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Research paper

A Study on the Factors influencing insulin resistance in obese adolescents

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Abstract

Objective: To explore the factors influencing insulin resistance in obese Chinese children. **Methods:** We randomly selected 53 children with uncomplicated obesity between 9 to14 years of age, and 29 normal healthy children, matched for age and sex. Anthropometric and plasma biochemical variables(including lipid profiles, glucose and insulin) were measured using standard methods. We calculated insulin resistance(IR) index using homeostasis model assessment(HOMA) methods and measured plasma high-sensitivity C-reactive protein(hs-CRP) levels using nephelometric methods. All statistical analyses were conducted using the statistical package SPSS. **Results:** Levels of fasting serum insulin, hs-CRP, total cholesterol(TC), low density lipoproteins cholesterol(LDL-C) and IR index were higher in obese children than in controls, while high-density lipoprotein cholesterol(HDL-C) values were lower in the obese children. There was no significant difference in levels of fasting blood glucose between the two groups. HOMA-IR was used as the dependent variable in multivariate regression analysis. Significant independent predictors for insulin resistance adjusted for waist/hip ratio, diastolic pressure (DBP), BMI, triglycerides and HDL-C level were waist circumference(WC), weight and systolic pressure(SBP). **Conclusion:** Waist circumference, weight and SBP are predictors of insulin resistance syndrome in Chinese adolescents

Key words: Obesity; Insulin resistance; Adolescents

INTRODUCTION

Overweight and obesity prevalence is increasing in children worldwide, and China is not spared. Ji et al[1] reported the prevalence of obesity was increasing more quickly in Chinese children. In most metropolitan areas the prevalence of being overweight is two to three folds more than that of 10 years ago. Since 2000, most of the Chinese metropolitan areas have started the so called "overall increment period" of obesity. The prevalence rates of obesity has already reached the average level seen in the medium-developed countries in the world for boys aged 7-9 and 10-12 years of age, a trend echoed in other countries[2].

It has been reported that obese children exhibit resistance to insulin(within the context of metabolic syndrome)[3,4], low-grade systemic inflammation[5,6] and dyslipidemia[7], all of which are risk factors for the development of cardiovascular disease. Insulin resistance is believed to be a central factor in the development of the disease[8]. There is considerable interest in the evaluation of insulin resistance in childhood. In China, on the whole, limited information is available about the prevalence of insulin resistance in obese children and adolescents.

The aim of our study was to examine the insulin resistance status, based on glucose and insulin levels evaluated under fasting conditions, and to explore the relationship between obesity, insulin resistance status and plasma high sensitivity C-reactive protein(hs-CRP) levels in a sample of obese adolescents.

METHODS

Study sample

We studied 53(44 male) obese Chinese children and

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adolescents(mean age 11.1 ± 1.6years, range 9-14 years) recruited from the Department of Pediatrics at the First Affiliated Hospital of Anhui Medical University, Hefei. Subjects were eligible with a BMI at the 95th percentile of the referenced BMI of metropolitan children of the same age and sex[1]. Exclusion criteria were secondary or genetic obesity and the use of any drug therapy. Twenty-nine(20 male) normal weight, healthy subjects(mean age 11.5 ± 0.6 years, range 11-13 years) were the control group, matched to sex and age. All of the participating children completed a structured questionnaire detailing their personal history of disease, pubertal development and lifestyle characteristics.

The Ethical Committee of the Anhui Medical University approved this study and the parents of the children gave their informed consent for the children to participate in the study.

Anthropometric measurements

Anthropometric measurements were carried out in the morning with the children wearing light indoor clothing and barefoot .Height, weight, WC(at the umbilicus) were recorded to the nearest 0.5 cm, 0.1 kg and 0.1 cm, respectively. We calculated their body mass index(BMI) as body weight(kg) divided by the square of their height(m). Overweight is defined as the 85th percentile BMI with age- and gender-specification. Obesity is the 95th percentile BMI[1]. WHR is the waist-hip circumference ratio. Systolic blood pressure(SBP) and diastolic blood pressure(DBP) were measured twice at the right arm after a 5-minute rest in the supine position using a calibrated sphygmomanometer and the values were averaged. Pubertal development was assessed by physical examination according to Tanner's criteria[9].

Biochemical measurements

After a 12-h overnight fast, measurements for plasma glucose and insulin, serum triglycerides(TG), total cholesterol(TC), high-density lipoprotein cholesterol (HDL-C), low density lipoproteins cholesterol(LDL-C) and high-sensitivity C-reactive protein(hs-CRP) were made in all subjects.

