1. Introduction

In previous studies, the relationship between aspartate aminotransferase to alanine aminotransferase ratio (AST/ALT ratio) and liver disease has been evaluated. In viral hepatitis, alcoholic liver disease and primary biliary cirrhosis, AST/ALT ratio has been proven to be an indicator of liver cirrhosis.\(^1\textsuperscript{-3}\) AST/ALT ratio was a potential value in differentiating nonalcoholic steatohepatitis from alcoholic liver disease. The value < 1 suggested nonalcoholic steatohepatitis, a ratio of ≥ 2 was strongly suggestive of alcoholic liver disease.\(^4\)

Nonalcoholic fatty liver disease (NAFLD) is the most common cause of elevated liver enzymes and also one of the most common forms of liver disease in the world.\(^5\) The AST/ALT ratio of the ultrasound-diagnosed NAFLD patients was lower than controls.\(^6\) AST/ALT ratio < 1 was a common NAFLD-related feature.\(^7\) NAFLD is now considered the hepatic manifestation of the metabolic syndrome. When compared with individuals without NAFLD, individuals with NAFLD had significantly higher fasting glucose, insulin, low-density lipoprotein cholesterol, triglycerides, systolic blood pressure and diastolic blood pressure.\(^8\) Recently, NAFLD marker the AST/ALT ratio have attracted great interest as potential novel marker of metabolic syndrome.\(^9\)

Very little information was available about the association of AST/ALT ratio with metabolic syndrome in Han young adults. Thus, this study evaluated the relationship between AST/ALT ratio and metabolic syndrome in Han young adults.
2. Materials and methods

2.1 Subjects

After obtaining the informed consent from all subjects, a cross-sectional, population-based study was conducted. The study population was determined according to 2-stage cluster sampling. In the first stage, a random sample of universities in Qinhuangdao, Hebei Province, China, were obtained; in the second stage, young adults aged 19 to 24 years, randomly selected from these schools, were invited to participate. In the end, 425 Han young adults (males/females 216/209) participated in 2009. Subjects with evidence of alcohol intake, hepatitis B (hepatitis B surface antigen), hepatitis C (hepatitis C antibody), autoimmune hepatitis (antinuclear antibody and anti-smooth muscle antibody) and drug toxicity were excluded. The study protocol was approved and supervised by the ethical committee of the First Hospital of Qinhuangdao.

2.2 Measurements

Anthropometric measurements, including height, weight and waist circumference (WC) were performed when subjects were without shoes and in light clothing. Height and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively. Standing height without shoes was measured three times with a stadiometer, and the three measurements were averaged for analysis. Body mass index (BMI) was defined as weight (kg) divided by height (m) squared. Blood pressure was measured three times with a mercury sphygmomanometer while the subjects were seated after 10 min of rest, and the three measurements were averaged for analysis.

After an overnight fast of 10–12h, blood samples were drawn from an antecubital vein in each subject into vacutainer tubes. Fasting plasma glucose (FPG) concentration was measured using the glucose oxidase method, serum lipids and alanine aminotransferase (ALT) and aspartate alanine aminotransferase (AST) were measured using enzymatic procedures with an autoanalyzer (Hitachi, Tokyo, Japan). Serum true insulin (TI) was measured using enzyme linked immunosorbent assay (ELISA) with model 680 microplate reader (BIO-RAD, America). The ELISA kits were purchased from USCNLIFE company, America. The following equation for homeostasis model assessment of insulin resistance (HOMA-IR) was used: fasting insulin level (μU/ml) x fasting glucose level (mmol/l)/22.5.

2.3 Definition for metabolic syndrome

Metabolic syndrome was defined as having ≥ 3 of the 5 factors with the following cut points: abdominal obesity (waist circumference ≥ 90 cm in males and 80 cm in females); high triglycerides (≥ 1.70 mmol/L [150 mg/dL]); low high density lipoprotein cholesterol (HDL-C) (< 1.03 mmol/L [40 mg/dL] for males and < 1.30 mmol/L [50 mg/dL] for females); elevated blood pressure (systolic blood pressure ≥ 135 mmHg and/or diastolic blood pressure ≥ 85 mmHg) and impaired fasting glucose (≥ 5.6 mmol/L [100 mg/dL]).

