Original Article

Lower Birth Weight and Visceral Fat Accumulation Are Related to Hyperinsulinemia and Insulin Resistance in Obese Japanese Children

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This study aimed to reveal the relation of birth weight (or the birth weight standard deviation score [BWSDS]) and visceral fat accumulation to hyperinsulinemia and insulin resistance. We examined obese Japanese children (650 boys and 317 girls) with a mean age of 10.3 years (range, 6–15 years). The mean percentage of overweight to the standard body weight of Japanese children was 52.1% in boys and 51.4% in girls. Abdominal fat thickness (maximum preperitoneal fat thickness; P_{max}) was measured using ultrasonography. The fasting serum insulin and plasma glucose levels were measured, and the homeostasis model assessment-insulin resistance (HOMA-R) and quantitative insulin sensitivity check index (QUICKI) were calculated. We divided the subjects into four groups according to their birth weight or BWSDS, and compared anthropometric measurements, P_{max}, blood pressure, serum insulin levels, HOMA-R and QUICKI among the quartiles. The relationships of both birth weight (or BWSDS) and P_{max} to serum insulin levels (or HOMA-R, QUICKI) were examined with multiple regression analyses. The fasting serum insulin level and HOMA-R were highest in the quartile with the lowest birth weight or BWSDS. The birth weight and BWSDS were inversely related to the serum insulin levels and HOMA-R, positively related to QUICKI, and independent of P_{max}. Our findings suggest that both lower birth weight and visceral fat accumulation may be independently related to hyperinsulinemia and insulin resistance in obese Japanese children. (*Hypertens Res* 2005; 28: 529–536)

***Key Words*: birth weight, insulin, obesity, children, visceral fat**

Introduction

The prevalence of obesity in Japanese school children has increased from 5% to more than 10% over the last two decades (*1*). This is a serious public health problem, since childhood obesity, which is the most common cause of hyperinsulinemia and insulin resistance (*2*), is associated with hypertension (HT), dyslipidemia, type 2 diabetes mellitus (DM), and long-term vascular complications (*3*–*5*). Visceral fat accumulation plays an important role in the development of hyperinsulinemia and insulin resistance and contributes to the acceleration of atherosclerosis in obese subjects (*6*). Metabolic syndrome (MS) has been described as a link between insulin resistance and HT, dyslipidemia, type 2 DM, and other metabolic abnormalities associated with visceral fat accumulation in obese individuals (*7*). Criteria for defining MS in adults were published by the World Health Organization (WHO) in 1998 and the National Cholesterol Education Program Adult Treatment Panel III (NCEP) in 2001 (*8*, *9*). How-

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Table 1. Clinical Characteristics of Subjects

	Obese boys (n=650)		Obese girls (n=317)	
	Mean±SD	Range	Mean±SD	Range
Birth weight (g)	3,258±429	1,740 to 4,875	3,151±415	1,845 to 4,110
Birth weight SDS	+0.46±0.96	−3.0 to +4.19	+0.13±0.82	−2.36 to +2.06
Gestational week	39.2±1.3	33.0 to 42.0	39.1±1.4	32.0 to 42.0
Age (years)	10.4±2.1	6.6 to 15.6	10.1±2.2	6.6 to 15.5
Height (cm)	143.2±13.1	110.3 to 184.6	140.0±11.7	109.8 to 165.0
Weight (kg)	56.3±16.1	27.0 to 109.9	53.0±15.4	26.8 to 114.0
Height SDS	+0.92±1.09	−3.00 to +4.13	+0.78±1.06	−3.51 to +3.13
Percentage of overweight (%)	+52.1±13.2	+27.5 to +116.7	+51.4±14.4	+21.9 to +118.1
Waist circumferences (cm)	85.2±10.2	59.5 to 119.5	81.1±10.2	63.0 to 129.5
Hip circumferences (cm)	89.1±9.2	67.0 to 123.0	88.2±10.5	71.0 to 120.0
P_{max} (mm)	11.3±3.4	3.6 to 24.9	11.0±3.5	1.4 to 21.3
SBP (mmHg)	116±13	74 to 158	113±13	76 to 154
DBP (mmHg)	57±8	35 to 83	57±9	40 to 84
Serum insulin (μU/ml)	17.5±13.3	2.5 to 181.0	18.6±10.8	3.0 to 72.8
HOMA-R	3.8±2.8	0.5 to 34.0	4.0±2.4	0.6 to 16.4
QUICKI	0.33±0.03	0.24 to 0.43	0.32±0.03	0.26 to 0.42

