constant	0.716	0.280		2.558	0.012	0.162–1.270	
Ghrelin	0.788	0.188	0.351	4.193	0.000	0.416–1.159	0.082
HOMA-IR	0.106	0.031	0.288	3.440	0.001	0.045–0.167	0.161

Dependent variable: soluble intercellular adhesion molecule-1

FHD+ subjects, sICAM-1 still correlated with ghrelin in two groups (FHD− group: $r = 0.538$, $P = 0.000$ versus FHD+ group: $r = 0.457$, $P = 0.000$). When sICAM-1 was considered as the dependent variable in a multiple regression analysis with age, gender, BMI, WC, SBP, DBP, TG, TC, HDL-C, LDL-C, FPG, fasting insulin, HOMA-IR and ghrelin as independent variables, the ghrelin ($\beta = 0.788$, 95 % CI: 0.416–1.159, $P = 0.000$) and HOMA-IR ($\beta = 0.106$, 95 % CI: 0.045–0.167, $P = 0.001$) maintained an independent association with sICAM-1 (Table 7).

Discussion

The results of the present study show that sICAM-1 levels were increased in adolescents with FHD. The endothelium is an important locus for the control of vascular function. It actively regulates vascular tone, permeability to leukocytes and macromolecules, the balance between coagulation and fibrinolysis, composition of the subendothelial matrix, and proliferation of vascular smooth muscle cells [11]. Intercellular adhesion molecule-1 (ICAM-1) is a transmembrane adhesion molecule involved in leukocyte migration to sites of inflammation [12]. As the result of endothelial activation, ICAM-1 is overexpressed. These molecules are shed from the surface and can be measured, as soluble forms in serum. Therefore, they can be regarded as early markers of endothelial dysfunction. sICAM-1 has also been known to be involved in the development of vascular diseases that are associated with vascular smooth muscle cell migration, such as hypertension and atherosclerosis. sICAM-1 increased rat aortic smooth muscle cells migration through spleen tyrosine kinase pathways [13], and may directly enhance membrane permeability to Ca^{2+} and increase Ca^{2+} inflow in smooth muscle fiber cells, thus inducing vasoconstriction in the smooth muscle cells [14]. Adolescents with FHD had significantly higher levels of sICAM-1 as well as endothelial activation indices compared with adolescents without FHD. Changes in endothelial function preceded the development of diabetes.

Our results showed that adolescents with FHD had decreased circulating levels of ghrelin and increased FPG than adolescents without FHD. We also report that FPG, fasting insulin, and HOMA-IR were negatively associated with plasma ghrelin levels. Moreover, FPG was a factor independent of ghrelin levels as determined by multiple

regression analysis. This result was supported by several previous studies [15, 16] and suggests that blood glucose suppresses circulating ghrelin in adolescents with FHD. Nanjo et al. [17] also found that FPG was inversely associated with ghrelin in a Japanese general population. The lower ghrelin levels in subjects with FHD may be the result of elevated FPG, causing a negative feedback to inhibit appetite and body weight [3].

Ghrelin has a close relationship with endothelial function. However, these claims are controversial, and study results tend to differ. Tesauro et al. found that administration of exogenous ghrelin acutely improves endothelial function by increasing nitric oxide bioavailability and normalizing the alternating balance between endothelin 1/nitric oxide within the vasculature of individuals with metabolic syndrome. In addition, in endothelial cell cultures, it has been shown that ghrelin directly stimulates nitric oxide production using a signaling pathway that involves GHSR-1a, PI 3-kinase, Akt, and eNOS [18, 19]. However, some researchers found different results. Skilton et al. [20] found that ghrelin increase endothelial cell adhesion molecule expression, possibly contributing to the increased atherosclerosis risk. Pöykkö et al. [21] also found that plasma ghrelin concentrations are positively associated with carotid artery atherosclerosis in middle-aged males and appear to be a novel risk factor for atherosclerosis. However one particular scholar also thinks that the effects of ghrelin are influenced by the presence of tumor necrosis factor-alpha. Ghrelin treatment increased adhesion of calcein-labeled THP-1 monocytes to EA.hy 926 endothelial cells. Simultaneously, ghrelin increased the expression of intercellular adhesion molecule-1 measured by quantitative reverse transcriptase polymerase chain reaction. However, in the presence of tumor necrosis factor-alpha stimulation, opposite effects of ghrelin were observed: decrease in both monocyte adhesion and expressions of vascular cell adhesion molecule-1 and monocyte chemoattractant protein-1, suggesting that ghrelin may also have an anti-inflammatory role in the presence of increased inflammation, for example, during the progressively increasing phases of atherogenesis [22]. The endothelial effects of ghrelin are quite complex and variable.

Ghrelin was positively correlated with sICAM-1. The finding in our study was similar to Skilton et al. [20] and Pöykkö et al. [21]. Interestingly, a lower level of ghrelin and a positive correlation of sICAM-1 with the ghrelin level in adolescents with FHD were observed. This finding may be interpreted as a protection mechanism for endothelial function in adolescents with FHD.

Insulin resistance is associated with endothelial dysfunction in youth [10, 23]. The association between sICAM-1 expression and insulin resistance found in this study is consistent with clinical evidence relating insulin resistance and endothelial dysfunction. These findings suggest that insulin resistance may be a potential risk factor for endothelial dysfunction in adolescents with FHD, which may lead to atherosclerosis and coronary artery disease in the future. On the other hand, elevated plasma level of ICAM-1 reflecting endothelial dysfunction was also powerful independent predictors of type 2 diabetes [24].

A limitation of our study was that this research is chiefly a case–control study. We could not determine the causal relationship between ghrelin and endothelial dysfunction. Further experimental and prospective studies are warranted to elucidate the role of ghrelin in endothelial dysfunction in adolescents with FHD. Ghrelin circulates in acylated and desacylated forms. Acylated form in excess may negatively modulate insulin action in children, and may contribute to the association of insulin resistance and metabolic syndrome [25]. Only total ghrelin levels were assayed in our study. We were unable to detail the differential between acylated and desacylated forms. It constitutes another limitation in our study.

In conclusion, endothelial dysfunction and decline of ghrelin were found in adolescents with family history of diabetes. The decline of ghrelin maybe a protection mechanism for endothelial function in adolescents with family history and should be examined in future studies.

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Conflict of interest None.

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