Plasma glucose concentrations, lipid profiles and the high sensitive C-reactive protein(hs-CRP) levels were analyzed immediately after blood sampling; plasma insulin was performed within 3 days of the blood samples being stored at -4℃. The estimate of insulin resistance was calculated by a homeostasis model assessment (HOMA-IR) index (fasting insulin-fasting glucose/22.5), as described by Matthews and colleagues[10]. To distinguish normal from impaired insulin sensitivity, HOMA-IR > 4.0 was employed as the cut-off levels in adolescents, according to the normal values provided by a recent national study[11]. Impaired fasting glycaemia (IFG) was defined as a fasting plasma glucose level > 110 and <126 g/L.

Statistical analysis

We used mean and standard deviation(SD) to describe the distributions of age, body weight, BMI, hs-CRP, HOMA-IR, lipids, glucose and insulin levels, Correlation between variables was evaluated using Spearman correlation coefficient and regression analysis. Multivariate regression analysis was performed using the stepwise method. For each variable, potential confounding factors were evaluated by an analysis of raw and adjusted regression coefficients.

Statistical analysis was conducted using SPSS version 11.0(Statistical Package for Social Science Inc., Chicago, IL, USA).

RESULTS

Table 1 shows the anthropometric data and selected biochemical parameters of the obese and control groups. Weight, weight status(BMI), waist circumference, waist/hip ratio, SBP and DBP were significantly higher in the obese group(***Table 1***) than control group. Obese and control non-obese children were pubertal and obese children did not differ significantly from the non-obese children in age, sex and pubertal status.

Fasting glucose levels were in the normal range and there was not significant differences between obese and control children. However, fasting insulin concentrations and HOMA-IR values were significantly higher in the obese children than in the non-obese children. The obese children showed significantly higher TC, LDL-C and hs-CRP concentrations, whereas their HDL-C concentrations were significantly lower when com-pared with normal weight children(***Table 1***).

Table 2 shows coefficients of simple correlation(r) between HOMA-IR and different variables in the obese children. In the single linear correlation, for the obese group, HOMA-IR was positively correlated with triglycerides, weight, BMI, waist circumference, waist/hip ratio, systolic and diastolic pressures, and negatively correlated with high-density lipoproteins, but not with hs-CRP, low density lipoproteins and total cholesterol. However, when HOMA-IR was used as the dependent variable in multiple linear regression analyses, the significant independent predictors for insulin resistance adjusted for waist/hip ratio, diastolic BP, BMI, triglycerides and HDL level were waist circumference, weight and SBP(***Table 3***).

Table 4 shows the Spearman correlation of plasma hs-CRP levels with anthropometric measures, biochemical variables and insulin resistance status in obese children. Plasma hs-CRP levels were significantly positively

Table 1 **Clinical characteristics of the study population**

	Obese children	Non-obese children
No	53	29
sex(F/M)	10/43	9/20
age(y)	11.10 ± 1.60	11.50 ± 0.60
weight(kg)	64.80 ± 15.71***	48.24 ± 8.56
BMI(kg/m²)	28.30 ± 3.29***	20.28 ± 2.48
WC(cm)	90.60 ± 9.59***	70.54 ± 7.48
WHR	0.96 ± 0.06***	0.73 ± 0.03
SBP(mmHg)	127.20 ± 11.90***	104.00 ± 8.20
DBP(mmHg)	81.40 ± 8.60***	70.00 ± 4.90
insulin(mmol/L)	17.07 ± 12.24***	7.29 ± 2.22
glucose(mmol/L)	5.11 ± 1.61	4.75 ± 0.49
HOMA-IR	3.71 ± 2.96***	1.54 ± 0.67
TG(mmol/L)	1.01 ± 0.81	0.83 ± 0.03
TC(mmol/L)	3.68 ± 0.74***	3.27 ± 0.54
HDL-C(mmol/L)	1.47 ± 0.25**	1.57 ± 0.28
LDL-C(mmol/L)	1.87 ± 0.61***	1.48 ± 0.42
hs-CRP(mmol/L)	2.66 ± 2.90**	1.41 ± 0.66

Abbreviations: BMI, body mass index; HOMA-IR, insulin resistance by homeostasis modeling; TC=total cholesterol; LDL-C=low density lipoproteins cholesterol; HDL-C=high density lipoproteins cholesterol; TG=triglycerides; SBP=systolic pressure(mmHg); DBP=diastolic pressure(mmHg); WHR=waist/hip ratio; WC=waist circumference; hs-CRP=high sensitivity C-reactive protein; Means ± s; $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$.

Table 2 **Coefficients of simple correlation(r) between HOMA-IR and different variables of the obese**

	r	P
Weight	0.305	0.028
BMI	0.461	0.001
WC	0.576	0.000
WHR	0.369	0.010
SBP	0.461	0.001
DBP	0.284	0.041
hs-CRP	−0.095	0.504
TC	0.024	0.868
TG	0.515	0.000
LDL-C	0.059	0.676
HDL-C	−0.307	0.027

Abbreviations: BMI, body mass index; HOMA-IR, insulin resistance by homeostasis modeling; TC=total cholesterol; LDL-C=low density lipoproteins cholesterol; HDL-C=high density lipoproteins cholesterol; TG=triglycerides; SBP=systolic pressure(mmHg); DBP=diastolic pressure(mmHg); WHR=waist/hip ratio; WC=Waist circumference; hs-CRP=high sensitivity C-reactive protein.

correlated with HR, plasma TC and LDL and negatively correlated with waist circumference, weight, and BMI. We used multivariate regression analyses to evaluate the association of plasma hs-CRP with these variable, Plasma hs-CRP levels were significantly associated with plasma LDL and HR.

