Original Paper

HORMONE RESEARCH

Horm Res 2009;71:83–88
DOI: 10.1159/000183896

Received: September 10, 2007
Accepted: March 14, 2008
Published online: January 8, 2009

Triglycerides and Alanine Aminotransferase as Screening Markers for Suspected Fatty Liver Disease in Obese Children and Adolescents

Ana M. Oliveira[a, b] Nelson Oliveira[b] Jussara C. Reis[c] Marcos V. Santos[b]
Agnaluce M. Silva[d] Luis Adan[a]

[a]Department of Pediatrics, Federal University of Bahia School of Medicine, Salvador; [b]Department of Health, State University of Feira de Santana, and [c]Cleriston Andrade General Hospital, Feira de Santana, and [d]Clinical Pathology Laboratory, Salvador, Bahia, Brazil

Key Words
Metabolic syndrome · Obesity · Suspected fatty liver disease · Screening procedures · Pediatrics

Abstract
Background/Aims: Metabolic syndrome (MS) and fatty liver disease (FLD) are on the rise. The association between these conditions in Brazilian youth is analyzed. ***Methods:*** 354 subjects (11.2 ± 3.1 years) were evaluated. FLD was suspected by ultrasound and computed tomography; weight and MS by BMI z-score and NCEP-ATPIII respectively. ***Results:*** Subjects were classified as: group 1 with suspected FLD and group 2 without and group 2 as 'a' (overweight/obese) and 'b' (normal weight). Comparing group 1 with 2a and 2b, differences in age ($p = 0.016$; $p = 0.075$), triglycerides (TG) ($p = 0.021$; $p = 0.002$), insulin ($p = 0.652$; $p = 0.015$) and homeostasis model assessment method of IR (HOMA-IR) ($p = 0.737$; $p = 0.003$) were found. Group 2a was divided into low/high alanine aminotransferase (ALT). A decrease in waist circumference and TG was found going from those with suspicion of FLD to obese with high and low ALT. Insulin and HOMA-IR in group 1 and high ALT were similar. Gender (OR 6.6; CI 1.9–22.5; $p = 0.025$), age (OR 1.3; CI 1.1–1.6; $p = 0.006$), TG (OR 10.4; CI 3.1–34.4; $p = 0.005$) were associated with suspected FLD. For every 10 U/l increase in ALT, there was a 4-fold greater chance of probable FLD (OR 4.01; CI 2.06–9.40; $p < 0.001$). ***Conclusion:*** Measurements of ALT and TG should be considered as screening for suspected FLD in overweight/obese youth.

Introduction

Over the last two decades the prevalence of obesity has increased and has become epidemic also in developing countries [1, 2]. A previous study of our group reported a prevalence of 13.7% of excessive weight in Brazilian children [3].

Related to obesity, fatty liver disease (FLD) is on the rise and has been reported worldwide (10–51%) and recent data based upon histological findings showed a prevalence of 9.6% for subjects aged 2–9 years, increasing with age and weight [4, 5]. In this way, FLD has become the most common chronic liver condition and an important cause of unexplained abnormal liver function tests, particularly alanine aminotransferase (ALT) among youth [4, 6, 7].

FLD comprises a broad spectrum of liver damage and probably this fat accumulation in the liver per se is not a

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

0301–0163/09/0712–0083$26.00/0

Accessible online at:
www.karger.com/hre

Ana Mayra Oliveira
Av. Maria Quitéria, 1660
Feira de Santana, BA 44025-250 (Brazil)
Tel./Fax +55 75 3625 4027
E-Mail anamayra@uol.com.br

benign condition [8]; studies have confirmed the association of FLD with a pronounced dyslipidemic profile [9] and suggested that high ALT may serve as a surrogate marker for metabolic syndrome (MS) [10].

The histological confirmation of FLD is still the gold standard for diagnosis but noninvasive diagnostic tests, such as measurement of hepatic enzymes and radiological imaging, are commonly used in children [11] with suspected FLD. Its pathogenesis is poorly understood and as yet, limited information is available on its natural history in the pediatric population [12]. Hyperinsulinemia, associated with insulin resistance (IR) appears to be an important component of its pathogenetic mechanism. FLD has been found to be associated with the MS, even in children [13].

