A Study of AST/ALT Ratio in Metabolic Syndrome

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ABSTRACT

Introduction: Features of metabolic syndrome and non alcoholic fatty liver disease (NAFLD) are strongly associated with one another. NAFLD has also been proposed as a component of metabolic syndrome. Hepatocyte damage as a consequence of hepatic fat accumulation is characterized by the release of aspartate transaminase (AST) and alanine transaminase (ALT) enzymes from damaged liver cells into the blood. AST/ALT ratio can be used to differentiate alcoholic liver disease from NAFLD. The present study aimed to determine AST/ALT ratio in individuals with metabolic syndrome and in healthy controls and to correlate it with the components of metabolic syndrome.

Material and methods: 50 subjects with metabolic syndrome and 50 healthy, age and gender matched individuals without features of metabolic syndrome were enrolled for the study. Fasting venous samples collected from the study group were estimated for glucose, AST, ALT, total bilirubin and lipid profile.

Results: AST/ALT ratio was significantly lower in individuals with metabolic syndrome when compared to controls ($p<0.001$). A marked association of metabolic syndrome with decreased AST/ALT ratio was observed with odd's ratio of 16.6. AST/ALT ratio also showed a significant negative correlation with waist circumference, blood pressure, fasting blood glucose and triglycerides and a positive correlation with HDL.

Conclusion: In the present study, AST/ALT ratio was found to be significantly reduced in subjects with metabolic syndrome. Determination of AST/ALT ratio could thus help to predict the development of NAFLD in individuals with metabolic syndrome.

Keywords: ALT, AST, AST/ALT ratio, metabolic syndrome, NAFLD

INTRODUCTION

Metabolic Syndrome is a cluster of interrelated risk factors. The National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III) guidelines have described the characteristic features of metabolic syndrome. It is defined as the presence of following three or more risk factors in an individual: abdominal obesity (waist circumference >102 cm in men; >88 cm in women), elevated blood pressure (systolic BP ≥ 130 mmHg; diastolic BP ≥ 85mmHg), elevated triglycerides (≥ 150 mg/dl), reduced HDL cholesterol (< 40mg/dl in men; < 50 mg/dl in women) and fasting blood glucose (≥ 100 mg/dl).[1]

Worldwide, nonalcoholic fatty liver disease (NAFLD) is the most common liver disease. Metabolic syndrome is strongly associated with NAFLD.[2] It is also considered as a hepatic manifestation of metabolic syndrome.[3] It is characterized by increased fat accumulation within hepatocytes in a person with negligible or no alcohol intake.[4]

The prevalence of NAFLD ranges from 5% to 30% in the Asia-Pacific region.[5] NAFLD is associated with an increased risk of developing insulin resistance, type 2 diabetes mellitus and cardiovascular disease. Accumulation of fat in NAFLD occurs as a result of insulin resistance.[6,7] Tumour necrosis factor-α, a cytokine produced by fat cells correlates with body fat and is important in obesity for the development of insulin resistance.[8] About 20-30% of persons with NAFLD develop nonalcoholic steatohepatitis (NASH) which in turn can progress to end stage liver disease and even hepatocellular carcinoma.[9] Chronic inflammation mediated by visceral adipose tissue and elevated free fatty acids are the key factors that lead onto progression of liver injury in NAFLD.[10]

In the current clinical settings, the diagnosis of NAFLD can be established only by liver biopsy. Identification of noninvasive measures to detect and monitor disease progression will minimize the need for liver biopsy in NAFLD. Often, the occurrence of NAFLD is suspected by the combination of fat in the liver seen on imaging studies (especially ultrasound) along with an absence of obvious cause for elevated liver enzymes.[4]

Upto 90% of persons with NAFLD have an asymptomatic elevation of aminotransferase levels. Previous studies have correlated AST/ALT (aspartate amino transferase/alanine amino transferase) ratio with metabolic syndrome and insulin resistance. AST/ALT ratio can differentiate the etiology and severity of liver damage; a value of <1 implies NAFLD whereas a value of >2 indicates alcoholic liver disease.[11] The present study was undertaken to evaluate the association of AST/ALT ratio in individuals with metabolic syndrome.

MATERIAL AND METHODS

The study was conducted at Thanjavur Medical College, Thanjavur, Tamilnadu after getting approval from the ethical committee. 50 subjects (25 males and 25 females) with metabolic syndrome were selected as cases. 50 healthy age and gender matched individuals without features of metabolic syndrome were taken as controls.

Metabolic syndrome was diagnosed based on the NCEP-ATPIII criteria. Subjects with evidence of hepatitis, alcohol consumption and hepatotoxic drug intake were excluded from the study. Informed consent was obtained prior to the study from all the subjects.

Anthropometric measurements like height, weight and waist circumference were measured. Height was measured without shoes in standing posture to the nearest 0.5cm by a standard stadiometer. Weight was measured to the nearest 0.1 kg with subjects in light clothing and without shoes using a digital weighing scale. Waist circumference (WC) was measured to the nearest 0.5cm at the end of normal expiration, midway between

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the superior border of the iliac crest and inferior margin of the ribs using a steel tape. Body mass index (BMI) was calculated by dividing the weight in kilograms by height in square meters (kg/m^2). Blood pressure was recorded on the right arm with a standard sphygmomanometer in the sitting position after the person had relaxed for about 10 minutes. The measurement was repeated after 10 minutes and the average of the two readings were noted.

