SERUM ALANIN AMINOTRANSFERASE (ALT) ACTIVITY IN OVERWEIGHT AND OBESE SUBJECTS

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Abstract

Introduction: ALT activity is frequently observed among overweight obese subjects, and has been used as a marker of nonalcoholic fatty liver disease and nonalcoholic steato-hepatitis. The present study aimed to know the prevalence of ALT elevation in overweight and obese subjects and to determinate the association between ALT level and anthropometric and biochemical parameters.

Methods: This cross-sectional was conducted among a sample of 100 overweight (BMI in kg/m2 >25) adults, 47 male (47%) and 53 female (53%), with median age 46.40+/-10.89 years. Blood samples were drown for the measurements of total bilirubin, ALT, glucose, insulin, cholesterol, HDL-cholesterol and triglycerides. Insulin resistance (IR) was calculated by means of the homeostasis model assessment. It was assumed IR when the HOMA-IR >3.7 and BMI >27.5kg/sqm. Fatty liver was diagnosed by ultrasonography detection of the most characteristic features of fatty infiltration of the liver, regarding to its echo texture, echo penetration, live-diaphragm differentiation of echo amplitude and the clarity of the liver blood vessel structure. The scoring system was used in order to graduate the severity of liver pathology. Hi-square test were used for comparison of mean values of ALT by the number of components to the metabolic syndrome. Logistic regression analysis was performed to determinate the risk of elevated ALT according to the number of component of anthropometric and metabolic syndrome. $P > 0.005$ was considered statistically significant.

Results: Overall 34 were (34%) overweight, 36 had obesity (36%) grade I, 19 grade II (19%) and 11 obesity (11%) grade III. Elevated ALT levels was seen in 23% of the subjects and were documented mostly in the category of obesity grade II (12 of 19 subjects) and obesity grade III (11 of 11 participants), respectively 48.8+/-4.56UI/l and 89.7+/- UI/l. ALT concentration was significantly correlated with anthropometric criteria, such as BMI ($p<0.001$) and abdominal parameter ($p<0.001$), severity of fatty liver infiltration ($p<0.001$) and insulin resistance ($p<0.001$). Logistic regression model shown that the prevalence of ALT elevation was positively associated with increasing BMI ($p=0.028$) and blood concentration of insulin ($p=0.028$).

Conclusions: The current study established overweight and obesity as a major risk factors for ALT elevation and that BMI and fasting insulin were the strongest risk factors for that elevation of serum concentration ALT.

Key words: ALT, overweight, obesity, fatty liver infiltration, non-alcoholic steato-hepatitis.

Introduction

TThe prevalence of overweight and obesity in adults, as well in children, are rapidly increasing, nearly doubled since 1980, becoming a very serious health problem. Overweight and obesity are in fact the fifth leading risk for global health. The WHO estimates that in 2005 approximately 1.6 billion people worldwide were overweight and at least 400 million adults were obese. They further project that by 2015, approximately 2.3 billion adults will be overweight and that at least 700 million will be obese (1).

Non-alcoholic steato-hepatitis is considered as hepatic manifestation of the metabolic syndrome, a set of disorders which include obesity, diabetes mellitus, dyslipidemia, atheroschlerosis and hypertension and etiologically associated with insulin resistance (2,3). Non-alcoholic steato-hepatitis is classified into 2 categories : simple fatty liver, which has a favorable clinical outcome, and non-alcoholic steato-hepatitis, which can result in chronic liver disease, with the risk of progression to liver cirrhosis or hepatocelullar carcinoma (4,5).

Non-alcoholic steato-hepatitis is considered the major cause of abnormal liver function test of unknown

origin. ALT is the liver enzyme with the closest association with the liver fatty accumulation, which is frequently observed among overweight and obese subjects, and has been used as a circulating marker of non-alcoholic fatty liver disease and non-alcoholic steato-hepatitis (6,7,8,9). The present study aimed to know the prevalence of serum ALT elevation in overweight and obese subjects and to determine the assessment between ALT level and anthropometric and biochemical parameters.

Methods

This cross-sectional study was conducted among a sample of 100 overweight and obese adults (body mass index in kg/m2>25), 47 male (47%) and 53 female (53%), with median age 46.40+/-10.49 years, who had visited the specialized policlinic nr.2 between April 2010-March 2011. Subjects who were found to have diabetes mellitus, TBC, evidence of hepatitis B or C infection, drug toxicity, autoimmune hepatitis or concomitant corticosteroid therapy were excluded. Inform consensus was obtained for each subject.