The aim of this study was to analyze metabolic and hepatic parameters in a sample of overweight and obese Brazilian school-aged youngsters. We further evaluated the association of probable FLD with IR, and the components of the MS in this relatively large sample of Brazilian children and adolescents from northeastern Brazil.

Methods

The study was conducted in state and private schools in Feira de Santana, Bahia, Brazil, and 354 students (202 girls; 200 with excessive weight; 11.2 ± 3.1 years) were included in the protocol. Data on duration of obesity were self-reported. To be eligible the subjects were required to fulfill the following criteria: no history of current or past excessive alcohol drinking as defined by an average daily consumption of >20 g of alcohol and absence of history and clinical, biochemical or ultrasound (US) findings consistent with cirrhosis and other chronic liver diseases. None of them were taking drugs known to affect liver function.

The local Human Research Ethics Committee reviewed and approved the study and written informed consent/assent was obtained from guardians and children/adolescents.

Protocol

The students attended the clinic initially to undergo a clinical and anthropometric examination, followed by US and computed tomography (CT) liver evaluation. A standard 2-hour oral glucose tolerance test was performed, in accordance with the American Diabetes Association guidelines [14]. Blood samples were withdrawn for the fasting measurement of glucose, insulin, aspartate aminotransferase (AST), ALT, γ-glutamyltranspeptidase (γ-GT), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG) and at 120 min, to measure glucose. In addition, individuals with suspected FLD had a complete evaluation of iron status (serum iron, transferrin and ferritin concentrations) and serology to exclude hemochromatosis and viral hepatitis (hepatitis B surface antigen [HBsAg], hepatitis B-C total [HBC-t], antibody against hepatitis A virus; immunoglobulin G [HAVC-IgG] and hepatitis C virus immunoglobulin G [HCV-IgG]).

Assessment of Suspected Fatty Liver Disease

FLD was suspected by the appearance of the liver on US, and by CT in those in whom the US suggested FLD [11]. ALT was chosen as the principal marker of liver injury even though AST and γ-GT were also measured. The cut-off point for abnormal serum enzymes was defined as: AST >35 and >41 U/l; ALT >35 and >40 U/l; γ-GT >40 and >60 U/l for girls and boys, respectively [15].

Ultrasonographic Evaluation

A real-time US examination of the liver was performed in all subjects using a 5-MHz curvilinear transducer in younger children and a 3.75-MHz transducer in older or markedly obese children. All US procedures were performed with an Aloka SSD 5500 US machine, used by the same, experienced sonographer, who was unaware of the aims of the study and blind to clinical and laboratory analyses.

The suspicion of FLD was assessed qualitatively as being present or absent. Steatosis was suspected on the basis of liver echotexture, liver-diaphragm differentiation in echo amplitude, hepatic echo penetration and clarity of hepatic blood vessels [16].

Computed Tomography Imaging

All individuals suspected of FLD by US underwent a CT evaluation, performed with a single-detector row helical scanner (Siemens; Model Somatom Sprit). Contiguous transverse images were acquired through the liver with 5 mm collimation, during a single breath-hold, without intravenous administration of a contrast agent, using these parameters: Pitch = 2; Kv = 130; Mas = 105, and rotation time 1.5 s.

The unenhanced CT images were retrospectively reviewed by only one radiologist, blind to clinical, biochemical and US findings. For each case, the hepatic attenuation was measured by means of a random selection of circular regions of interest that ranged between 8.72 and 19.05 cm^2, selecting areas of most interest and avoiding areas of visible hepatic vascular and biliary structures. The liver attenuation index (difference between mean hepatic attenuation and mean splenic attenuation) was used to predict the degree of steatosis [17]. Suspicion of FLD was assessed qualitatively as being present or absent.

Definitions

In accordance with the criteria of the National Cholesterol Education Program – Adult Treatment Panel III [18] modified for age, the MS was diagnosed by the concomitant presence of at least three of the following five clinical features: waist circumference (WC) >75th percentile [19]; fasting plasma glucose ≥100 mg/dl, or 2 h glucose post-challenger between 140 and 199 and ≥200 mg/dl [14]; TG >100 and >130 mg/dl for younger than 10 years and between 10 and 19 years, respectively [20]; high-density lipoprotein cholesterol (HDL-C) <40 and <35 mg/dl for younger than 10 years and between 10 and 19 years, respectively [20], and arterial systolic/diastolic blood pressure (BP) ≥95th percentile by height percentile for age and gender [21].

