Associations between iron status and insulin resistance in Chinese children and adolescents: findings from the China Health and Nutrition Survey

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ABSTRACT

Background and Objectives: Iron homeostasis abnormalities are associated with insulin resistance (IR), but studies on such associations in children and adolescents are limited and have contrasting results. The purpose of this study was to determine the associations between indicators of iron status and IR, and assesse if there are sex disparities in these associations. **Methods and Study Design:** We selected data of 689 children and adolescents (367 boys and 322 girls) aged 6-18 years in the analysis. Serum ferritin, transferrin, and soluble transferrin receptor (sTfR) levels were determined. The level of glycated hemoglobin (HbA1c) was assessed using high-performance liquid chromatography. Homeostasis model assessment of insulin resistance (HOMA-IR) was used to indicate the status of insulin resistance. Stepwise and multivariate logistic regression analyses were computed to evaluate associations between iron status and glucose parameters. **Results:** The prevalence of IR (HOMA-IR >3.16) and high HbA1c (HbA1c ≥5.7%) were 29.8% and 16.4%, respectively. Serum transferrin and sTfR were significant associated with HbA1c (p<0.001), while serum transferrin was associated with HOMA-IR (p<0.001). Furthermore, the highest transferrin concentrations were associated with higher risks of both HOMA-IR and high HbA1c, while decreased sTfR concentrations were associated with a risk of higher HbA1c in both children and adolescents. **Conclusions:** Serum transferrin and sTfR were statistically significantly associated with glucose parameters, which may suggest that transferrin and sTfR levels should be taken into consideration when studying IR in both boys and girls.

Key Words: iron status, insulin resistance, HbA1c, children and adolescents, sex

INTRODUCTION

Iron plays a key role in many biological processes including oxygen transport, DNA synthesis, and electron transport.[1] Serum ferritin levels reflect the status of iron storage, with low serum ferritin indicating depleted iron stores. Transferrin (the iron-binding protein in circulation) levels rise with increasing iron requirements.[2] Most iron is loaded with plasma transferrin, which binds to transferrin receptors (TfR) on target cells. Soluble TfR (sTfR) is released from microsomal membranes and reflects the cellular expression level of membrane TfR and cellular iron demands. Abnormalities in iron homeostasis have been shown to play a role in the development of insulin resistance (IR), type 2 diabetes mellitus (T2DM), and cardiovascular disease.[3-6]

The association between iron status and IR in adults has been reported in several studies.[7-14] Studies on Asian adults reported a higher serum ferritin level in the diabetes group than that in the prediabetes group, implying a decrease in circulating iron in diabetes.[8,9] The results were consistent with the findings of a large European cohort.[7] Higher levels of ferritin and transferrin were associated with high risks of impaired glucose metabolism and T2DM,[11] while the relationship between the risks and sTfR were significantly influenced by BMI.[15] However, related studies evaluating such associations in children are limited, and the results are controversial.[5,17,18]

There has been a concerning increase in the prevalence of obesity among children and adolescents globally.[19-21] One of the important consequences of obesity is the development of IR.[22] In recent studies, serum ferritin and sTfR levels were used as body iron indicators for iron sufficiency or iron depletion in overweight or obese adolescents.[23-24] By contrast, a cross-sectional study conducted on Korean children failed to find associations of serum ferritin and sTfR levels with IR.[5] In addition, previous evidence showed possible sex disparity in the associations between iron status and glucose parameters in adults.[25-26] However, whether there is also a sex disparity in children and adolescent was unclear.

Therefore, this study aimed to determine the relationships between indicators of iron status and IR and to identify the indicators of iron status associated to childhood IR and whether the associations were affected by sex in Chinese children and adolescents.

MATERIALS AND METHODS

Study population

Cross-sectional data from the China Health and Nutrition Survey (CHNS) 2019 were used. CHNS was a community-based study which included a series of economic, sociological, demographic, and health questions.[27] The CHNS imitated in 1989 and collected health data in nine diverse provinces (Guangxi, Guizhou, Heilongjiang, Henan, Hubei, Hunan, Jiangsu, Liaoning, and Shandong) throughout China. The sampling methods were described previously.[28] Children and adolescents with missing data on weight, height, waist circumference (WC), and biochemical measurements were excluded from our analysis. In addition, we excluded the participants who were on iron supplements and medications known to influence iron metabolism. A total of 828 children and adolescents aged 6-18 years were included in the 2009 survey. Of these, 139 (16.7%) were excluded, and thus 689 children and adolescents were included in the analysis. All subjects' parents gave written informed consent for their children's participation in the survey. The study was approved by the Institutional

Review Boards of the University of North Carolina at Chapel Hill and the Chinese Center for Disease Prevention and Control. Individuals provided written informed consent for participation.