SDS, standard deviation score; P_{max}, maximum preperitoneal fat thickness; SBP, systolic blood pressure; DBP, diastolic blood pressure; HOMA-R, homeostasis model assessment-insulin resistance (FBG [mg/dl]×IRI [μU/ml]/405); QUICKI, quantitative insulin sensitivity check index (1/{log IRI [μU/ml]+log FBG [mg/dl]}); FBG, fasting blood glucose; IRI, immunoreactive insulin.

Table 2. Characteristics of 650 Obese Boys after Being Divided into Four Groups According to Birth Weight

	MA (n=162)	MB (n=163)	MC (n=162)	MD (n=163)	ANOVA p
Range of birth weight (g)	1,740–3,005	3,006–3,250	3,254–3,505	3,508–4,875	—
Birth weight SDS	−0.55±0.76¶,†,*	+0.14±0.33†,*	+0.64±0.33*	+1.63±0.64	<0.0001
Gestational week	38.3±1.5¶,†,*	39.2±1.1†,*	39.5±1.0*	39.8±1.2	<0.0001
Age (years)	10.2±2.4	10.4±2.2	10.6±1.9	10.4±1.9	NS
Height (cm)	141.3±14.2*	142.3±12.4*	143.9±12.9	145.4±12.8	<0.05
Weight (kg)	53.9±15.9†,*	54.9±14.7*	58.1±17.3	58.6±16.0	<0.05
Height SDS	+0.73±1.07*	+0.79±1.15*	+0.87±1.09*	+1.31±0.96	<0.0001
Percentage of overweight (%)	+50.8±12.2†	+51.5±11.3†	+54.2±15.7	+51.9±13.2	NS
Waist circumferences (cm)	84.0±10.4†,*	84.3±9.4	86.3±11.1	86.5±9.6	<0.05
Hip circumferences (cm)	87.7±9.2†,*	88.1±8.4†,*	90.4±10.1	90.3±8.9	<0.01
P_{max} (mm)	11.1±3.2¶	11.8±3.4	11.3±3.4	11.2±3.5	NS
SBP (mmHg)	116±14	116±12	115±13	115±12	NS
DBP (mmHg)	58±9	58±8	57±9	56±7	NS
Serum insulin (μU/ml)	20.2±19.5†,*	17.4±10.4	16.5±11.4	15.8±9.1	<0.05
HOMA-R	4.3±3.9†,*	3.8±2.3	3.7±2.6	3.4±2.0	<0.05
QUICKI	0.32±0.03	0.32±0.03	0.33±0.03	0.33±0.03	NS

¶p<0.05 *vs.* the value of the MB group, †p<0.05 *vs.* the value of the MC group, *p<0.05 *vs.* the value of the MD group using Bonferroni/Dunn's *post hoc* test. NS, not statistically significant. Other abbreviations are the same as in Table 1.

ever, no criteria have been published for defining MS in Japanese children, despite the fact that hyperinsulinemia and insulin resistance have been shown to play an important role in MS in children just as in adults (*10*).

Barker and Osmond found that there was a close causality between intrauterine growth retardation (IUGR) and future cardiovascular disease onset (*11*). And low birth weight has been associated with increased risk for type 2 DM, HT, and dyslipidemia in adults (*12*, *13*). Some studies have reported that retarded fetal growth and accelerated growth during childhood contributed to the onset and progression of these diseases (*14–16*). In children and adolescents from different countries, a relationship between birth weight and both insulin resistance and type 2 DM has been reported (*17–20*). And

in our previous studies, we reported that there was an association between birth weight and blood pressure (BP) in healthy children (*21*), and between birth weight and insulin resistance or hyperinsulinemia in obese boys (*22*).