To compare body mass index (BMI) across different ages and in both boys and girls, BMI z-score was calculated and a threshold of 1.5 SD or more defined excessive weight. The subjects were then classified as overweight (z-score of 1.5–2.0 SD) or obese (z-score >2.0 SD).

The WC was measured using the methodology described by the National Center of Health Statistics [22] and the blood pres-

Table 1. Baseline anthropometric, clinical and metabolic characteristics of the study

Variables	Group 1 (n = 10)	Group 2a (n = 190)	p[1]	Group 2b (n = 154)	p[2]
Age, years	13.4 ± 2.5	10.7 ± 3.2	0.016	11.7 ± 2.8	0.075
Boys/girls	8/2	98/92	0.015	46/108	0.003
Ethnic group (White/Mulatto/Black)	9/1/0	85/62/43	0.022	47/68/39	<0.001
BMI (z-score)	2.0 ± 0.3	2.1 ± 0.3	0.646	0.1 ± 1.2	<0.001
WC, cm	100.3 ± 12.1	90.2 ± 13.3	0.004	72.3 ± 11.6	<0.001
Triglycerides, mg/dl	159.5 ± 54.8	126.0 ± 66.6	0.021	93.8 ± 58.1	<0.001
HDL-C	37.0 ± 9.2	38.8 ± 7.9	0.557	41.5 ± 8.6	0.164
HOMA-IR, log	4.6 ± 3.6	4.3 ± 3.3	0.737	2.2 ± 1.8	0.030
Insulin, μU/ml	27.6 ± 23.1	23.0 ± 16.5	0.652	12.1 ± 10.1	0.015
AST, U/l	49.5 ± 23.9	28.6 ± 8.1	0.001	25.9 ± 6.4	0.006
γ-GT, U/l	22.0 ± 8.6	16.6 ± 6.8	0.004	13.4 ± 4.6	0.006
ALT means, U/l	52.0 ± 28.8	26.1 ± 9.0	<0.001	23.3 ± 6.8	0.006
ALT median, U/l	42.0	28.0	<0.001	22.5	<0.001

Data are expressed as mean ± SD (range) and frequencies (%). Frequencies for 'yes' group. Groups: 1 = with suspected FLD; 2a = with excessive weight and without FLD; 2b = normal weight and without FLD.
[1] Comparison of group 1 with group 2a. [2] Comparison of group 1 with group 2b.

sure according to the Task Force on Blood Pressure Control in Children [21]. The anthropometric measurements were taken in triplicate and the mean value was used.

The homeostasis model assessment method of IR (HOMA-IR) based on serum fasting glucose and insulin levels (product of glucose concentrations [expressed as milligrams per deciliter] and insulin [expressed as milliunits per milliliter] divided by a constant [405]) was used as a measure of IR. The cut-off used was 3.16, as described by Keskin et al. [23].

Laboratory Analyses

Sera were stored at –70°C until they were analyzed. AST, ALT and γ-GT concentrations were measured using a standard automated kinetic enzymatic assay. Plasma glucose, HDL-C and TG concentrations were measured by automated enzymatic photometry; serum insulin levels with a solid phase radioimmunoassay unit (Linco Laboratories); iron, ferritin and transferrin, respectively by the ferrozine, immunoluminometry and nephelometry methods, and markers, such as HBsAg, by automatic immunoluminometry, HBC-t by microparticle enzymometric assay, HAVG-IgG and HCV-IgG by immunoenzymometric assay.

Statistical Analysis

A descriptive analysis was performed, continuous variables being expressed as mean values ± SD and categorical variables as frequencies and proportions. χ^2 test or Fisher's exact test were used whenever appropriate. Multivariate analysis was done using logistic regression. In the model, variables that attained 20% of significance in the univariate analysis were included plus the five individual components of MS and IR. In the final model only the statistically significant covariables were maintained. SPSS (Statistical Packard for Social Sciences) for Windows statistical software version 10.0 was used for all calculations. A p value <0.05 defined statistical significance.