Assessment and measures

Each child's weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, by trained staff during the detailed physical examination with the child wearing light indoor clothing and without shoes. BMI was calculated by dividing the body mass in kilograms by the square of height in meters (kg/m^2). WC was measured at a point midway between the lowest rib and the iliac crest in a horizontal plane using a non-elastic tape. The waist-to-height ratio (WHtR) was calculated as WC (cm)/height (cm).

After an overnight fast, 12 mL blood was collected via venipuncture. Whole blood was immediately centrifuged, and the serum was tested for related measurements. The fasting serum glucose measurements (enzymatic method) and routine blood examinations were performed at local hospitals. The glycated hemoglobin (HbA1c) level was assessed via high-performance liquid chromatography. An elevated HbA1c was defined as >5.7%.[29] The calibrators and control serums provided by the department of laboratory medicine of China-Japan Friendship Hospital had the same lot number. Glucose was measured with a Hitachi 7600 analyzer using a glucose oxidase phenol 4-aminoantipyrine peroxidase kit (Randox, Crumlin, UK). Serum triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol were detected using the enzymatic colorimetric method (Kyowa, Japan). High-sensitivity C-reactive protein (hsCRP) was measured using the immunoturbidimetric immunoassay method (Denka Seiken, Japan). sTfR and transferrin were detected using the nephelometry method (Siemens, Germany). The concentrations of fasting serum insulin and ferritin were evaluated via a commercial radioimmunoassay kit (Beijing North Institute of Biological Technology, China). Serum creatinine and uric acid (UA) were measured using the picric acid method and enzymatic colorimetric method (Hitachi 7600, Japan). Serum alanine aminotransferase was measured using the International Federation of Clinical Chemistry and Laboratory Medicine enzyme method (Hitachi 7600, Japan). The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as the fasting insulin concentration (μIU/mL) × fasting glucose concentration (mmol/L) / 22.5. The HOMA-IR cutoff point for the diagnosis of IR is 3.16.[30]

Statistical analysis

Descriptive analyses were presented as mean and standard deviation (SD) or median (interquartile range) for continuous variables, as appropriate. Student t-test or Mann-Whitney U test was used for between-group comparisons. Pearson correlation coefficients were computed between serum iron parameters (ferritin, transferrin, sTfR, and sTfR/ferritin) and subject characteristics and further controlled for age and sex. Stepwise linear regression analyses were performed to assess the associations of serum iron parameters (independent variables) with glucose parameters (dependent variables). Multivariate logistic regression models were performed to estimate the odds ratios (ORs) of quantiles of transferrin and sTfR with IR and elevated HbA1c. All analyses were performed using Stata 15 (StataCorp., College Station, TX, USA), and $p<0.05$ was considered significant.

RESULTS

The characteristics of the subjects are presented in Table 1. The mean age was 12.0 (2.9) years, with no difference in mean age between boys and girls. Boys had significantly lower levels of TC, TG, and sTfR/ferritin and significantly higher levels of ferritin, sTfR, glucose, alanine aminotransferase (ALT), UA, and creatinine than girls did ($p<0.05$). No differences in other characteristics were observed between girls and boys.

Associations of anthropometric and biochemical variables with iron indicators are summarized in Table 2. Serum ferritin was significantly correlated to fasting glucose (r=0.083, $p=0.030$), ALT (r=0.164, $p<0.001$), and CRP (r=0.142, $p<0.001$) levels after adjusting for age and sex. Serum transferrin levels were positively associated with age (r=0.100, $p=0.009$), BMI (r=0.187, $p<0.001$), WC (r=0.159, $p<0.001$), WHtR (r=0.157, $p<0.001$), fasting insulin (r=0.232, $p<0.001$), HOMA-IR (r=0.229, $p<0.001$), HbA1c (r=0.088, $p=0.021$), and ALT (r=0.163, $p<0.001$) after adjusting for age and sex. Furthermore, a significant and negative relationship independent of age and sex was observed between serum sTfR and HbA1c (r=-0.082, $p<0.001$). The ratio of sTfR and ferritin was negatively related to the fasting glucose level (r=-0.116, $p=0.002$), HbA1c (r=-0.082, $p=0.033$), and ALT (r=-0.185, $p<0.001$), while the relationship between TfR/ferritin and HbA1c became borderline significant after adjusting for age and sex.

