Body Fat Distribution in Childhood Obesity: Association with Metabolic Risk Factors

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ABSTRACT

Objectives: *To evaluate the clinical significance of body fat distribution in childhood obesity, we investigated the associations of subcutaneous and intraabdominal (preperitoneal and visceral) fat, estimated by ultrasonography, with metabolic risk factors.* ***Subjects:*** *Fifty-one obese (age 11.5±2.6 years) and 33 non-obese (age 12.2±2.7 years) children.* ***Study Design:*** *Case control study.* ***Methods:*** *Ultrasonographic measurements of fat thickness [maximum and minimum preperitoneal fat thicknesses (Pmax, Pmin), maximum and minimum subcutaneous fat thicknesses (Smax, Smin), visceral fat thickness (V), triceps (Tr) and subscapular (Ss) skin fold thicknesses] were documented. Blood pressures, lipid profiles, fasting insulin levels, glucose/insulin ratio and $HOMA_{IR}$ (homeostasis model assessment for insulin resistance) were evaluated in both groups and these parameters were correlated with body fat distribution.* ***Results****: In the obese group, fasting insulin level was correlated to Smin, Smax, and Pmin. HOMA, accordingly, was also correlated to Smin, Smax, and Pmin. Fasting insulin level and HOMA showed no correlation with either Pmax or visceral fat thickness.* ***Analysis****: Abdominal subcutaneous fat thickness measurements were the best predictors of hyperinsulinemia (R^2: 0.32).* ***Conclusion:*** *We did not observe a significant correlation between blood pressure, lipid parameters and body fat distribution in obese group. Abdominal subcutaneous fat thickness might be a better predictor of the risk for hyperinsulinemia in childhood obesity.*

Key words: *Anthropometry, Body fat distribution, Hyperinsulinemia, Metabolic risk factors, Obesity, Ultrasound.*

INTRODUCTION

Obesity is strongly linked to cardiovascular disease and non-insulin-dependent diabetes mellitus through the promotion of insulin resistance and other associated physiological abnormalities, including dyslipidemia, elevated blood pressure, and increased left ventricular mass(1). A close relationship between high morbidity and intraabdominal (visceral) fat obesity, rather than extra-abdominal (subcutaneous) fat obesity, has been observed in adults(2). Although body fat patterning has been related to adverse health outcomes in adults, its importance in children and adolescents is less certain. Various fat patterns have been associated with concentrations of lipids and insulin and with blood pressure in some studies, but negative results have also been reported(3-8). Computed tomography (CT) and magnetic resonance imaging (MRI) are accurate imaging techniques for assessing body fat distribution, but the disadvantages are cost, radiation exposure (for CT), and use limited to a research setting(9,10). Ultrasonography (US) has been proposed as an alternative non-invasive technique to measure subcutaneous and visceral fat thickness because it may overcome some limitations of the anthropometric measurements(11-17). US scanners are capable of measuring subcutaneous fat at depths

of 100 mm or more without tissue compression and can reliably detect density interfaces with an accuracy of 1 mm(16). Fanelli, *et al.*(11) reported that the caliper and US techniques are equally effective in predicting body density and, hence total body fat of lean man. We previously reported that the validity of anthropometric measurement of skinfold thickness is low in obese children when compared to US measurements(17). Visceral fat thickness measured by US was strongly correlated with the amount of visceral fat and the cardiovascular risk factors(18). Ferrozzi, *et al.*(19) reported that US was as useful as CT in evaluating body fat distribution in pediatric obesity. In this study, we investigated the association of body fat distributions, estimated by US, with metabolic risk factors. The aim was to evaluate the clinical significance of visceral fat accumulation in childhood obesity with respect to the development of metabolic derangements.

METHODS

Fifty one obese (21 F, 30 M) and 33 non-obese children (17 F, 16 M) were recruited as study and control groups, respectively. The control group was selected from subjects of same age with normal growth and development and no endocrinalogical problems but with acute non-serious illnesses, who were admitted to general pediatric polyclinics. The same investigator performed anthropometric measurements and complete physical examination including pubertal staging, neurological, mental and dysmorphic findings. Tanner classification was used for pubertal staging(20,21). Blood pressure (BP) was measured in each subject three times by the same observer, using a mercury-gravity manometer with proper cuff size in standard conditions. BP measurements were compared with reference values prepared according to age and sex(22).