Results

Twelve subjects (3.4%) with probable FLD (by US) underwent the CT evaluation; 10 of them (2.8%, group 1) fulfilled the criteria for this suspicion. The remaining 344 subjects were included in two comparison groups: 2a (n = 190), with excessive weight, and 2b (n = 154), with normal weight.

There were significant differences in clinical, laboratory, and anthropometric data among the groups (table 1). Of note: those with suspected FLD (group 1) were older (p = 0.016) and had higher WC (p = 0.004) than the obese (group 2a). The preponderance of boys (n = 8) and Whites (n = 9) was significantly different from the comparison groups (table 1).

Subjects with suspected FLD had higher levels of TG (p = 0.021), ALT (p < 0.001), AST (p = 0.001) and γ-GT (p = 0.004), when compared with the excessive weight subjects (group 2a), and the normal weight subjects in group 2b (except for age). The mean fasting insulin levels and HOMA-IR values (27.6 ± 23.1 μU/ml; 4.6 ± 3.6) in the suspected FLD group were higher than those in group 2a (23.0 ± 16.5 μU/ml; 4.3 ± 3.3) and 2b (12.1 ± 10.1 μU/ml; 2.2 ± 1.8), but statistical significance was reached only between groups 1 and 2b.

The prevalence of MS in groups 1, 2a and 2b was 40.0, 27.4 and 0% respectively. No case of diabetes melllitus, impaired glucose tolerance or impaired fasting glucose was diagnosed. The other variables related to the MS

Table 2. Baseline anthropometric, clinic and metabolic characteristics of subjects with suspected FLD compared with two subgroups (high or low ALT) of non-FLD obese subjects

Variables	Group 1 (n = 10)	Group 2a high ALT (n = 94)	p^1	Group 2a low ALT (n = 96)	p^2	p^3
Age, years	13.4 ± 2.5	10.9 ± 3.4	0.024	10.6 ± 3.1	0.015	0.834
Boys/girls	2/8	55/39	0.105	43/53	0.011	0.289
Ethnic group (White/Mulatto/Black)	9/1/0	44/35/15	0.044	41/36/19	0.015	0.243
Duration of obesity, years	8.5 ± 4.0	6.4 ± 4.5	0.090	6.4 ± 4.2	0.075	0.747
BMI (z-score)	3.6 ± 0.8	2.1 ± 0.4	0.878	2.0 ± 0.3	0.333	0.014
WC, cm	100.3 ± 12.1	91.6 ± 13.2	0.016	88.9 ± 13.4	0.002	0.018
SBP, mm Hg	117.3 ± 11.0	112.6 ± 15.1	0.144	110.0 ± 16.9	0.033	0.104
DBP, mm Hg	74.3 ± 13.4	70.5 ± 11.7	0.278	69.8 ± 13.6	0.119	0.118
Glucose, mg/dl	71.0 ± 9.7	75.2 ± 9.8	0.282	76.2 ± 9.8	0.159	0.274
Triglycerides, mg/dl	159.5 ± 54.8	131.3 ± 68.0	0.049	120.7 ± 65.2	0.012	0.133
HDL-C, mg/dl	37.0 ± 9.2	37.9 ± 8.5	0.452	39.6 ± 7.2	0.303	0.199
HOMA-IR	4.6 ± 3.6	4.8 ± 3.5	0.935	3.9 ± 3.0	0.495	0.030
MS components, n	2.3 ± 0.6	2.1 ± 0.9	0.257	1.9 ± 0.9	0.073	0.215
Insulin, μU/ml	27.6 ± 23.1	25.5 ± 17.8	0.928	20.5 ± 14.8	0.457	0.014
ALT, U/l	52.0 ± 28.8	33.0 ± 7.6	0.002	19.5 ± 3.9	<0.001	<0.001
AST, U/l	49.5 ± 23.9	31.8 ± 8.5	0.007	25.4 ± 6.4	<0.001	<0.001
γ-GT, U/l	22.0 ± 8.6	17.9 ± 7.2	0.025	15.3 ± 6.3	0.001	0.003

Data are expressed as mean ± SD (range).

Groups: 1 = with suspected FLD; 2a = with excessive weight and without FLD; 2b = normal weight and without FLD; high and low ALT were based on ALT median from group 2a.

