Clinical characteristics of obese boys and girls in a high school: focused on abdominal fat indices, fatty liver and carotid intima-media thickness

Jung Eun Oh, MD[1], Jiyoung Jung, MD[1], Hae Soon Kim, MD[1], Young Mi Hong, MD[1], Jung Hyun Yoo, MD[2], Young Whan Song, MD[3], Jo Won Jung, MD[4], Nam Su Kim, MD[5], Chung Il Noh, MD[6]

Departments of [1]Pediatrics and [2]Radiology, Ewha Womans University School of Medicine, Seoul, [3]Department of Pediatrics, Inje University College of Medicine, Busan, [4]Department of Pediatrics, Ajou University School of Medicine, Suwon, [5]Department of Pediatrics, Han Yang University College of Medicine, Seoul, [6]Department of Pediatrics, Seoul National University College of Medicine, Seoul, Korea

Purpose: Our study aimed to evaluated sex differences in clinical features of obese high school students,

Methods: One hundred three obese high school students (body mass index [BMI]≥85th percentile) and 51 control students (BMI<85th percentile) were enrolled in this study. Anthropometric measurements were performed. Fasting serum glucose, insulin, aspartate aminotransferase, alanine aminotransferase, total cholesterol, triglyceride, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and high-sensitive C-reactive protein were measured. Abdominal fat thickness, degree of fatty liver, and carotid intima-media thickness were measured by ultrasound.

Results: In control and obese groups, waist circumference was significantly longer in boys but body fat mass was significantly higher in girls. In the control group, total cholesterol and LDL-C were higher in girls. In the obese group, however, aspartate aminotransferase, alanine aminotransferase and triglyceride were higher and HDL-C was lower in boys. Preperitoneal fat thickness was significantly higher in obese girls. In obese group, the degree of fatty liver was significantly higher in boys. Carotid intima-media thickness was not significantly different between boys and girls.

Conclusion: Obese adolescents had distinguishable sex differences in body measurements, metabolic abnormalities, abdominal fat thickness and fatty liver. We can infer that these characteristics may extend into adult obesity.

Key words: Adolescent, Obesity, Abdominal fat, Fatty liver, Carotid artery disease

Introduction

Recently in Korea, childhood and adolescent obesity has increased rapidly because of socio-economic development, westernization of eating lifestyles, and the increased use of computers. Obesity leads to complications such as hypertension, hyperlipidemia, insulin resistance, and non-alcoholic hepatitis. The prevalence of these complications has increased and they are life-threatening factors on adolescent health, on which lifelong health is based. Childhood obesity ultimately contributes to the prevalence of adult diabetes, hypertension, and cardiovascular disease.

Marked sex differences have been reported in regards to the degree of insulin resistance, body composition and energy balance in adults[1]. Adolescents in high school present some features like abdominal fat distribution of both childhood and adulthood. To date, most researches have focused on adolescent obesity itself without mentioning sex differences. Physiological changes during this period include increased secretion of sex hormone and growth hormone, and the development of insulin resistance, which influences differences in sex hormone and subcutaneous fat between the two sexes[2-5].

In this study, we evaluated clinical features of obese high school students according to the sex, and we focused on the finding relations between metabolic index, cardiovascular risk factors and abdominal fat indices.

Materials and methods

1. Subjects

One hundred fifty four students (68 boys, 86 girls) aged between 15 and 17 in a high school participated in this study. They were divided into two groups: the obese group and control group. The obese group (48 boys, 55 girls) included those who had body mass index (BMI) above the 85th percentile for age and sex and the control group (20 boys, 31 girls) included those who had BMI below the 85th percentile for age and sex by the survey of Korean Centers of Disease Control and Prevention in 2007. Persons with endocrine dysfunction or other illnesses were excluded. We obtained informed consents from the guardians after explaining the procedure and purpose of the test thoroughly, and the study was approved by the Institutional Review Board.

2. Methods

1) Anthropometric measurement

We obtained height, weight, BMI, and body composition with Segmental Multi-frequency Bioelectrical Impedance Analysis (InBody J10, Biospace, Seoul, Korea). Waist circumference was measured with a tapeline at the expiratory phase on the horizontal plane between the lowest margin of the 12th rib and the mid portion of the superior iliac crest to the nearest 0.1 cm on standard physician's beam scales, and hip circumference was measured from the most protruding part of the hip to the nearest 0.1cm on standard physician's beam scales.