Stepwise regression analysis was performed to determine the factors that were significantly associated with HOMA-IR and HbA1c (Table 3). Serum transferrin and WC were found to be significantly associated with HOMA-IR ($p<0.001$), while BMI, transferrin, sTfR, hsCRP, and ALT were significantly associated with HbA1c ($p<0.05$).

The prevalence of insulin resistance (HOMA-IR >3.16) and high HbA1c (HbA1c ≥5.7%) were 29.8% and 16.4%, respectively, for this age group. Table 4 and Table 5 show the adjusted ORs and 95% confidence interval for IR and elevated HbA1c according to serum transferrin and sTfR levels. The highest odds for risk of IR and elevated HbA1c were found in the highest serum transferrin tertile groups in both girls and boys. Meanwhile, the highest odds for elevated HbA1c (HbA1c ≥5.7%) were found in the lowest sTfR tertile group in both girls and boys.

DISCUSSION

In the present study, we observed that serum transferrin and sTfR, but not serum ferritin levels, were significantly related with glucose metabolism. Increased serum transferrin remained to be associated with IR and elevated HbA1c after adjusting for several confounding factors in both boys and girls.

Associations between iron status and IR in adults have been investigated in several studies.[7-15] Previous evidence showed that people with impaired glucose metabolism or diabetes have higher serum ferritin and transferrin levels.[11,15] Furthermore, several studies have demonstrated that the baseline serum ferritin and transferrin are not only related to IR, but are also indicators of future impaired glucose metabolism in adulthood.[12-14] However, the associations between iron status and IR in children and adolescents have not been deeply investigated, and the results were controversial.[5,17,18]

The prevalence of obesity and diabetes has profoundly increased over the past two decades in China, with a faster increase in children than that in adults.[20-21] IR, previously considered a problem in older ages, is also becoming a serious issue in children.[22] Early detection of IR is important for the prevention of non-communicable diseases. Serum ferritin and sTfR levels, as indicators of body iron sufficiency or depletion, were investigated in obese adolescents.[18, 23-24] Aigner et al[17] found that sTfR/ferritin level was inversely related to HOMA-IR in teenage girls, but this association was not observed in teenage boys. In the present study, we found that sTfR/ferritin level was negatively related to the fasting glucose and HbA1c level, but not with HOMA-IR. Moreover, a cross-sectional study conducted on Korean children failed to find associations of serum ferritin and sTfR levels with IR.[5] The results were consistent with our findings. In the present study, higher serum transferrin, but not ferritin and sTfR levels, was associated with IR. In addition, serum transferrin and sTfR were associated with HbA1c, which presents the glucose status in the last 2-3 months. The associations were independent of obesity factors. Inflammation of body tissues has an impact on iron metabolism and iron

homeostasis. The changes of serum transferrin and sTfR levels, mainly induced by hepcidin, might be beneficial for the host and prevent oxidative damage, which indicates that the iron homoeostasis is associated with insulin resistance.

Previous studies have indicated that the associations between iron status and glucose parameters in adults have sex disparity.[25-26] This is different from our results in children and adolescents. Bonfils et al[26] found that ferritin was associated with IR in men, but not in women, while Sheu et al[25] reported that the relationship was observed in women, but not in men. A previous study indicated that differences in sex hormones may partly contribute to the sex difference.[31] However, due to the limited evidence on the influence of iron status on glucose metabolism in children and adolescents, a clear mechanism could not be established.[32] Moreover, the previous findings of sex disparity in the association between iron status and glucose parameters were refuted by other researchers.[32] Significant changes in iron status could be due to differences in the baseline characteristics of subjects or the lower reference values of the iron status indicators, but not just simple sex differences.