Anthropometry: Body weight was measured to the nearest 0.1 kg with a balance scale (Baurer, PS 07), and height was measured to the nearest 0.1 cm with stadiometer (Hyssna Limfog, AB) with subjects lightly dressed and without shoes. Body mass index (BMI) was calculated as weight (kg) divided by height square (m^2). The degree of obesity was quantified using Cole's reference data(23). BMI higher than 95th percentile was defined as obesity. All measurements were taken 3 times at each site, and the mean of the 3 values was used.

Ultrasonography: All participants underwent ultrasonographic measurements of fat thicknesses [maximum and minimum preperitoneal fat thicknesses (Pmax, Pmin), maximum and minimum subcutaneous fat thicknesses (Smax, Smin), visceral fat thickness (V), triceps (Tr) and subscapular (Ss) skinfold thicknesses]. A 7.5 MHz linear-array probe was used to measure the subcutaneous and preperitoneal fat layers. Skinfold thickness was measured at the following sites: Tr-halfway between the acromion and the olecranon; and Ss-1 cm below the inferior angle of scapula. It was placed perpendicular to the skin on the mid-upper abdominal wall. Midline longitudinal scans were obtained from the xiphoid process to the navel along the linea alba. Smin and Pmax were measured just below the xiphoid process. Smax and Pmin were measured 5 cm above the umbilicus. The measurements of Smin and Smax were taken directly from the screen using electronic calipers placed at the skin-fat and fat-linea alba interfaces. Pmax was measured in the region just below the xiphoid process between the posterior aspect of linea alba and the anterior surface of the left lobe of the liver. Pmin was obtained 5 cm above the umbilicus between the posterior aspect of the linea alba and the peritoneum which is displayed as an echogenic layer(15). A 3.5 MHz convex-array probe was used to evaluate V, which was measured just above the umbilicus between the posterior aspect of the abdominal wall and the anterior wall of the abdominal aorta(15).

Laboratory investigations: Blood glucose, serum insulin and lipid levels were determined from blood samples taken after an overnight fast of 12 hours. Glucose, total cholesterol (TC), triglyceride (TG) measurements were performed by using enzymatic assays (Instrumentation Lab, MA, USA). High-density cholesterol (HDL-C) was measured by a direct enzymatic assay without precipitation (Instrumentation Lab, MA, USA). Low-density cholesterol (LDL-C) was estimated by using Friedewald formula. Serum alanine aminotrans-ferase (ALT) and aspartate aminotransferase (AST) were measured by Herry's method and serum gama-glutamyl transpeptidase

(GGT) by Szasz method. Lipid and liver enzyme values were compared with reference values(24,25). Insulin measurement was done by using solid phase chemiluminesance immunoassay. Glucose/insulin ratio (G_0 / I_0) and homeostasis model assessment for insulin resistance ($HOMA_{IR}$) were estimated by using glucose (mg / dK) / insulin (mmol/L), and insulin (mmol/L) × glucose (mmol/L) / 22.5 formulae, respectively (26,27).

In both groups systolic and diastolic BP, lipid and fasting insulin levels, G_0 / I_0 and $HOMA_{IR}$ were determined and these parameters were correlated with body fat distribution.

Statistical analysis: Independent *t* test was used to analyze the significance of differences between the groups. Pearson's correlation coefficients were calculated to assess the association of changes in metabolic risk factors and ultrasonographic measurements. Multiple linear regression analysis was used to investigate the effect of body fat distribution on metabolic risk factors. *P* value of less than 0.05 was regarded as significant.

RESULTS

Clinical and laboratory characteristics of the obese and the control group are shown in ***Table* I**. When groups were compared, BMI and all ultrasonographic measurements differed significantly. There was no significant difference between the groups with respect to systolic and diastolic BP, ALT, AST, HDL-C and glucose. However, GGT, TC, TG, LDL-C, VLDL-C, insulin, G_0 / I_0 ve $HOMA_{IR}$ mean values were significantly different.