2) Blood pressure measurement

We checked each subject's blood pressure in his/her right arm with a standard mercury sphygmomanometer. A cuff with a width that encircles 40 to 50% of the upper arm was chosen. After the subject was stabilized for at least 5 minutes, we checked blood pressure twice and used the average.

3) Biochemical analysis

Venous blood was drawn after overnight fasting. Samples were kept at -70°C for subsequent assay. The serum concentrations of glucose, insulin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total cholesterol, triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and high-sensitive C-reactive protein (hs-CRP) were evaluated.

4) Abdominal ultrasound for abdominal fat indices and fatty liver

We used abdominal ultrasound Acuson XP128 (Acuson, Mountain View, CA, USA) and placed it above the navel and measured abdominal fat thickness including subcutaneous fat thickness, visceral fat thickness and preperitoneal fat thickness. The measurements were taken by an experienced radiologist. The subjects were comfortably placed in a supine position and we measured subcutaneous fat thickness from skin to anterior abdominal muscle, visceral fat thickness from posterior abdominal muscle to abdominal anterior wall of aorta, and preperitoneal fat thickness from the subcutaneous layer to the peritoneum, by placing a 3.5 MHz linear-array probe 1 cm above the navel at the end-expiratory phase. Fatty liver grading was recorded: grade 0 - no fatty liver; grade 1 - mild; grade 2 - moderate; and grade 3 - severe[6].

5) Carotid artery ultrasound

Carotid intima-media thickness (IMT) was measured when the subjects were supine for at least 30 minutes with neck ultrasound iU22 (Intelligent Ultrasound System, Philips Medical System, Amsterdam, The Netherlands) on 3 points of the thickest part of the intima-media 1 cm below, and the average was recorded.

6) Statistical analysis

The average and standard deviation of all measurements were collected. Statistic analysis between the groups was processed using SPSS ver. 16.0 (SPSS Inc., Chicago, IL, USA). We used the Mann-Whitney nonparametric method to compare the average between the obese group and the control group. The degree of the fatty liver in obese group was compared between boys and girls using Chi-square test. Spearman's rho nonparametric correlation analysis was used to confirm the relationship between cardiovascular risk factors and visceral fat thickness measured by ultrasound. A P value of less than 0.05 was regarded as significant.

Results

1. Anthropometric analysis

In control and obese groups, there was no significant difference of BMI between boys and girls, but waist circumference, waist-hip circumference ratio and blood pressure were higher in boys

Table 1. Anthropometric Measurements of the Subjects

	Control			Obese		
	Boys (n=20)	Girls (n= 31)	P value	Boys (n=48)	Girls (n=55)	P value
Age (yr)	16.5±0.3	16.5±0.3	NS	16.6±0.9	16.4±0.9	NS
BMI (kg/m^2)	20.3±1.8	20.8±2.2	NS	27.8±4.2	26.5±2.7	NS
WC (cm)	69.1±4.4	65.0±4.4	<0.01	89.1±10.2	77.0±5.9	<0.01
WHR	0.78±0.04	0.73±0.03	<0.01	0.86±0.1	0.787±0.04	<0.01
Fat (g)	10.4±3.3	17.3±3 .9	<0.01	25.2±10.5	26.8±5.9	<0.05
% Body Fat	17.5±4.5	32.2±4.6	<0.01	29.8±6.4	39.5±4.5	<0.01

Values are presented as mean±SD.
BMI, body mass index; WC, waist circumference; WHR, waist hip ratio; NS, not significant.

Table 2. Metabolic Parameters of the Subjects

	Control			Obese		
	Boys (n=20)	Girls (n= 31)	P value	Boys (n=48)	Girls (n=55)	P value
Insulin (U/mL)	7.4±3.7	9.4±5.3	NS	17.2±12.2	13.6±9.3	NS
Glucose (mg/dL)	87.0±6.5	87.5±.9	NS	88.5±8.1	87.3±5.3	NS
HOMA-IR	1.7±0.7	1.9±1.1	NS	3.9±1.9	3.3±2.8	NS
AST (U/L)	19.9±5.3	20.3±2.9	NS	32.5±47.2	21.4±11.3	<0.001
ALT (U/L)	17.7±0.6	13.7±3.1	NS	34.1±25.1	19.67±24.1	<0.001
TC (mg/dL)	144.7±15.9	158.4±27.1	<0.01	156.1±31.9	168.1±29.2	NS
TG (mg/dL)	65.1±34.4	74.4±27.5	NS	97.4±51.1	77.5±43.2	<0.05
HDL-C (mg/dL)	61.6±9.6	65.5±12.7	NS	49.8±6.2	57.7±11.2	<0.001
LDL-C (mg/dL)	72.6±16.1	101.1±19.3	<0.01	94.6±25.8	98.8±26.9	NS
hs CRP (mg/L)	1.2±2.2	0.6±1.2	NS	1.5±2.2	1.3±1.8	NS

Values are presented as mean±SD.
HOMA-IR, homeostasis model assessment of-insulin resistance; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; hs CRP, high-sensitive C-reactive protein; NS, not significant.