The purpose of this study was to clarify the relation of birth weight and visceral fat accumulation to hyperinsulinemia and insulin resistance in obese Japanese children. Elucidation of the pathophysiology of hyperinsulinemia and insulin resistance in obese children would contribute to prevention of MS and cardiovascular disease in adults.

Methods

Subjects

This study examined 650 (15.0%) of the 4,320 obese boys (mean age, 10.4 years; range, 6–15 years) and 317 (9.1%) of the 3,470 obese girls (mean age, 10.1 years; range, 6–15 years) who resided in Niigata Prefecture, Japan and received regular medical examinations in conjunction with "The Prevention of Cardio- and Cerebrovascular Diseases in Childhood" program in September 2001. The Department of Pediatrics of Niigata University School of Medicine and the School Health Division of the local governments in Niigata Prefecture undertake this program every year. All subjects were more than 20% of percentage of overweight (POW, the ratio of overweight to the age- and sex-specific standard bodyweight for the height, expressed as a percentage) and were simply obese, with fasting blood glucose levels below 110 mg/dl, and an hemoglobin A1c (HbA1c) of below 5.6%. Informed consent was obtained from the parents or guardians of all subjects. The Ethical Committee of the Niigata University Graduate School of Medicine and Dental Sciences approved this study.

Methods

We measured the body height and weight with a portable standiometer and a digital scale to the nearest 1 mm and 0.1 kg, respectively. POW was calculated based on the table published in 1990 by the Ministry of Education, Science and Culture of Japan (*23*, *24*). Waist and hip circumferences were measured to the nearest 1 mm. Abdominal fat thickness was measured using ultrasonography (*25*). Subjects were kept in the supine position, the linear-array probe was kept perpendicular to the skin on the upper median abdomen, and a longitudinal scan was done from the xyphoid process to the navel along the linea alba. Scanning was performed at the optimal position, and the surface of the liver was kept almost parallel to the skin by having the subjects hold their breath. The maximum thickness of the fat layer between the linea abla and the liver surface was defined as the maximum preperitoneal fat thickness (P_{max}). P_{max} was measured directly from the screen with electronic calipers (*26*). Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured three times from the right arm with the subjects in a seated position using an automated recorder (Dinamap Model 8104; Critikon Inc., Tampa, USA). The third measurement of BP was used for analysis in this study.

The fasting serum levels of insulin and fasting plasma glucose were measured. The serum levels of insulin were measured by a commercial radioimmunoassay using a commercially available kit (LS Eiken Insulin Kit; Eiken Chemical Co., Ltd., Tokyo, Japan). The homeostasis model assessment-insulin resistance (HOMA-R) (*27*) and the quantitative insulin sensitivity check index (QUICKI) (*28*) were calculated.

Birth weight and gestational weeks were checked using maternity record books. The birth weight standard deviation score (BWSDS) was calculated using the fetal growth curve of Japanese (*29*).

Statistical Analysis

Data were expressed as the mean±SD. Birth weight, height, weight, POW, waist and hip circumference, P_{max}, SBP, DBP, and QUICKI were normally distributed. The fasting serum insulin levels and HOMA-R were not in normal distribution, and were therefore log-transformed before the data analyses.

We divided the subjects into four groups according to their birth weight or BWSDS. Quartiles of birth weight ranged from the MA group (lowest) to the MD group (highest) in boys, and from the FA group (lowest) to the FD group (highest) in girls. Quartiles of BWSDS ranged from the M1 group (lowest) to the M4 group (highest) in boys, and from the F1 group (lowest) to the F4 group (highest) in girls. Comparisons of SBP, DBP, serum insulin levels, HOMA-R, QUICKI, waist and hip circumference, and P_{max} were made using parametric one-way analysis of variance (ANOVA). *Post hoc* comparisons between pairs of means were made using Bonferroni/Dunn's test.