All subjects were underwent physical examination, anthropometric measurements, biochemical and ultrasonography of the liver. The components of metabolic syndrome were: abdominal obesity (abdominal perimeter >98 cm in man and >84 cm in

percentile), normal weight (5-th<BMI< 84 percentile), overweight (85th<BMI<95 percentile) and obese (BMI-th> 95 percentile).

Blood samples were drown from the forearm in the fasting condition for the measurement of total bilirubin, ALT, glucose, insulin, cholesterol, HDL-cholesterol and triglycerides. Insulin resistance (IR) was calculated by means of the homeostasis model assessment using the formula for the HOMA-IR (HOMA-IR=fasting plasma insulin in microunity/ml X fasting plasma glucose in mg/dL:405. It was assumed IR when the HOMA-IR >3.7 and BMI>27.5 kg/m2.

Real time ultrasonography of the liver was performed in fasting condition by a physician with CT-scanner of 3.5 MHz transductor. Fatty liver was diagnosed by ultrasonography detection of the most characteristics features of fatty infiltration of the liver, regarding to its echo texture, echo penetration, liver-diaphragm differentiation of the echo amplitude and the clarity of the liver blood vessel structure. The scoring system was used in order to graduate the severity of the liver pathology, similar to that described by Tominga (10).

Descriptive data were exposed as mean +/- standard deviation (SD) for continuous variables. Hi-square test were used for comparison of mean values of ALT by the number of components of metabolic syndrome. Logistic regression analysis was performed to determinate

Table nr.1 Baseline characteristics of the study subjects according to the BMI

VARIABLES	BMI CATEGORY				p VALUE
	Overweight (n=34)	Obesity I (n=36)	Obesity II (n=19)	Obesity III (n=11)	
Weight (kg)	79+/-14	91+/-16	89+/-17	117+/-19	<0.001
Height (cm)	163+/-17	168+/-16	154+/-17	163+/-19	NS
Waist (cm)	97+/-9	109+/-9	105+/-11	125+/-14	<0.001
BMI (kg/m2)	27+/-4	32+/-5	36+/-6	44+/-8	<0.001
Bilirubin (mg/l)	0.7+/-0.1	0.7+/-0.4	0.8+/-0.5	0.8+/-0.6	NS
ALT (UI/l)	27.9+/- 9.2	24.4+/-6.3	48.8+/-4.5	89.7+/-8.7	<0.001
Glucose (mg/dl)	78+/-7	86+/-9	88+/-10	110+/-12	<0.001
Insulin (mmUI/ml)	17+/-1	19+/-4	29+/-6	30+/-7	<0.001
T Chol (mmol/l)	223+/-27	230+/-21	220+/-19	205+/-20	NS
TG (mmol/l)	163+/-18	167+/-16	215+/-20	190+/-19	NS
HOMA-IR	3.5+/-0.6	4.5+/-1.5	9.3+/-1.8	8.8+/-1.4	<0.001

women), hipertrigliceridemia >150 mg/dL, HDL-chol <40mg/dl in man and < 50mg?dL in women, TA >130/85 mmHg and blood glucose > 126 mg/dl. BMI was calculated as the weight (kg) divided by the square of height (m). Weight status was determined using the Diseases Control Center and Prevention 2000 growth curves that define as : underweight (BMI <5-th

the risk of elevated ALT according to the number of components of anthropometric and metabolic syndrome. P<0.005 as considered statistically significant.

Results

The study participants comprised 100 overweight and obese adults including 47 male (47%) and 53 female

Table nr.2 Characteristics of study sample by serum ALT status

VARIABLES	SUBJECTS (n=100)	GROUPS		p VALUE
		ALT>40 UI/l (n=25)	ALT <40UI/l (n=75)	
ALT (UI/l)	36.5+/-24.7	67.6+/-24.6	23.8+/-7.5	<0.001
Age (y)	46.4+/-10.8	44.3+/-10.1	47.3+/-11.1	NS
BMI (kg/m2)	31.9+/-6.7	37.7+/-6.5	29.5+/-5.4	<0.001
Waist (cm)	105.3+/-16.8	115.4+/-11.7	101.1+/-16.8	<0.001
Glucose (mg/dl)	93.6+/-23.2	96.7+/-23.2	93.2+/-23.3	NS
Insulin(mUI/ml)	13.1+/-9.9	18.7+/-9.2	10.9+/-11.2	NS
Bilirubin(mg/ml)	07+/-0.1	0.8+/-0.2	0.8+/-0.2	NS
T Chol (mmol/L)	219.3+/-47.5	209.2+/-59.4	223.4+/-41.3	NS
LDL-Chol (mmol/L)	145.5+/-50.8	136.2+/-63.1	149.4+/-44.7	NS
HDL-Chol(mmol/L)	40.1 +/-18.3	35.9+/-8.4	41.8+/-20.9	NS
Triglycer (mmol/L)	175.5+/-98.8	228.9+/-82.2	154.2+/-71.5	<0.001
Steatosis score	2.5+/-1.9	4.2+/-1.8	1.9+/-1.1	<0.001
HOMA-IR	3.1+/-1.9	4.9+/-2.2	2.3+/-1.3	<0.001

(53%) with a mean (SD) age of 46.40+/-10.89 years. Overall 34 were (34%) overweight, 36 had (36%) obesity grade I, 19 obesity (19%) grade II and 11 obesity (11%) grade III.