Table 3. Abdominal Fat Thickness and Grade of Fatty Liver of the Subject

	Control			Obese		
	Boys (n=20)	Girls (n= 31)	P value	Boys (n=48)	Girls (n=55)	P value
VFT (mm)	30.3±10.1	16.5±9.8	NS	36.7±17.5	32.5±7.4	NS
SFT (mm)	7.8±4.1	8.4±5.3	NS	19.8±7.5	19.2±5.0	NS
PFT (mm)	5.5±2.2	6.8±3.4	NS	11.4±4.6	13.5±3.9	<0.05
Fatty liver grade	0.12±0.3	0.13±0.3	NS	1.3±1.1	0.8±0.6	NS

Values are presented as mean±SD.
VFT, visceral fat thickness; SFT, subcutaneous fat thickness; PFT, peritoneal fat thickness; NS, not significant.
Fatty liver grade 0-3[32]

than in girls. However, body fat mass and body fat percentage were significantly higher in girls than in boys in both groups (Table 1).

2. Biochemical analysis

In the control group, there was no significant difference in insulin, glucose, homeostasis model assessment of-insulin resistance (HOMA-IR) , AST, ALT, TG, HDL-C and hs-CRP between boys and girls, but total cholesterol and LDL-C were higher in girls than in boys. In the obese group, there was no significant difference in insulin, glucose, HOMA-IR, total cholesterol, LDL-C and hs-CRP between boys and girls, but AST, ALT and TG were higher and HDL-C was lower in boys than in girls (Table 2).

3. Abdominal fat thickness and fatty liver

In the control group, visceral fat thickness, subcutaneous fat thickness and preperitoneal fat thickness showed no significant sex difference. In the obese group, there was no significant sexual difference in visceral fat thickness and subcutaneous fat thickness but preperitoneal fat thickness was significantly larger in girls than in boys (Table 3).

In obese group, the degree of fatty liver was thicker in boys compared to girls but, there was no significant difference between boys and girls. However, cross-analysis of the degree of fatty liver in the obese group showed that boys had a higher degree of fatty liver compared to girls (Table 4).

4. Blood pressure and carotid intima-media thickness

In control and obese groups, systolic and diastolic blood pressure was higher in boys than in girls. In control and obese groups, carotid

IMT was higher in boys than in girls but there was no significant difference (Table 5). In obese group, the incidence of carotid IMT over 0.6 mm, which is over the 2 standard deviations of carotid IMT of the control group, was higher in boys (26.7%) than in girls (16.7%) but there was no significant difference.

Discussion

For a given body mass index, men are reported to have more lean mass, and women to have higher adiposity[7]. Men are also found to have more visceral and hepatic adipose tissue, whereas women have more peripheral or subcutaneous adipose tissue. These differences as well as differences in sex hormones and adipokines may contribute to the more insulin-sensitive environment in women than in men[8]. In our study, although the BMI between boys and girls are not different in control and obesity group, waist circumference and waist-hip ratio were higher in boys but fat masses were higher in girls.

BMI is commonly used as a tool for the evaluation of obesity, but cannot discriminate body fat and muscle mass, and is inaccurate in that it is correlated more with subcutaneous fat than with abdominal fat, which is linked to metabolic disorders. Abdominal visceral fat is known to be a risk factor of insulin resistance and diabetes in both men and women. Waist circumference is easy to estimate and is a common index for epidemiologic research, but is not a direct reflection of visceral fat because abdominal fat is divided into visceral fat and subcutaneous fat. To measure visceral fat correctly, waist circumference, waist-hip circumference ratio, and the length of abdominal median-plane should be used together as they are simple and non-invasive anthropometric methods[9].

It has already been reported that waist circumference is more closely correlated with hypertension or metabolic disorder and insulin resistance compared to BMI[10]. Waist circumference is a good parameter for abdominal obesity, but cannot always be related with cardiovascular risk because waist circumference has a high correlation not only with visceral fat but also with subcutaneous fat[11].