The relationships of both birth weight (or BWSDS) and P_{max} to serum insulin levels (or HOMA-R, QUICKI) were examined with multiple regression analyses. Birth weight (or BWSDS) and P_{max} were entered as independent variables, and serum insulin levels, HOMA-R and QUICKI were entered as dependent variables.

All statistical evaluations were made using StatView software (version 5.0; Abacus Concepts, Berkeley, USA) on a personal computer. For all analyses, probability (p) values below 0.05 were considered to indicate statistical significance.

Results

The characteristics of the subjects are shown in Table 1. The mean POW was 52.1% for boys and 51.4% for girls. Twenty-four boys and 20 girls were low birth weight infants (less than 2,500 g), 13 boys and 9 girls were preterm gestational week infants (less than 37 weeks), and 13 boys and 7 girls were

Table 3. Characteristics of 650 Obese Boys after Being Divided into Four Groups According to Birth Weight SDS

	M1 (n=162)	M2 (n=163)	M3 (n=162)	M4 (n=163)	ANOVA p
Range of birth weight SDS	−3.05 to −0.11	−0.10 to +0.39	+0.39 to +1.03	+1.03 to +4.19	—
Birth weight (g)	2,774±276¶,†,*	3,149±143†,*	3,347±189*	3,758±314	<0.0001
Gestational week	39.1±1.3	39.2±1.2	39.2±1.4	39.3±1.4	NS
Age (years)	10.3±2.4	10.3±2.1	10.3±2.1	10.7±1.9	NS
Height (cm)	141.4±14.0*	141.8±12.1*	142.9±13.1*	146.7±12.7	<0.001
Weight (kg)	54.0±15.8*	54.6±13.8*	56.3±17.5*	60.5±16.3	<0.01
Height SDS	+0.71±1.12†,*	+0.80±1.20*	+0.95±1.03*	+1.23±0.94	<0.0001
Percentage of overweight (%)	+50.8±11.7	+52.3±11.7	+52.3±14.7	+52.9±14.5	NS
Waist circumferences (cm)	83.9±10.4*	84.5±8.6*	84.6±11.2*	87.9±10.0	<0.01
Hip circumferences (cm)	87.6±9.3*	88.5±7.8*	88.9±10.0*	91.4±9.3	<0.01
P_{max} (mm)	11.0±3.0	11.6±3.4	11.1±3.7	11.6±3.3	NS
SBP (mmHg)	116±13	116±13	115±13	116±12	NS
DBP (mmHg)	57±8	59±9†,*	57±9	57±7	NS
Serum insulin (μU/ml)	21.7±19.5¶,†,*	15.9±10.7	16.1±9.8	16.2±10.0	<0.0001
HOMA-R	4.7±3.9¶,†,*	3.5±2.3	3.6±2.3	3.5±2.2	<0.001
QUICKI	0.32±0.03¶,†,*	0.33±0.03	0.33±0.03	0.33±0.03	<0.001

¶p<0.05 *vs.* the value of the M2 group, †p<0.05 *vs.* the value of the M3 group, *p<0.05 *vs.* the value of the M4 group using Bonferroni/Dunn's *post hoc* test. NS, not statistically significant. Other abbreviations are the same as in Table 1.

Table 4. Characteristics of 317 Obese Girls after Being Divided into Four Groups According to Birth Weight