Under aseptic precautions, 5 ml of fasting venous samples were collected from the study groups and centrifuged after retraction of the clot. The serum was estimated for glucose, AST, ALT, total bilirubin and lipid profile. Glucose was estimated by Glucose oxidase-peroxidase method, AST and ALT by enzymatic methods, Total Cholesterol by Cholesterol oxidase PAP method, Triglycerides by GPO-PAP method, HDL by direct method Total Bilirubin by Jendrassik-Grof's method in XL 300 auto analyser. LDL was calculated by Friedwald's formula.

STATISTICAL ANALYSIS

Data were statistically analysed using SPSS software (13) and expressed in terms of mean and standard deviation. Student's t-test was employed for the analysis of data. 'P' value less than 0.05 was taken as the significant value. Correlation between AST/ALT ratio and the components of metabolic syndrome was assessed using Pearson's correlation coefficient.

RESULTS

Table 1 shows the baseline characteristics of the study group. AST/ALT ratio was significantly lower in individuals with metabolic syndrome when compared to healthy control subjects ($p<0.001$).Metabolic syndrome showed a marked association with decreased AST/ALT ratio with odds ratio of 16.6. Table 2 shows the gender wise distribution of AST/ALT ratio in the study group. AST/ALT ratio was significantly lower in both males and females with metabolic syndrome.

Table 3 shows the Pearson's coefficient of correlation between AST/ALT ratio and the different components of metabolic syndrome. AST/ALT ratio showed a significant negative correlation with waist circumference, blood pressure, FBG and triglycerides and a significant positive correlation with HDL.

Parameters	Controls (n=50)	Metabolic syndrome (n=50)	P value
	Mean±S.D	Mean±S.D	
Age (years)	39.78±8.6	42.14±9.08	0.433
BMI (kg/m^2)	21.18±2.36	25.8±3.2	0.04
WC (cm)	84.3±4.24	96.7±7.06	0.006
SBP (mmHg)	104.6±9.0	126.36±20.21	<0.001
DBP (mmHg)	74.56±3.85	81.88±8.85	<0.001
FBG (mg/dl)	86±9.5	104±7.76	0.004
TC (mg/dl)	170.76±18.25	181.52±20.03	<0.001
TGL (mg/dl)	134.81±17.64	188.16±25.85	<0.001
HDL (mg/dl)	42.6±3.1	37.2±4.3	0.03
VLDL (mg/dl)	27.8±3.3	37.32±6.1	<0.001
LDL (mg/dl)	101.67±13.06	106.8±18.07	0.04
AST (U/L)	18.2±4.1	32.3±5.7	<0.001
ALT (U/L)	13.4±6.3	44.7±9.21	<0.001
AST/ALT Ratio	1.13±0.07	0.81±0.23	<0.001
Total bilirubin (mg/dl)	0.8±0.3	0.9±0.32	0.67

Table-1: Descriptive statistics of the study group

Gender	Groups	Mean±SD	P value
Males	Controls (n=25)	1.22±0.07	<0.001
	Metabolic syndrome (n=25)	0.81±0.23	
Females	Controls (n=25)	1.13±0.07	<0.001
	Metabolic syndrome (n=25)	0.82±0.24	

Table-2: Gender-wise distribution of AST/ALT ratio in the study group

Parameters	'r' value	'P' value
WC	-0.686	<0.01
SBP	-0.536	<0.01
DBP	-0.394	<0.01
FBG	-0.411	<0.01
TGL	-0.612	<0.01
HDL	0.499	<0.01

Table-3: Pearsons correlation coefficient for AST/ALT ratio with components of Metabolic Syndrome

DISCUSSION

NAFLD is considered as one of the morbid conditions of metabolic syndrome. It is typically characterized by elevated aminotransferase levels. In the present study, AST/ALT ratio was observed to be significantly reduced in persons with metabolic syndrome ($P<0.001$). Previous studies have demonstrated similar findings.[11,12]

NAFLD is strongly correlated with visceral adiposity (reflected by waist circumference).[10] The accumulation of fat in the abdomen predicts fat deposition in hepatocytes irrespective of a person's total body fat content and thus contributes to the pathogenesis of NAFLD.[13] In our study, we observed a significant negative correlation between AST/ALT ratio and waist circumference.

We also observed a significant negative correlation between AST/ALT ratio and fasting blood glucose and triglycerides and a significant positive correlation with HDL. Samuel et al demonstrated the causal role of hepatic fat accumulation in the development of insulin resistance.[14] Hyperlipidemia and fatty change in the liver promote inflammation through nuclear factor-κB signaling pathways ultimately leading onto insulin resistance.[10] In addition, we observed a significant negative correlation between AST/ALT ratio and blood pressure. Hsiao et al demonstrated the significant correlation of severe fatty liver with hypertension, triglyceride metabolism and abnormal glucose levels.[15]

The results of the present study show that the AST/ALT ratio was strongly associated with all the components of metabolic syndrome. This is in accordance with the Insulin Resistance Atherosclerosis Study which proved that the AST/ALT ratio independently predicted metabolic syndrome in a well characterized multiethnic cohort.[16]

Our study had some limitations. One limitation is the lack of dietary habit evaluation in the study group which could modify the association of AST/ALT ratio with metabolic syndrome. Liver biopsy and imaging studies like ultrasound were not performed to establish the diagnosis of NAFLD which is the second limitation.

CONCLUSION

The present study shows that AST/ALT ratio is significantly associated with metabolic syndrome. Since the onset and progression of NAFLD is associated with multiple cardiovascular risk factors, AST/ALT ratio could be used as a marker to predict NAFLD in metabolic syndrome.

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