Characteristics of the study population according to the BMI category are presented in table nr.1.

As shown in table nr.1, from overweight to higher categories of obese subjects, anthropometric measurers (weight, abdominal parameter and BMI), ALT level, glucose, insulin concentration and HOMA-IR increased significantly. Total bilirubin, cholesterol and triglycerides were not significantly different between overweight group and obese categories of the subjects. Elevated ALT levels were seen in 25% of the subjects and were documented mostly in the category of obesity grade II (14 of 19 subjects) and grade III (11 of 11 participants), respectively 48.8+/-4.5 UI/l and 89.7+/-7 UI/l. Characteristics of participants with and without elevated serum ALT activity are shown in table nr. 2.

Although ALT concentrations were not significantly correlated with age, serum glucose, insulin, total bilirubin, total cholesterol, LDL-Cholesterol, HDL-Cholesterol and triglycerides, ALT levels were positively correlated with anthropometric parameters, such as BMI (p<0.001) and abdominal perimeter (p<0.001) and severity of liver steatosis (p<0.001) and insulin resistance (p<0.001).

Logistic regression model of the association of elevated ALT activity with anthropometric and metabolic variables shown that the prevalence of elevated ALT activity was positively associated with increasing BMI (OD:1.11; Cl 95%: 1.07 +/-2.31, p=0.028) and increasing of blood insulin (OD: 1.11; CL95%: 1.03+/-3.24, p=0.028).

NASH diagnosed by defined criteria was seen in 29 of obese adults (29%) of grade II and III.

Discussion

Obesity, insulin resistance and metabolic syndrome have been reported as factors associated with non-alcoholic fatty liver disease (2,3). Although in the most cases fatty liver does not progress to more severe liver disease, approximately 20% to 30% of patients have histologic sings of fibrosis and necroinflamation, indicating the presence of nonalcoholic steato-hepatitis (11). These patients are at high risk of developing cirrhosis and hepatocelullar carcinoma (4,5).

In most cases, nonalcoholic fatty liver disease/ nonalcoholic steato-hepatitis causes elevation of ALT concentration, which is closely related to liver fatty accumulation and insulin resistance, and consequently ALT has been used as a marker of NAFLD/NASH (6,7). Insulin resistance, increased proinflammatory cytokine production, oxidative stress and mitochondrial dysfunction leading to hepatocytes damage or destruction are all posed as important pathophysiological mechanisms of NAFLD/NASH (12). So that, an elevated ALT in obesity has the physiologic significance in terms of the potential of the fatty liver that is common in the metabolic syndrome.

The present observation study shows the abnormal activity in 25% of the obese adult subjects. This finding suggests that NAFLD/NASH, a part of metabolic syndrome, are common in adult obese population.

Our study indicates that ALT concentration were significantly correlated with anthropometric parameters (BMI, abdominal perimeter), severity of fatty liver accumulation and insulin resistance. Interestingly, this correlation was more apparent in the upper high of BMI range. In fact, the subjects attributable fraction of elevated ALT activity was much more among obese than overweight persons. Likewise, elevated serum activity was strongly related with abdominal perimeter suggested a role for body fat distribution in the development of NAFLD/NASH. In fact, abdominal perimeter is correlated with visceral adipose tissue, which provides a greater supply of potentially hepatotoxic fatty acids to the liver (6). Visceral adipose tissue lipolysis is also less sensitive to insulin suppression than other fat deposits (13).

Several studies have shown that ALT is related to features of the metabolic syndrome (14,15) and that insulin resistance plays an important role in the pathogenesis of NAFLD/NASH (16,17). Our findings show significant association between ALT concentrations as a marker for NAFLD/NASH and fasting insulin and HOMA-IR as markers for insulin resistance. Furthermore, a higher fasting serum insulin concentration was associated with elevated ALT activity independent of BMI and fat distribution. At last, our finding show that elevated ALT activity was positively correlated to the severity of fatty liver diagnosed by ultrasonography.

In conclusion, the current study established overweight ad obesity as a major risk factor for elevated ALT and that BMI and fasting blood insulin were the strongest risk factor for the elevation of serum concentration of ALT.

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