Abdominal fat, especially, visceral fat is known to be a risk factor of metabolic disorder, which increases the degradation of fatty acid and is related to the increase of insulin resistance, and visceral fat cells

Table 4. Comparisons of Incidence of Fatty Liver Grades in the Obese Subjects

Obese subjects	Fatty liver grade				χ^2
	0	1	2	3	
Boys (n=48)	14 (30.0)	13 (26.7)	13 (26.7)	8 (16.7)	11.914
Girls (n=55)	17 (30.6)	32 (58.3)	6 (11.1)	0 (0.0)	

Values are presented as n (%).
$P<0.01$ between boys and girls.

Table 5. Blood Pressure and Carotid Intima-Media Thickness of the Subjects

	Control			Obese		
	Boys (n=20)	Girls (n=31)	P value	Boys (n=48)	Girls (n=55)	P value
Systolic BP (mmHg)	118.1±6.9	108.6±7.0	<0.01	124.2±12.9	114.6±8.9	<0.001
Diastolic BP (mmHg)	72.6±6.9	68.4±4.9	<0.05	77.4±10.4	71.4±6.4	<0.001
IMT (mm)	0.45±0.1	0.39±0.1	NS	0.57±0.18	0.49±0.14	NS

Values are presented as mean SD.
BP, blood pressure; IMT, intima-media thickness; NS, not significant.

secrete many cytokines and increase the cardiovascular factor[12].

Visceral fat and subcutaneous fat have not only a histological difference but also a difference in metabolic activities: visceral fat is more sensitive to lipolysis by catecholamine than to the anti-lipolytic effect of insulin[13]. Visceral fat transfers fatty acid to the portal circulation, increases glucogenesis and LDC, and reduces insulin degradation in the liver. As abdominal fat lipolysis increases, fatty acid in the portal and systemic circulation increases and finally induces hyperlipidemia, glucogenesis, and insulin resistance[14]. Visceral fat is known to increase with age and weight gain in both boys and girls. The waist-hip ratio is generally higher in boys, and it seems that visceral fat is larger in boys compared to girls[15]. In our study, waist circumference and waist-hip ratio were higher in boys than in girls, but body fat mass was larger in girls than in boys, which is similar to the distribution of body fat mass in adults. In addition, it is known that men have much more visceral fat and much less subcutaneous fat than women[8,16]. Our study revealed that abdominal fat thickness measured by ultrasound was thicker in boys than in girls among high school students but the difference was not significant. Subcutaneous fat thickness and preperitoneal fat thickness were higher in girls than in boys but were not significant. We think that the characteristic difference of fat distribution between normal men and women may be altered by obesity in adolescence. In the regulation of growth and development of puberty, estrogen and growth hormone interact closely. During growth spurt, estrogen and growth hormone take an action and change the physical development and then make a result sex different body composition change[17].

Adolescent obesity is known to be a major risk factor of non-alcoholic fatty liver and atherosclerosis, and combined with hyperlipidemia, hypertension, elevation of liver enzymes, and insulin resistance. Non-alcoholic steatohepatitis is a chronic liver dysfunction and has been reported to progress finally to fibrosis, hepatocirrhosis[18]. Jang et al.[19] reported that obese first-year high school students have an abnormal ALT level, 23.7% in boys and 11.8% in girls. In the obesity group, boys had a statistically higher abnormal rate of AST, ALT, and total cholesterol, but in the normal weight group, the abnormal rate of AST, ALT, and total cholesterol was significantly higher in girls than in boys. In a large cohort of overweight and obese European children and adolescents, the markers of nonalcoholic liver disease, especially elevated ALT, were frequently predicted by severe obesity group and male gender[20,21].

Recent studies study about estrogen effect to obesity. Pediatric non-alcoholic steatohepatitis is common in boys[22] and this sex difference may be due to the defense mechanism of estrogen as non-alcoholic steatohepatitis appears to be more common in menopause women than in premenopausal women as estrogen can reduce the oxidation of fat[20].

We can elude that lipid metabolism of sex steroid may start from the adolescent period; eventually these differences can be related with sex steroid, cytokine and lipid metabolism. The association of elevated ALT in obese boys supports the hypothesis that the pubertal increase of sex steroid may be important in predisposition for pediatric non-alcoholic steatohepatitis[22]. The underlying mechanisms of sex difference appeared to be due to the change of gene expression, which is dependent on estrogen. Estrogen reduced reactive oxygen species with increased antioxidant gene expression and reduced proinflammatory cytokine production[24].