In the obese group, fasting insulin level was correlated to Smin, Smax, and Pmin. $HOMA_{IR}$, accordingly, was also correlated to Smin, Smax, and Pmin. Fasting insulin level and $HOMA_{IR}$ showed no correlation with either Pmax or visceral fat thickness. G_0 / I_0 showed negative correlation with Smin, Smax and Pmin. In the control group, systolic BP was correlated to Pmax, Pmin, Smax and V. ALT was correlated to V.

Multiple linear regression analysis model, using $HOMA_{IR}$ as the dependent variable and ultrasonographic measurements of fat thickness as the independent variables, that best estimated $HOMA_{IR}$ from the predictor variables included abdominal subcutaneous fat thickness measurements (Smin and Smax) were the best predictors of hyperinsulinemia [R^2 (adjusted): 0.32].

DISCUSSION

The present study clearly confirms that cardiovascular risk factors are more common in obese children than in controls. When compared to control group, mean HDL-C value in obese group was not as low as expected. These finding might be related to the fact that Turkish population has genetically low HDL-C levels(28). Some previous investigations have demonstrated that the changes in lipids which occur throughout adolescence may be more explained by a sexual maturity index than chronologic age(29).

Obesity is an important factor in the development of hypertension(3). In our study, BP measurements did not differ significantly in both groups, but we think it seems inappropriate to compare the mean BP measurements in such a group with a wide age distribution. For this reason, BP measurements were compared with reference values prepared according to age and sex. Systolic hypertension was detected in 6 (11.6%), diastolic hypertension in 10 (19.6%) subjects in the obese group. On the other hand, there was no significant correlation between regional fat accumulation and blood pressure in the obese group. Contrary to this observation, an interesting finding was that systolic BP was positively related to body fat thicknesses in the control group. Because the fat thicknesses are closely associated with elevated systolic BP in non-obese children, maintaining an ideal increase in the fat thickness in childhood is important in preventing elevated BP.

In cross-sectional population studies, higher fasting serum insulin levels are directly related to increases in body fatness, particularly in those with central adiposity(30,31). Yamaguchi, *et al.*(8) investigated the relation between intraabdominal fat/extraabdominal fat thickness (V/S) and metabolic indices and found the V/S displayed no correlation with serum lipids, blood glucose, insulin and BP. Asayama, *et al.*(7) reported that there is a relation

TABLE I CLINICAL AND LABORATORY CHARACTERISTICS OF BOTH GROUPS

	Obese (n=51) Mean ±SD	Control (n=33) Mean ±SD
Age (year)*	11.5 ± 2.6	12.2 ± 2.7
BMI (kg/m^2)†	28.8 ± 3.4	18.5 ± 2.3
Pmax (mm)†	11.4 ± 3.6	6.3 ± 5.0
Pmin (mm)†	3.8 ± 1.5	2.4 ± 1.2
Smax (mm)†	29.5 ± 7.6	9.3 ± 5.4
Smin (mm)†	18.1 ± 5.3	5.3 ± 4.2
V (mm)†	44.3 ±12.9	23.0 ± 9.4
Tr (mm)†	10.6 ± 4.7	5.2 ± 2.9
Ss (mm)†	11.7 ± 5.4	3.0 ± 4.1
SBP (mmHg)*	109.9± 7.6	106.5± 9.9
DBP (mmHg)*	71.6 ± 5.8	70.3 ± 6.2
ALT (IU/L)*	28.0 ±29.5	19.1 ± 6.5
AST (IU/L)*	26.18±13.2	23.5 ± 8.0
GGT (IU/L)†	20.6 ±19.4	11.3 ± 5.5
TC (mg/dL)†	164.7±36.0	143.0± 8.5
TG (mg/dL)†	104.8±50.6	65.4 ± 3.7
HDL-C (mg/dL)*	46.0 ±12.2	48.9 ± 3.6
LDL-C (mg/dL)†	94.6 ±32.9	77.3 ± 8.8
VLDL-C (mg/dL)†	21.0 ±10.9	15.7 ±14.3
Glucose (mg/dL)*	92.2 ±40.4	94.4 ± 6.7
Insulin (μU/mL)†	10.6 ± 5.1	6.3 ± 3.3
G_0 / I_0†	10.5 ± 5.1	19.8 ± 2.8
$HOMA_{IR}$†	2.51 ± 0.2	1.5 ± 0.8