	FA (n=79)	FB (n=78)	FC (n=81)	FD (n=79)	ANOVA p
Range of birth weight (g)	1,845–2,918	2,920–3,165	3,174–3,422	3,430–4,110	—
Birth weight SDS	−0.73±0.71¶,†,*	−0.15±0.42†,*	+0.32±0.34*	+1.06±0.43	<0.0001
Gestational week	38.3±1.8¶,†,*	39.1±1.2	39.3±1.1	39.6±1.1	<0.0001
Age (years)	10.2±2.3	9.6±2.0	10.3±2.3	10.5±2.2	NS
Height (cm)	138.8±11.5*	137.5±11.1*	140.8±12.3	142.9±11.3	<0.05
Weight (kg)	51.7±14.5	49.8±13.5*	54.3±16.0	56.1±17.0	NS
Height SDS	+0.52±1.16†,*	+0.88±0.79	+0.77±1.13	+0.94±1.09	NS
Percentage of overweight (%)	+51.3±15.9	+50.6±10.7	+52.2±13.7	+51.4±16.8	NS
Waist circumferences (cm)	81.0±9.4	79.9±9.0	81.1±9.9	82.3±12.2	NS
Hip circumferences (cm)	87.6±10.3	86.1±9.9*	89.3±10.7	89.8±10.7	NS
P_{max} (mm)	11.4±3.2¶	10.0±3.0†,*	11.2±3.5	11.4±3.9	<0.05
SBP (mmHg)	112±15	112±13	113±13	113±11	NS
DBP (mmHg)	58±9	57±9	56±8	58±8	NS
Serum insulin (μU/ml)	20.7±13.0	17.5±9.6	18.3±10.0	18.0±10.1	NS
HOMA-R	4.5±3.0	3.7±2.2	3.9±2.2	3.9±2.3	NS
QUICKI	0.32±0.03	0.32±0.03	0.32±0.03	0.32±0.03	NS

¶p<0.05 *vs.* the value of the FB group, †p<0.05 *vs.* the value of the FC group, *p<0.05 *vs.* the value of the FD group using Bonferroni/Dunn's *post hoc* test. NS, not statistically significant. Other abbreviations are the same as in Table 1.

light for their gestational age (birth weight less than −1.5 SD for gestational age).

Table 2 shows the relationship of anthropometric measurements, P_{max}, SBP, DBP, serum insulin levels, HOMA-R and QUICKI among birth weight quartiles in obese boys. There were no significant differences in age, POW, SBP, DBP or P_{max} among the four groups. The mean height and weight of the MD group were significantly greater than those of the MA group. The mean waist circumference of the MA group was less than that of the MD group, but the mean serum insulin level and HOMA-R of the MA group were significantly higher than those of the MD group. Significant downward trends in the mean serum insulin level and HOMA-R across birth weight quartiles were observed.

Table 3 shows the relationship of anthropometric measurements, P_{max}, SBP, DBP, serum insulin levels, HOMA-R and QUICKI among BWSDS quartiles in obese boys. There were no significant differences in age, POW, SBP, DBP or P_{max}

Table 5. Characteristics of 317 Obese Girls after Being Divided into Four Groups According to Birth Weight SDS

	F1 (n=79)	F2 (n=78)	F3 (n=80)	F4 (n=80)	ANOVA p
Range of birth weight SDS	−0.44 to −2.36	−0.41 to +0.08	+0.09 to +0.69	+0.71 to +2.06	—
Birth weight (g)	2,675±299¶,†,*	3,056±168†,*	3,281±225*	3,583±284	<0.0001
Gestational week	39.2±1.5	39.1±1.2	39.2±1.3	38.9±1.7	NS
Age (years)	10.0±2.2	10.4±2.4	9.8±2.0	10.4±2.2	NS
Height (cm)	138.6±12.0*	141.2±12.2	137.6±10.7*	142.8±11.5	<0.05
Weight (kg)	52.0±15.2*	54.7±16.4†	48.9±11.8*	56.3±16.9	<0.05
Height SDS	+0.61±0.98*	+0.88±0.79	+0.73±1.05	+0.97±1.08	NS
Percentage of overweight (%)	+52.9±16.6†	+52.0±13.9	+48.0±8.5*	+52.7±16.8	NS
Waist circumferences (cm)	82.1±10.1†	81.4±9.8	78.3±7.5*	82.5±12.4	<0.05
Hip circumferences (cm)	87.7±10.7	89.5±11.5†	85.6±8.2*	90.1±10.8	<0.05
SBP (mmHg)	114±14	112±14	110±12	113±11	NS
DBP (mmHg)	59±9†	57±8	56±8	57±9	NS
P_{max} (mm)	11.0±3.5	11.2±3.4	10.3±3.2	11.4±3.7	NS
Serum insulin (μU/ml)	21.9±13.1†,*	18.9±9.8	16.5±8.9	17.3±10.3	<0.01
HOMA-R	4.8±3.0†,*	4.0±2.2	3.5±1.9	3.7±2.3	<0.01
QUICKI	0.31±0.03†,*	0.32±0.02	0.33±0.03	0.33±0.03	<0.05