Nonalcoholic fatty liver disease (NAFLD) is a disorder associated with obesity. Studies reported the prevalence rate of suspected fatty liver in overweight children between 6 and 23%[25].

Interestingly, epidemiological studies and most of published case series demonstrate a clear male predominance in the diagnosis of nonalcoholic fatty liver disease. In this study, the incidence of fatty liver in obese adolescents measured by ultrasound was 30% in both sexes. However, compared to the severity of fatty liver, the boys showed a mild to severe degree but the girls showed mostly a mild or moderate degree and no severe degree. This led to the assumption that estrogen might be an important mediator in the pathogenesis of nonalcoholic fatty liver disease. Changes in estrogen metabolism and physiological insulin resistance may determine susceptibility to fatty liver disease and contribute to the gender-specific prevalence pattern which is supported by previous studies[26,27].

Carotid intima-media thickness is a measure of subclinical atherosclerosis and predictive of future myocardial infarction and stroke. Obesity during childhood has been associated with higher carotid IMT during adulthood[28,29]. Caserta et al.[30] reported that NAFLD, BMI, waist circumference, and systolic blood pressure are independent markers of increased IMT in a random sample of adolescents.

Lee et al.[31] reported that obesity in adolescence was related to an increase in carotid IMT among healthy young Korean men but not in women. In our study, the incidence of carotid IMT over 0.6 mm, which is over the 2 standard deviations of carotid IMT of the control group, was higher in obese boys (26.7%) than in obese girls (16.7%) but there was no significant difference.

Limitations of this study were first, only 154 of a high school in Seoul were included and the number of the objectives was small. Second, although, the mean BMI of boys was not different from that of girls, we did not adjust the BMI on the results statistically.

In conclusion, comorbidities of obesity in adolescents are more prevalent and severe in the male sex. We can infer that these characteristics reflect some parts of adult obesity.

References

1. Moller DE, Flier JS. Insulin resistance--mechanisms, syndromes, and implications. N Engl J Med 1991;325:938-48.

2. Beauloye V, Zech F, Tran HT, Clapuyt P, Maes M, Brichard SM. Determinants of early atherosclerosis in obese children and adolescents. J Clin Endocrinol Metab 2007;92:3025-32.

3. Tershakovec AM, Kuppler KM, Zemel BS, Katz L, Weinzimer S, Harty MP, et al. Body composition and metabolic factors in obese children and adolescents. Int J Obes Relat Metab Disord 2003;27:19-24.

4. Moran A, Jacobs DR Jr, Steinberger J, Hong CP, Prineas R, Luepker R, et al. Insulin resistance during puberty: results from clamp studies in 357 children. Diabetes 1999;48:2039-44.

5. Travers SH, Jeffers BW, Bloch CA, Hill JO, Eckel RH. Gender and Tanner stage differences in body composition and insulin sensitivity in early pubertal children. J Clin Endocrinol Metab 1995;80:172-8.

6. Rumack CM, Wilson SR, Charbonean JW. Diagnostic ultrasound. 3rd ed. St. Louis: Elsevier Mosby, 2005:95-7.

7. Geer EB, Shen W. Gender differences in insulin resistance, body composition, and energy balance. Gend Med 2009;6 Suppl 1:60-75.

8. Garaulet M, Pérex-Llamas F, Fuente T, Zamora S, Tebar FJ. Anthropometric, computed tomography and fat cell data in an obese population: relationship with insulin, leptin, tumor necrosis factor-alpha, sex hormone-binding globulin and sex hormones. Eur J Endocrinol 2000;143:657-66.

9. Seidell JC, Cigolini M, Charzewska J, Ellsinger BM, Deslypere JP, Cruz A. Fat distribution in European men: a comparison of anthropometric measurements in relation to cardiovascular risk factors. Int J Obes Relat Metab Disord 1992;16:17-22.

10. Pouliot MC, Després JP, Lemieux S, Moorjani S, Bouchard C, Tremblay A, et al. Waist circumference and abdominal sagittal diameter: best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. Am J Cardiol 1994;73:460-8.

11. Janssen I, Heymsfield SB, Allison DB, Kotler DP, Ross R. Body mass index and waist circumference independently contribute to the prediction of nonabdominal, abdominal subcutaneous, and visceral fat. Am J Clin Nutr 2002;75:683-8.