*BMI, body mass index; Pmax & Pmin, maximum and minimum preperitoneal fat thickness, respectively; Smax & Smin, maximum and minimum subcutaneous fat thickness, respectively; V, visceral fat thickness; Tr, triceps-ultrasound; Ss, subscapular-ultrasound; SBP, systolic blood pressure; DBP, diastolic blood pressure; ALT, alanine amino-transferase; AST, aspartate aminotransferase; GGT, gama-glutamyl transpeptidase; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VLDL-C, very low-density lipoprotein cholesterol; G_0/I_0, glucose/insulin ratio; $HOMA_{IR}$, homeostasis model assessment for insulin resistance; *Not significant; † < 0.05..*

between total, subcutaneous, visceral fat thicknesses and insulin, lipid values and that visceral fat thickness measurement is a more sensitive index to predict metabolic risk. Tershakovec, *et al.*(6) reported visceral abdominal and subcutaneous fat thicknesses were not correlated with insulin level or $HOMA_{IR}$ in the obese children and adolescents. Tamura, *et al*.(4) implied that evaluating Pmax by US may be the most sensitive and reliable method of predicting insulin-resistance associated metabolic derangements in children. Nishina, *et al*.(5) reported the relationships among systolic BP, serum insulin and Pmax. In our study, while hyper-insulinemia was correlated to all abdominal subcutaneous fat thicknesses, only Pmin among measurements of preperitoneal fat thickness had relation with hyperinsulinemia. No correlation was found between V and hyperinsulinemia. Lovejoy, *et al.*(32) showed subcutaneous abdominal fat was significantly correlated with insulin sensitivity and fasting insulin in the young African-American women. Yanovski, *et al*.(33) reported that both basal and 2h OGTT serum insulin were significantly correlated with subcutaneous adipose tissue as assessed by MRI in black girls but not in white girls. Different results in the literature might be related to different age, sex and ethnic characteristics in these studies and to various techniques used to detect body fat and to different indices used to determine hyperinsulinemia.

Our results show that the increase in total body fat leads to fat deposition in both subcutaneous and visceral areas. It has been proposed that excessive subcutaneous fat may be less harmful than the visceral fat in obese adults(34). However, our finding that abdominal subcutaneous fat thickness was positively correlated with fasting insulin and $HOMA_{IR}$, suggests a synergistic effect of sub-cutaneous fat on the development of hyper-insulinemia, which contradicts the mentioned theory above. Therefore, the role of subcutaneous fat in childhood obesity is more likely to differ than in adult obesity. We did not observe a significant correlation between BP, lipid parameters and body fat distribution. As compared to children, the relatively higher amount of visceral abdominal fat of adults might make it physiologically more important in adults. Goran, *et al.*(35) reported that body fat in general is the predominant factor influencing insulin sensitivity, but visceral fat may have additional effects on fasting insulin. The lack of major effects of visceral fat on insulin sensitivity in children may be explained by lower levels of visceral fat or because visceral fat affects aspects of whole body insulin action that are not measured by the minimal model. In addition, in obese children, obesity might be of too short duration for central fat deposition to produce metabolic disorders. In conclusion, although the

WHAT IS ALREADY KNOWN?

- There is a close relationship between high morbidity and intraabdominal (visceral) fat obesity in adults.

WHAT THIS STUDY ADDS?

- Abdominal subcutaneous (extra-abdominal) fat thickness might be a better predictor of the risk for hyperinsulinemia in childhood obesity.

sample size was small, our findings indicate that abdominal subcutaneous fat thickness might be a better predictor of the risk for hyperinsulinemia in childhood obesity.

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