[1] Comparison of group 1 with group 2a high ALT. [2] Comparison of group 1 with group 2a low ALT. [3] Comparison of group 2a low ALT and group 2a high ALT.

were compared between subjects in groups 1 and 2a, both with excessive weight; hypertriglyceridemia was the only one significantly higher in patients with suspected FLD (159.5 ± 54.8 vs. 126.0 ± 66.6; p = 0.021). As expected, the comparison with normal weight controls (2b) showed significant differences for all the variables evaluated, except for the HDL-C levels (37.0 ± 9.2 vs. 38.8 ± 7.9, p = 0.557).

Hypertriglyceridemia was positively correlated with AST (r = 0.20, p < 0.001), ALT (r = 0.16, p = 0.002), γ-GT (r = 0.20, p = 0.002) and BMI z-score (r = 0.31, p < 0.001), and negatively with HDL-C levels (r = –0.20, p < 0.001) in the whole population.

In view of the wide variation in ALT in group 2a (without a positive CT examination suggestive of FLD) the authors elected to further classify it as high or low ALT based on the median of ALT (25 U/l). When differences in demographic, anthropometric and metabolic variables (table 2) were assessed between these two subgroups and group 1, significant differences were found for age (p = 0.024; p = 0.015), ethnic group (p = 0.044; p = 0.015), WC (p = 0.016; p = 0.002), TG (p = 0.049; p = 0.012), AST (p = 0.007; p < 0.001) and γ-GT (p = 0.025; p = 0.001) (table 2). The highest level of fasting insulin and HOMA-IR were found in group 1, followed by group 2a high ALT and group 2a low ALT (with no statistical significance). There was a positive correlation between TG and ALT in group 2a high ALT (r = 0.224, p = 0.015).

The comparisons between the two subgroups showed that the 2a high ALT had higher levels of BMI (p = 0.014), WC (p = 0.018), fasting insulin (p = 0.014), HOMA-IR (p = 0.030), AST (p < 0.001) and γ-GT (p = 0.003) than group 2a low ALT (table 2).

In a multiple logistic regression analysis, including the covariates with statistical significance in the bivariate analysis (see table 1), gender (OR 6.6; CI 1.9–22.5; p = 0.025), age (OR 1.3; CI 1.1–1.6; p = 0.006), and TG (OR 10.4; CI 3.1–34.4; p = 0.005) were the covariates independently associated with the presence of suspected FLD. Furthermore, using the same analysis, adjusted for age, gender and ethnic group, an increase of 10 U/l in ALT was significantly associated with the presence of suspected FL (OR 4.01; CI 2.06–9.40, p < 0.001).

Discussion

The escalating rise in the prevalence of obesity in children and adolescents in developing countries is of great concern [1–3]. The myth that chronic disease, such as obesity, and its consequences affect only developed countries and only the elderly is no longer true [24].

According to the International Diabetes Federation [25], to be defined as having MS, a person must have central obesity as measured by WC. In addition, biochemical measurements of fasting hyperglycemia and dyslipidemia ought to be present. Although not an essential part of the definition of MS, the presence of elevated ALT, as a surrogate marker of liver injury or FLD, has often also been considered. In the present study, the prevalence rate of suspected FLD was 2.8% and all of the subjects were obese. In addition, the abdominal obesity and the duration of excessive weight were significantly associated with fatty liver accumulation. This prevalence of suspected FLD is lower than that described in other studies. Whether ethnicity, the short duration of obesity in the sample and the apparent low sensitivity of US have influenced or not this finding deserves further investigation.

Data from pediatric clinical series support the contention that nonalcoholic fatty liver disease (NAFLD) is more common in boys than in girls [26], which has been confirmed in the present study (4:1 ratio). One possible explanation for this finding is that men are more likely to distribute excess body fat in the intra-abdominal compartment. This hypothesis has, however, not yet been tested in the pediatric age range. The high prevalence of White subjects in the group with suspected FLD and the absence of Afro descendents, in spite of a total of 18.6% in the sample, is consistent with a clinical series conducted with NAFLD in which a lower rate of FLD in obese Black children and adolescents was demonstrated [26].