DISCUSSION

Obesity leads to insulin resistance causing impaired glucose tolerance(IGT) over time, and ultimately type 2 diabetes. The presence of the metabolic syndrome in children and adolescents has also been reported[12-14]. Thus with the obesity epidemic, the incidence of type 2

Table 3 **Multiple Linear Regression Analysis(Stepwise Method)***

	β coefficient	95% confidence interval	P
WC	0.342	0.207–0.477	0.000
weight	−0.149	(−0.231)–(−0.066)	0.001
systolic BP	0.072	0.007–0.136	0.030

Abbreviations: BP, blood pressure; HOMA-IR, insulin resistance by homeostasis modeling; WC, waist circumference.
*Dependent variable, HOMA-IR

Table 4 **Spearman correlation(r) between hs-CRP and different variables of the obese**

	r	P
Age	−0.261	0.063
Weight	−0.407	0.003
BMI	−0.389	0.004
WC	−0.325	0.019
WHR	−0.052	0.727
SBP	0.003	0.984
DBP	0.058	0.685
TC	0.341	0.013
TG	0.127	0.371
LDL-C	0.295	0.033
HDL-C	0.180	0.202
Glucose	0.223	0.112
Insulin	−0.039	0.782
HR	0.401	0.005
HOMA-IR	−0.056	0.695

Abbreviations: BMI, body mass index; HOMA-IR, insulin resistance by homeostasis modeling;TC=total cholesterol; LDL-C=low density lipoproteins cholesterol; HDL-C=high density lipoproteins cholesterol; TG=triglycerides; SBP=systolic pressure(mmHg); DBP=diastolic pressure(mmHg);WHR=waist/hip ratio; WC=Waist circumference; hs-CRP=high sensitivity C-reactive protein; HR=heart rate.

diabetes mellitus in children has increased alarmingly. It seems essential to discover the early indicators of insulin resistance in obese children and adolescents. Our study is designed to document the extent of the metabolic consequences of obesity among obese children and adolescents in our community.

In this study insulin resistance status was assessed by HOMA-IR, which is a simplified tool to estimate insulin sensitivity[15]. The obese pubertal children in our study had higher fasting insulin and HOMA-IR than the controls, similar to those obtained in another group of obese children[16]. We found that 23.08% of the obese adolescents were insulin-resistant, using a cut-off value of >4.0, based on the Italian reference values for adolescents[11] since there is not enough knowledge about the cut-off value of insulin-resistant in obese children in China. At variance with other studies in obese adolescents, Valerio et al[17], using a HOMA-IR cut-off value of 4.0, found 41.2% of their cases were insulin-resistant. We did not find any case of insulin resistance among normal adolescents. One case of diabetes and impaired fasting glucose(IFG) was found in our sample, 1.9%(1/53). Childhood and adolescent diabetes melli-

tus reports from Europe range from 0% to 1.5%[18, 19], while in the United States, adolescents with diabetes mellitus(DM) is 4.0%[20].

In our sample multivariate regression analyses performed to evaluate the factors associated with insulin resistance indicated that the variables independently associated with HOMA-IR were waist circumference, weight and SBP. Similar results were obtained in a study done by Valeria and collegues[21] analyzing the relationship between waist circumference and insulin resistance syndrome in children and adolescents. They administered a homeostasis assessment model of insulin resistance(HOMA-IR) in 40 obese, 28 overweight and 16 non-obese children and adolescents, and found waist circumference and SBP to be significant independent predictors for insulin resistance, but not BMI. It appears that waist circumference is a predictor of insulin resistance syndrome in children and adolescents and could be included in clinical practice as a simple tool to help identify children at metabolic risk of cardiovascular disease and type 2 diabetes mellitus(T2DM).

In our sample, TG, LDL-C and hs-CRP levels were significantly higher in obese than control, but were not correlated with insulin resistance. Plasma hs-CRP levels were positively correlated with body weight, BMI, waist circumference, total cholesterol and low density lipoproteins among obese children. The lack of association between hs-CRP level and HOMA-IR suggests that obesity may precede the elevation of these markers in the evolution of insulin resistance.

In conclusion, the results of the present study suggest that waist circumference and weight were the main predictors of insulin resistance in these 9 to 14 year old obese children. Early treatment and improvement of insulin sensitivity may prevent type2 diabetes and metabolic syndrome.

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