The sTfR is the part of the transferrin receptor that gets separated and released into the circulation, and its levels increase as iron stores are deplete.[33] High serum sTfR concentrations play a role in the development of impaired glucose metabolism.[16] Furthermore, in the present study, we also observed an inverse relationship between sTfR and HbA1c, which is in contrast to the findings in adults. Fernandez-Real et al. found that sTfR level was positively correlated to HbA1c level in 221 men, and more than 50% of these men had impaired glucose tolerance.[16] Previous studies have indicated that serum sTfR concentrations appear to be regulated by inflammatory status, and glucose regulatory medication could also obscure this relationship.[34] The subjects in our study are generally healthy children and adolescents with relatively lower inflammatory status compared with adults in the CHNS study (median CRP: 0.0 vs. 1.0 mg/L).[35]

The present study has some limitations. First, because this study used a cross-sectional study design, the ability to establish a causal relationship between iron status and insulin resistance was limited. Second, influence of puberty on iron status was not taken into consideration due to its unavailability. Third, a further subgroup analysis was not allowed since the sample size was relatively small. Furthermore, serum iron concentration was not tested. Therefore, transferrin iron saturation data were unavailable for analysis of changes in iron metabolism. A further cohort study with proper large sample size is warranted to investigate such relationship in children and adolescents.

Conclusion

In conclusion, our investigation of the iron status and glucose homoeostasis in Chinese children and adolescents showed that elevated serum transferrin was associated with IR and higher HbA1c in both boys and girls; Serum sTfR was associated with HbA1c but not IR. The results had no sex disparity. These findings suggest that transferrin and sTfR, rather than ferritin, may contribute to the development of impaired glucose homeostasis in children and adolescents.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest.

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Table 1. Basic characteristics of the study population by sex †

	Total	Boys	Girls	*p*-value
	N=689	N=367	N=322	
Age (years)	12.0 (2.9)	11.9 (3.0)	12.0 (2.9)	0.76
Height (cm)	146.7 (16.1)	147.2 (17.3)	146.2 (14.7)	0.42
Weight (kg)	39.5 (13.5)	39.8 (14.2)	39.1 (12.7)	0.52
BMI (kg/m^2)	17.8 (3.5)	17.8 (3.6)	17.8 (3.4)	0.88
WC (cm)	63.4 (9.7)	64.0 (10.2)	62.8 (9.1)	0.13
WHtR	0.43 (0.05)	0.43 (0.06)	0.43 (0.05)	0.14
TC (mmol/L)	3.9 (0.7)	3.8 (0.7)	3.9 (0.7)	0.024
Triglycerides (mmol /L)	0.8 (0.6-1.2)	0.8 (0.5-1.2)	0.9 (0.6-1.2)	0.002
HDL-C (mmol/L)	1.4 (1.2-1.6)	1.4 (1.2-1.6)	1.4 (1.2-1.6)	0.42
LDL-C (mmol/L)	2.2 (0.9)	2.2 (1.1)	2.2 (0.6)	0.63
Ferritin (nmol/L)	0.14 (0.09-0.20)	0.16 (0.11-0.22)	0.12 (0.08-0.18)	<0.001
Transferrin (mmol/L)	8.3 (1.4)	8.3 (1.4)	8.3 (1.4)	0.081
sTfR (mg/L)	1.6 (1.3-1.8)	1.6 (1.3-1.9)	1.5 (1.3-1.8)	0.024
sTfR/ferritin	0.04 (0.02-0.06)	0.04 (0.02-0.05)	0.04 (0.03-0.07)	<0.001
Glucose (mmol/L)	4.9 (0.8)	5.0 (1.0)	4.8 (0.5)	0.002
Insulin (uIU/mL)	10.98 (7.90-16.14)	10.79 (7.90-15.46)	11.30 (7.81-16.62)	0.46
HOMA-IR	2.34 (1.64-3.49)	2.33 (1.68-3.47)	2.36 (1.59-3.64)	0.97
HbA1c (mmol/L)	5.3 (0.5)	5.3 (0.6)	5.3 (0.4)	0.18
hsCRP (mmol/L)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	0.21
ALT (U/L)	13.0 (10.0-17.0)	14.0 (11.0-18.0)	12.0 (9.0-15.0)	<0.001
UA (mmol/L)	18.3 (5.0)	19.4 (5.3)	17.1 (4.3)	<0.001
Creatinine (mmol/L)	70.8 (12.5)	73.4 (14.0)	67.9 (9.8)	<0.001

BMI: body mass index; WC: waist circumference; WHtR: waist-to-height ratio; TC: total Cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; sTfR: soluble transferrin receptor; HbA1c: glycated hemoglobin; hsCRP: high-sensitivity CRP; ALT: alanine aminotransferase; UA: uric acid; HOMA-IR: homeostasis model assessment of insulin resistance.