2.4 Statistical analysis

Data are expressed as mean ± standard deviation (SD) or medians with interquartile ranges (IQR). When data was not normally distributed, they were ln transformed for
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3. Results

3.1 Clinical and laboratory characteristics

In this sample, AST/ALT ratio < 1 was detected in 146 subjects (34.4%). Males had a significantly higher frequency of AST/ALT ratio < 1 than females (48.6% vs 19.6%, \( \chi^2 = 39.595, P=0.000 \)). The age was similar in two groups (20.3±0.8 vs 20.3±0.8, \( t=0.057, P=0.955 \)). Table 1 showed clinical and laboratory characteristics in the study subjects. After adjustment for age and sex, young adults with AST/ALT ratio < 1 had higher BMI, WC, SBP, DBP, TG, TI and HOMA-IR than subjects with AST/ALT ratio ≥ 1. Subjects with AST/ALT ratio < 1 also had significantly lower HDL-C than subjects with AST/ALT ratio ≥ 1 (\( P<0.05 \)). The level of FPG was similar between subjects with AST/ALT ratio < 1 and ≥ 1 (\( P>0.05 \)).(Table 1)

Associations of AST/ALT ratio with anthropometric and metabolic variables were presented in Table 2. After adjustment for age and sex, AST/ALT ratio showed positive correlations with HDL-C and negative correlations with BMI, WC, TG, TI and HOMA-IR (\( P<0.05 \)). (Table 2)

3.2 AST/ALT ratio and metabolic syndrome

The prevalence of metabolic syndrome was 2.1% and was similar in males and females (2.3% vs 1.9%, \( \chi^2 = 0.082, P=0.774 \)). Subjects with AST/ALT ratio < 1 had a significantly higher frequency of abdominal obesity, high triglycerides, elevated blood pressure and metabolic syndrome (\( P<0.05 \)). (Table 3) After adjustment for age, sex and BMI, the frequency of metabolic syndrome among young adults with AST/ALT ratio < 1 was 6.975 (95%CI: 1.430 to 34.019, \( P=0.016 \)) times compared with young adults with AST/ALT ratio ≥ 1.

4. Discussion

Using Adult Treatment Panel III criteria’s definition, we estimated that approximately 2.1% of Han young adults have the metabolic syndrome. The prevalence of metabolic syndrome in this study was lower than previously report from Chinese adults and was similar to Chinese adolescents.\(^{11,12} \) It was because of a positive effect of age on the prevalence of metabolic syndrome.\(^{13,14} \) Abdominal obesity, elevated blood pressure and low HDL-C were common components of the metabolic syndrome in this sample. In the insulin resistance atherosclerosis study, NAFLD marker the AST/ALT ratio predict metabolic syndrome independently of potential confounding variables.\(^{15} \) In this study, we found that the
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metabolic syndrome was related with a lower AST/ALT ratio in Han young adults. Subjects with AST/ALT ratio < 1 had a significantly higher frequency of abdominal obesity, high triglycerides, elevated blood pressure and metabolic syndrome. The association was not modified by age, sex and BMI.

| variable                  | AST/ALT level ratio≥1 (n=279) | AST/ALT level ratio< 1 (n=146) | P       |
|---------------------------|--------------------------------|--------------------------------|---------|
| Age(years) mean(SD)       | 20.3(0.8)                      | 20.3(0.8)                      | 0.955   |
| Sex(male/female)          | 111/168                        | 105/41                         | 0.000   |
| BMI(kg/m²) mean(SD)       | 22.9(3.8)                      | 26.3(4.0)                      | 0.000   |
| WC(cm) mean(SD)           | 70.8(9.3)                      | 81.4(12.3)                     | 0.000   |
| SBP(mmHg) mean(SD)        | 109.3(10.7)                    | 115.2(11.5)                    | 0.004   |
| DBP(mmHg) mean(SD)        | 73.1(8.2)                      | 76.7(9.9)                      | 0.030   |
| FPG(mmol/L) mean (SD)     | 4.30(0.44)                     | 4.38(0.40)                     | 0.101   |
| TG(mmol/L) mean (SD)      | 0.69(0.24)                     | 0.83(0.46)                     | 0.000   |
| HDL-C(mmol/L) mean (SD)   | 1.42(0.22)                     | 1.30(0.24)                     | 0.001   |
| TI( uU/ml) median (IQR)   | 6.58(3.88)                     | 7.75(4.86)                     | 0.014   |
| HOMA-IR median(IQR)       | 1.25(0.76)                     | 1.53(1.08)                     | 0.006   |
| ALT(U/L) mean(SD)         | 10.6(5.0)                      | 30.6(17.3)                     | 0.000   |
| AST(U/L) mean(SD)         | 17.9(6.0)                      | 20.6(8.5)                      | 0.223   |

Data are expressed as mean ± standard deviation(SD) or medians with interquartile ranges(IQR). Continuous variables were analyzed with covariance adjustment for age and sex. When data was not normally distributed, they were ln transformed for analysis. ALT: alanine aminotransferase; AST: aspartate aminotransferase; BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; FPG: fasting plasma glucose; TG: triglycerides; HDL-C: high density lipoprotein cholesterol; TI: true insulin; HOMA-IR: homeostasis model assessment of insulin resistance; SD: standard deviation; IQR:indicates interquartile range.