Recent studies have shown that obesity, IR and MS and its components (hypertriglyceridemia, low HDL-C, high blood pressure, hyperglycemia) are associated with an increased prevalence of NAFLD, although it is not clear why simple hepatic steatosis develops in some subjects, whereas NAFLD and progressive disease develop in others, nor how the precise sequence of events leading to the development of FLD occurs [27]. The prevalence of MS was higher in patients with suspicion of FLD (40%) than in obese ones without this condition (27.4%). In spite of the similarities (insulin and HOMA-IR values) between the two groups, patients with probable FLD were older and had higher values of WC, indicating that the hepatic lesion could be an additional criterion for MS, clearly related with abdominal obesity and its duration. Also, it must be emphasized that no dysfunction on glucose metabolism was found in the present study, suggesting that this alteration appears later in life.

The lack of association between suspicion of FLD and MS in this sample is probably due to the subjects' low mean age and the short duration of excessive weight, which may indicate that more time is required for the metabolic disturbances to develop.

The authors reported here that the group with probable FLD had higher ALT levels in agreement with studies from other developed countries [28, 29]. It is worth noting that when the group without suspicion of FLD, but with excessive weight, was classified into two subgroups based on median ALT levels, those above median were more obese, had more abdominal obesity and had more IR, moreover a positive correlation between ALT and TG was found. Hence, the measurement of ALT in overweight and obese youngsters may represent not only possible liver injury but also a state of IR, with all of its known consequences. After adjustment for age, gender and ethnic group, this study showed that for an increase of 10 U/l in the level of ALT, there is a 4 times greater risk in children and adolescents with excessive weight for the development of probable FLD, and that high TG levels are strongly associated with its development (OR 10.4).

In conclusion, the present study shows that excessive weight in children and adolescents is related to hypertriglyceridemia, high ALT levels, IR state, and probable FLD. For an indisputable diagnosis, liver biopsy – not easily performed – would be necessary. However, our consistent results suggest that simultaneous measurements of ALT and TG are very valid screening tools for identifying states of IR and suspected FLD, especially in developing countries. Thus, low-cost and cost-effective programs should be implemented in order to improve outcomes.

Acknowledgments

The authors thank the children, parents, teachers and school authorities from Feira de Santana, BA, Brazil, as well as Clarimar Valle and her group from the Brazilian's University (UnB) and Prof. Sonia Caprio, for their cooperation. This study was supported by The Research Foundation of Bahia (FAPESB), Bahia, Brazil.