¶p<0.05 *vs.* the value of the F2 group, †p<0.05 *vs.* the value of the F3 group, *p<0.05 *vs.* the value of the F4 group using Bonferroni/Dunn's *post hoc* test. NS, not statistically significant. Other abbreviations are the same as in Table 1.

among the four groups. The mean height and weight of the M4 group were greater than those of the other groups. The mean waist circumference of the M4 group was greater than those of the other groups. In the M1 group, the mean serum insulin level and HOMA-R were significantly higher than those of the other groups, and the mean QUICKI was significantly lower than those of the other groups.

Table 4 shows the relationship of anthropometric measurements, P_{max}, SBP, DBP, serum insulin levels, HOMA-R and QUICKI among birth weight quartiles in obese girls. There were no significant differences in age, POW, waist circumference, SBP or DBP among the four groups. The mean height of the FD group was higher than that of the FA group.

Table 5 shows the relationship of anthropometric measurements, P_{max}, serum insulin levels, HOMA-R and QUICKI among BWSDS quartiles in obese girls. There were no significant differences in age, POW, SBP, DBP or P_{max} among the four groups. The mean height and weight of the F4 group were greater than those of the F1 group. In the F1 group, the mean serum insulin level and HOMA-R were significantly higher than those of the F4 group, and the mean QUICKI was significantly lower than that of the F4 group.

To reveal the relationships of both birth weight (or BWSDS) and P_{max} to the serum insulin levels (or HOMA-R or QUICKI), multiple regression analyses were carried out. The birth weight or BWSDS and P_{max} were entered as independent variables, and serum insulin levels, HOMA-R and QUICKI were entered as dependent variables. In both obese boys and girls, the birth weight and BWSDS were inversely related to the serum insulin levels and HOMA-R, and P_{max} was independently and positively related to the serum insulin levels and HOMA-R (Table 6). The birth weight and BWSDS were positively related to QUICKI, and P_{max} was independently and inversely related to QUICKI (Table 6). Both analyses revealed that P_{max} had a closer relationship to serum insulin levels, HOMA-R and QUICKI than did the birth weight or BWSDS.

Discussion

In this study, both birth weight (or BWSDS) and visceral fat accumulation were independently associated with serum insulin levels (or HOMA-R, QUICKI) in obese Japanese children. In other words, children who were born smaller and accumulated a substantial amount of visceral fat seemed to have a much higher risk for hyperinsulinemia and insulin resistance, as previously reported in other studies on children (*18*, *19*, *30*). The interaction of low birth weight and later overweight in childhood might be associated with the occurrence of MS, because hyperinsulinemia and insulin resistance play important roles in MS. Therefore, this study supported Barker's hypothesis that low birth weight is associated with type 2 DM and HT (*11*, *12*).

Otherwise this study revealed that P_{max} had a closer relationship to the serum insulin revel (or HOMA-R or QUICKI) than did the birth weight (or BWSDS). Visceral fat accumulation after birth might thus be a more important determinant of occurrence of MS in obese children than birth weight.

The serum insulin levels, HOMA-R and QUICKI showed greater variation among BWSDS quartiles than among birth weight quartiles. BWSDS tended to be more closely related to hyperinsulinemia and insulin resistance than was birth weight in this study, which suggests that IUGR may play an important role in forming insulin resistance.