†Data are presented as mean (standard deviation) or median (interquartile range). Significance tests for continuous variables between groups were performed using Student t-test or the Mann-Whitney U test.

Table 2. Pearson correlation coefficients between iron status parameters and metabolic factors[†]

	Ferritin		Ferritin (adjusted for sex and age)		Transferrin		Transferrin (adjusted for sex and age)		sTfR		sTfR (adjusted for sex and age)		sTfR /ferritin		sTfR/ferritin (adjusted for sex and age)	
	r	*p*	r	*p*	r	*p*	r	*p*	r	*p*	r	*p*	r	*p*	r	*p*
Age	-0.028	0.459			0.100	0.009			-0.045	0.243			0.009	0.817		
BMI[†]	-0.051	0.179	-0.043	0.258	0.211	<0.001	0.187	<0.001	-0.034	0.379	-0.015	0.702	0.032	0.396	0.031	0.409
WC	-0.005	0.902	-0.009	0.814	0.183	<0.001	0.159	<0.001	-0.050	0.198	-0.047	0.220	-0.015	0.706	-0.010	0.788
WHtR	0.040	0.300	0.025	0.523	0.140	<0.001	0.157	<0.001	-0.033	0.387	-0.042	0.281	-0.048	0.215	-0.037	0.337
Insulin[†]	-0.056	0.145	-0.044	0.251	0.249	<0.001	0.232	<0.001	0.010	0.802	0.023	0.540	0.053	0.168	0.047	0.219
FPG	0.109	0.004	0.083	0.030	0.037	0.338	0.046	0.230	-0.051	0.178	-0.062	0.106	-0.116	0.002	-0.096	0.012
HOMA-IR[†]	-0.035	0.363	-0.029	0.452	0.244	<0.001	0.229	<0.001	-0.002	0.963	0.009	0.819	0.030	0.434	0.028	0.462
HbA1c[†]	0.027	0.478	0.016	0.673	0.082	0.033	0.088	0.021	-0.151	0.001	-0.156	<0.001	-0.082	0.033	-0.074	0.052
ALT[†]	0.208	<0.001	0.164	<0.001	0.138	<0.001	0.163	<0.001	0.000	0.994	-0.020	0.605	-0.185	<0.001	-0.151	<0.001
hsCRP[‡]	0.143	<0.001	0.142	<0.001	-0.053	0.163	0.105	0.006	0.049	0.199	0.038	0.326	-0.101	0.129	-0.110	0.004

BMI: body mass index; WC: waist circumference; WHtR: waist-to-height ratio; FPG: fasting plasma glucose; HbA1c: glycated hemoglobin; sTfR: soluble transferrin receptor; hsCRP: high-sensitivity C-reactive protein; ALT: alanine aminotransferase; HOMA-IR: homeostasis model assessment of insulin resistance.

[†]BMI, insulin, HOMA-IR, HbA1c, and ALT were log transformed

[‡]Spearman correlation was used.

Table 3. Multiple linear regression analysis of HOMA-IR and HbA1c among children and adolescents †

	HOMA-IR		HbA1c	
	β±SE	*p*	β±SE	*p*
Age	-0.006±0.014	0.666	-0.003±0.002	0.151
Sex	-0.003±0.048	0.953	-0.012±0.007	0.069
BMI	0.002±0.009	0.853	-0.003±0.001	0.033
WC	0.024±0.006	<0.001	0.002±0.001	0.036
WHtR	-0.999±0.971	0.303	0.008±0.135	0.954
Transferrin	0.189±0.051	<0.001	0.020±0.007	0.005
sTfR	-0.012±0.054	0.820	-0.035±0.008	<0.001
sTfR/ferritin	0.110±0.270	0.261	0.015±0.036	0.669
hsCRP	0.001±0.005	0.865	0.002±0.001	0.045
ALT	0.001±0.001	0.333	0.001±0.001	0.030

BMI: body mass index; WC: waist circumference; WHtR: waist-to-height ratio; FPG: fasting plasma glucose; HbA1c: glycated hemoglobin; sTfR: soluble transferrin receptor; hsCRP: high sensitivity C-reactive protein; ALT: alanine aminotransferase; HOMA-IR: homeostasis model assessment of insulin resistance; TC: total Cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol.
†HOMA-IR, HbA1c, CRP, and ALT were log transformed. Multiple linear regressions were also adjusted for TC, triglycerides, HDL-C and LDL-C.