References

1 Hossain P, Kawar B, El Nahas M: Obesity and diabetes in the developing world – a growing challenge. N Engl J Med 2007;356:213–215.
2 Veiga GVV, Cunha AS, Sichieri R: Trends in overweight among adolescents living in the poorest and richest regions of Brazil. Am J Public Health 2004;94:1544–1548.
3 Oliveira AM, Oliveira AC, Almeida MS, Oliveira N, Adan L: Influence of the family nucleus on obesity in children from northeastern Brazil: a cross-sectional study BMC Public Health 2007;7:235.
4 Schwimmer JB, Deutsch R, Kahen T, Lavine JE, Stanley C, Behling C: Prevalence of fatty liver in children and adolescents. Pediatrics 2006;118:1388–1393.
5 Quiros-Tejeira RE, Rivera CA, Ziba TT, Mehta N, Smith CW, Butte NF: Risk for nonalcoholic fatty liver disease in Hispanic youth with BMI ≥ 95th percentile. J Pediatr Gastroenterol Nutr 2007;44:228–236.
6 Lavine JE, Schwimmer JB: Nonalcoholic fatty liver disease in the pediatric population. Clin Liver Dis 2004;8:549–588, viii–ix.
7 Adams LA, Angulo P, Lindor KD: Nonalcoholic fatty liver disease. CMAJ 2005;172:889–905.
8 Angulo P: Nonalcoholic fatty liver disease. N Engl J Med 2002;346:1221–1231.
9 Cali AM, Zern TL, Taksali SE, Oliveira AM, Dufour S, Otvos JD, Caprio S: Diab Care 2007;30:3093–3098.
10 Oliveira AC, Oliveira AM, Almeida MS, Silva AM, Adan L, Ladeia AM: Alanine aminotransferase and high sensitivity C-reactive protein: correlates of cardiovascular risk factors in youth. J Pediatr 2008;152:337–342.
11 Chan DF, Li AM, Chu WC, Chan MH, Wong EM, Liu EK, Chan IH, Yin J, Lam CW, Fok TF, Nelson EA: Hepatic steatosis in obese Chinese children. Int J Obes Relat Metab Disord 2004;28:1257–1263.
12 Burget TS, Taksali SE, Dziura J, Goodman TR, Yeckel CW, Papademetris X, Constable RT, Weiss R, Tamborlane WV, Savoye M, Seyal AA, Caprio S: Alanine aminotransferase levels and fatty liver in childhood obesity: associations with insulin resistance, adiponectin, and visceral fat. J Clin Endocrinol Metab 2006;91:4287–4294.
13 Wieckowska A, Feldstein AE: Nonalcoholic fatty liver disease in the pediatric population: a review. Curr Opin Pediatr 2005;17:636–641.
14 American Diabetes Association: Diagnosis and classification of diabetes mellitus. Diabetes Care 2006;29:S43–S48.
15 Tietz NW, Pruden EL, McPherson RA, Fuhrman SA: Clinical Guide to Laboratory Tests, ed 3. Philadelphia, Saunders, 1995, p 1096.
16 Tominaga K, Kurata JH, Chen YK, Fujimoto E, Miyagawa S, Abe I, Kusano Y: Prevalence of fatty liver in Japanese children and relationship to obesity: an epidemiological ultrasonographic survey. Dig Dis Sci 1995;40:2002–2009.
17 Limanond P, Raman SS, Lassman C, Sayre J, Ghobrial RM, Busuttil RW, Saab S, Lu DSK: Macrovesicular hepatic steatosis in living related liver donors: correlation between CT and histologic findings. Radiology 2004;230:276–280.
18 Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285:2486–2497.
19 Fernandez JR, Redden DT, Pitrobelli A, Allison DB: Waist circumference percentiles in nationally representative samples of African-American, European-American, and Mexican-American children and adolescents. J Pediatr 2004;145:439–444.
20 III Diretrizes Brasileiras sobre Dislipidemias e Diretriz de Prevenção da Aterosclerose do Departamento de Aterosclerose da Sociedade Brasileira de Cardiologia. Arq Bras Cardiol 2001;77(suppl 3):1–48.
21 Update on the 1987 Task Force Report on High Blood Pressure in Children and Adolescents: A working group report from the National High Blood Pressure Education Program. National High Blood Pressure Education Program Working Group on Hypertension Control in Children and Adolescents. Pediatrics 1996;98:649–658.
22 National Health and Nutrition Examination Survey: Anthropometry Procedures Manual. Available online at: http://www.cdc.gov/nchs/data/nhanes/bm.pdf.2002. Accessed on: Oct, 2005.
23 Keskin M, Kurtolgu S, Kendirci M, Atabek ME, Yazici C: Homeostasis model assessment is more reliable than the fasting glucose/insulin ratio and quantitative insulin sensitivity check index for assessing insulin resistance among obese children and adolescents. Pediatrics 2005;115:500–503.
24 Anderson GF, Chu E: Expanding priorities – confronting chronic disease in countries with low income. N Engl J Med 2007:356:209–211.
25 International Diabetes Federation: The IDF consensus worldwide definition of the metabolic syndrome. 2005. Available on line at: http://www.idf.org. Accessed on 02.08.2005.
26 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;115:561–565.
27 Angelico F, Ben MD, Conti R, Francioso S, Feole K, Fiorello S, Cavallo MG, Zalunardo B, Lirussi F, Alessandri C, Violi F: Insulin resistance, the metabolic syndrome, and nonalcoholic fatty liver disease. J Clin Endocrinol Metab 2005;90:1578–1582.
28 Yamada J, Tomiyama H, Yambe M, Koji Y, Motobe K, Shiina K, Yamamoto Y, Yamashina A: Elevated serum levels of alanina aminotransferase and γ-glutamyltransferase are markers of inflammation and oxidative stress independent of the metabolic syndrome. Atherosclerosis 2006;189:198–205.
29 Fraser A, Longnecker MP, Lawlor DA: Prevalence of elevated alanine aminotransferase among US adolescents and associated factors: NHANES 1999–2004. Gastroenterology 2007;133:1814–1820.