Table 6. Multiple Regression Analyses of Insulin and Insulin Resistance with P_{max} and Birth Weight (Birth Weight SDS)

Dependent variable	Independent variable	Obese boys (n=650)		Obese girls (n=317)	
		β	R	β	R
Insulin	P_{max}	0.470†	0.480†	0.500†	0.510†
	Birth weight	−0.105**		−0.104*	
	P_{max}	0.476†	0.484†	0.496†	0.520†
	Birth weight SDS	−0.125***		−0.144**	
HOMA-R	P_{max}	0.453†	0.463†	0.492†	0.502†
	Birth weight	−0.106**		−0.100*	
	P_{max}	0.459†	0.467†	0.489†	0.511†
	Birth weight SDS	−0.123***		−0.135**	
QUICKI	P_{max}	−0.449†	0.458†	−0.49†	0.500†
	Birth weight	0.098**		0.099*	
	P_{max}	−0.455†	0.461†	−0.487†	0.509†
	Birth weight SDS	0.112**		0.136**	

SDS, standard deviation score; HOMA-R, homeostasis model assessment-insulin resistance; QUICKI, quantitative insulin sensitivity check index; P_{max}, maximum preperitoneal fat thickness. β: standard partial regression coefficient; R: multiple correlation coefficient. *$p<0.05$, **$p<0.01$, ***$p<0.001$, †$p<0.0001$.

A poor intrauterine environment, such as that in a mother with malnutrition, a smoking habit, inappropriate dieting would affect fetal growth retardation. When the maternal-placental nutrient supply fails to match the fetal nutrient demand, the fetus changes the structure and function of the organs and placenta (*31*, *32*). This adaptation, called "programming," is beneficial to fetal survival, but it has a strong and permanent influence on the fetal structure, physiology and metabolism. For example, malnutrition of the fetus changes the structure of the muscles and increases type IIb fibers. Type IIb fibers have less capillary supply and less intake of glucose from capillaries than type I fibers. This change leads to insulin resistance (*33*). Some studies had suggested that tumor necrosis factor (TNF)-α plays a significant role in the tissue specificity and signal selectivity of insulin resistance. The pathway related to glucose metabolism is selectively impaired by TNF-α in skeletal muscle, and this impairment may induce compensatory hyperinsulinemia (*34*). Other studies have revealed an increase in the plasma insulin-like growth factor-1 (IGF-1) concentration in low birth weight children (*35–37*). Intrauterine resetting of the hypothalamic-pituitary-adrenal axis for postnatal catch-up growth may lead to a high IGF-1 concentration. This reprogramming may be one of the mechanisms linking reduced fetal growth and high BP in later life.

In this study, there was no relationship between birth weight (or BWSDS) and BP, because all subjects were obese children with a mean age of 10.3 years. However, a previous study reported that BP was associated with hyperinsulinemia and insulin resistance in obese children (*38*). It is possible that the relationship between birth weight and BP is amplified with age. Some studies have revealed that both fetal growth and early postnatal growth have a long-term impact on BP in adults (*16*, *39*, *40*). Law *et al*. found that lower birth weight and greater weight gain between 1 and 5 years of age were associated with higher SBP in young British adults (*39*). Adair and Cole found that larger weight increments from 8 to 11 years and 11 to 16 years were associated with increased odds of high BP in Filipino adolescent boys (*40*). It is thought that part of the risk of adult HT is set in fetal life.

Improvement of the intrauterine environment and fetal growth may prevent the metabolic derangements in obese children. To this end, it will be important to provide proper health education for children and adolescents, including instruction on maintaining an ideal body weight and avoiding smoking and sexually transmitted diseases, so that these children, when grown, will be more likely to have healthy children themselves. In conclusion, our findings suggest that both lower birth weight and visceral fat accumulation may be independently related to hyperinsulinemia and insulin resistance. Strategies that help obese children, especially those with lower birth weight, to reduce their visceral fat accumulation, such as exercise and reduction of fat intake, might help to prevent MS in adulthood.

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