12. Björntorp P. "Portal" adipose tissue as a generator of risk factors for cardiovascular disease and diabetes. Arteriosclerosis 1990;10:493-6.

13. Wajchenberg BL. Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. Endocr Rev 2000;21:697-738.

14. Ritchie SA, Connell JM. The link between abdominal obesity, metabolic syndrome and cardiovascular disease. Nutr Metab Cardiovasc Dis 2007;17:319-26.

15. Huang TT, Johnson MS, Figueroa-Colon R, Dwyer JH, Goran MI. Growth of visceral fat, subcutaneous abdominal fat, and total body fat in children. Obes Res 2001;9:283-9.

16. Machann J, Thamer C, Schnoedt B, Stefan N, Stumvoll M, Haring HU, et al. Age and gender related effects on adipose tissue compartments of subjects with increased risk for type 2 diabetes: a whole body MRI/MRS study. MAGMA 2005;18:128-37.

17. Leung KC, Johannsson G, Leong GM, Ho KK. Estrogen regulation of growth hormone action. Endocr Rev 2004;25:693-721.

18. Wanless IR, Lentz JS. Fatty liver hepatitis (steatohepatitis) and obesity: an autopsy study with analysis of risk factors. Hepatology 1990;12:1106-10.

19. Jang HO, Lee CG, Kang YJ. The prevalent rates of abnormal serum aminotransferase levels and total cholesterol levels among adolescents with obesity. J Korean Pediatr Soc 2002;45:1484-90.

20. Wiegand S, Keller KM, Röbl M, L'Allemand D, Reinehr T, Widhalm K, et al. Obese boys at increased risk for nonalcoholic liver disease: evaluation of 16,390 overweight or obese children and adolescents. Int J Obes (Lond) 2010;34:1468-74.

21. Clark JM, Brancati FL, Diehl AM. Nonalcoholic fatty liver disease. Gastroenterology 2002;122:1649-57.

22. Schwimmer JB, McGreal N, Deutsch R, Finegold MJ, Lavine JE. Influence of gender, race, and ethnicity on suspected fatty liver in obese adolescents. Pediatrics 2005;115:e561-5.

23. Shimizu I, Inoue H, Yano M, Shinomiya H, Wada S, Tsuji Y, et al. Estrogen receptor levels and lipid peroxidation in hepatocellular carcinoma with hepatitis C virus infection. Liver 2001;21:342-9.

24. Anezaki Y, Ohshima S, Ishii H, Kinoshita N, Dohmen T, Kataoka E, et al. Sex difference in the liver of hepatocyte-specific Pten-deficient mice: a model of nonalcoholic steatohepatitis. Hepatol Res 2009;39:609-18.

25. Strauss RS, Barlow SE, Dietz WH. Prevalence of abnormal serum aminotransferase values in overweight and obese adolescents. J Pediatr 2000;136:727-33.

26. Lavine JE, Schwimmer JB. NAFLD/NASH in children. In: Farrell G, George J, Hall P, McCollough AJ, editors. Fatty liver disease: NASH and related disorders. Oxford: Blackwell Publishing, 2004:229-40.

27. Bacon BR, Farahvash MJ, Janney CG, Neuschwander-Tetri BA. Nonalcoholic steatohepatitis: an expanded clinical entity. Gastroenterology 1994;107:1103-9.

28. Gnasso A, Irace C, Mattioli PL, Pujia A. Carotid intima-media thickness and coronary heart disease risk factors. Atherosclerosis 1996;119:7-15.

29. Raitakari OT, Juonala M, Kähönen M, Taittonen L, Laitinen T, Mäki-Torkko N, et al. Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. JAMA 2003;290:2277-83.

30. Caserta CA, Pendino GM, Amante A, Vacalebre C, Fiorillo MT, Surace P, et al. Cardiovascular risk factors, nonalcoholic fatty liver disease, and carotid artery intima-media thickness in an adolescent population in southern Italy. Am J Epidemiol 2010;171:1195-202.

31. Lee YJ, Nam CM, Kim HC, Hur NW, Suh I. The association between obesity indices in adolescence and carotid intima-media thickness in young adults: Kangwha Study. J Prev Med Public Health 2008;41:107-14.

32. Kim SK, Kim HJ, Hur KY, Choi SH, Ahn CW, Lim SK et al. Visceral fat thickness measured by ultrasonography can estimate not only visceral obesity but also risks of cardiovascular and metabolic disease. Am J Clin Nutr 2004;79:593-9.