Table 4. Multivariate logistic regression analyses between transferrin (mol/L) quantiles and insulin resistance (HOMA-IR >3.16) and elevated HbA1c (HbA1c ≥5.7%) in boys and girls†

	IR	Elevated HbA1c
All		
Q1 (<7.4 mol/L, n=171)	1	1
Q2 (7.4-8.2 mol/L, n=173)	1.66 (0.95-2.87)	1.64 (0.86-3.13)
Q3 (8.2-9.1 mol/L, n=171)	1.21 (0.69-2.13)	1.63 (0.85-3.15)
Q4 (≥9.1 mol/L, n=174)	2.82 (1.65-4.81)	2.33 (1.22-4.45)
Boys		
Q1 (<7.3 mol/L, n=88)	1	1
Q2 (7.3-8.1 mol/L, n=93)	1.55 (0.73-3.31)	1.46 (0.60-3.58)
Q3 (8.1-9.1 mol/L, n=93)	1.18 (0.54-2.57)	2.00 (0.82-4.87)
Q4 (≥9.1 mol/L, n=93)	2.49 (1.19-5.21)	2.49 (1.03-6.02)
Girls		
Q1 (<7.5 mol/L, n=79)	1	1
Q2 (7.5-8.3 mol/L, n=81)	1.49 (0.65-3.41)	1.90 (0.70-5.21)
Q3 (8.3-9.3 mol/L, n=80)	1.07 (0.46-2.47)	1.43 (0.50-4.10)
Q4 (≥9.3 mol/L, n=82)	2.70 (1.22-6.00)	3.11 (1.13-8.59)

HOMA-IR: homeostasis model assessment of insulin resistance; IR: insulin resistance; HbA1c: glycated hemoglobin.
†Data are presented as odds ratio (95% confidence intervals). Multivariate logistic regression were adjusted for age, residence, body mass index, waist-to-height ratio, total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein cholesterol, C-reactive protein and alanine aminotransferase (ALT).

Table 5. Multivariate logistic regression analyses between sTfR (mg/L) quantiles and insulin resistance (HOMA-IR >3.16) and elevated HbA1c (HbA1c ≥ 5.7%) in boys and girls[†]

	IR	Elevated HbA1c
All		
Q1 (<1.3 mg/L, n=169)	1	1
Q2 (1.3-1.55 mg/L, n=175)	0.58 (0.34-1.00)	0.55 (0.31-0.97)
Q3 (0.55-0.83 mg/L, n=168)	1.29 (0.78-2.13)	0.43 (0.24-0.80)
Q4 (≥1.83 mg/L, n=177)	0.81 (0.48-1.37)	0.39 (0.21-0.71)
Boys		
Q1 (<1.33 mg/L, n=90)	1	1
Q2 (1.33-1.57 mg/L, n=93)	0.57 (0.35-1.60)	0.25 (0.10-0.62)
Q3 (1.57-1.93 mg/L, n=91)	1.85 (0.91-3.75)	0.52 (0.24-1.12)
Q4 (≥1.93 mg/L, n=93)	1.05 (0.50-2.20)	0.32 (0.14-0.72)
Girls		
Q1 (<1.28 mg/L, n=79)	1	1
Q2 (1.28-1.51 mg/L, n=80)	0.57 (0.26-1.23)	0.92 (0.40-2.12)
Q3 (1.51-1.76 mg/L, n=78)	0.93 (0.44-1.96)	0.35 (0.13-0.96)
Q4 (≥1.76 mg/L, n=85)	0.70 (0.33-1.48)	0.36 (0.13-0.95)

HOMA-IR: homeostasis model assessment of insulin resistance; IR: insulin resistance; HbA1c: glycated haemoglobin.
[†]Data are presented as odds ratio (95% confidence intervals). Multivariate logistic regression analyses were adjusted for age, residence, body mass index, waist-to-height ratio, total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein cholesterol, C-reactive protein, and alanine aminotransferase.