Table 1. Clinical and laboratory characteristics of the subjects in different levels of AST/ALT ratio.
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| variable          | r    | P*  | r    | P** |
|-------------------|------|------|------|------|
| BMI (kg/m^2)      | -0.296 | 0.000 | -0.281 | 0.000 |
| WC (cm)           | -0.310 | 0.000 | -0.264 | 0.000 |
| SBP (mmHg)        | -0.141 | 0.004 | -0.072 | 0.134 |
| DBP (mmHg)        | -0.102 | 0.036 | -0.048 | 0.321 |
| FPG (mmol/L)      | -0.051 | 0.295 | -0.039 | 0.413 |
| TG (mmol/L)       | -0.134 | 0.006 | -0.134 | 0.006 |
| HDL-C (mmol/L)    | 0.174  | 0.000 | 0.125  | 0.010 |
| TI (uU/ml)        | -0.154 | 0.001 | -0.118 | 0.015 |
| HOMA-IR           | -0.158 | 0.001 | -0.121 | 0.012 |

*Pearson correlation. **Partial correlation analysis, adjustment for age and sex. ALT: alanine aminotransferase; AST: aspartate aminotransferase; BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; FPG: fasting plasma glucose; TG: triglycerides; HDL-C: high density lipoprotein cholesterol; TI: true insulin; HOMA-IR: homeostasis model assessment of insulin resistance.

Table 2 Correlation analysis of AST/ALT ratio with anthropometric and metabolic variables in Han young adults.

| Factor                          | AST/ALT level ratio≥1 (n=279) | AST/ALT level ratio<1 (n=146) | P    |
|---------------------------------|-------------------------------|-------------------------------|------|
| abdominal obesity(%)            | 9.7                           | 32.2                          | 0.000|
| high triglycerides(%)           | 0.0                           | 3.4                           | 0.008|
| low high density lipoprotein cholesterol(%) | 15.1                          | 21.2                          | 0.109|
| elevated blood pressure(%)      | 12.9                          | 25.3                          | 0.001|
| impaired fasting glucose(%)     | 0.7                           | 0.0                           | 0.548|
| metabolic syndrome(%)           | 0.7                           | 4.8                           | 0.016|

The χ² test was used to test for differences in proportions. ALT: alanine aminotransferase; AST: aspartate aminotransferase.

Table 3 Prevalence of metabolic syndrome in different levels of AST/ALT ratio(%).
In our study, AST/ALT ratio showed negative correlation with HOMA-IR. Insulin resistance is a central feature in the pathogenesis of metabolic syndrome, while insulin resistance is now considered the main link between metabolic disturbances and liver enzymes. Hanley AJ et al.\textsuperscript{16} reported that AST/ALT ratio was associated with directly measured insulin sensitivity when conventionally availables were adjusted. This result can be explained by the following possible mechanism. Liver markers were known to be significantly correlated with increased hepatic fat content.\textsuperscript{17} Liver fat content was a significant risk factor of HOMA-IR while BMI and waist circumference were not.\textsuperscript{18}

In our study, we found that young adults with AST/ALT ratio < 1 had higher TI than subjects with AST/ALT ratio \( \geq 1 \). But the level of FPG was similar between subjects with AST/ALT ratio < 1 and \( \geq 1 \). The liver plays an important role in maintaining normal glucose concentrations during fasting as well as postprandially. The loss of a direct effect of insulin to suppress hepatic glucose production and glycogenolysis in the liver causes an increase in hepatic glucose production.\textsuperscript{19} Increased insulin levels with increasing insulin resistance in subjects with AST/ALT ratio < 1 suggested that elevated insulin concentrations reflected increased beta cell output to the elevated insulin concentrations. The hyperinsulinemia can thus be seen as a compensatory mechanism for the preexisting insulin resistance, which represents a mechanism for protection against the development of impaired fasting glucose and diabetes. T2DM will result when there is insufficient insulin secretion to counter preexisting insulin resistance.\textsuperscript{20}

Diet habit modifies the relationship of the liver enzymes ratio with metabolic syndrome. For example, Mediterranean diet moderates the association of the liver enzymes ratio with the prevalence of the metabolic syndrome.\textsuperscript{9} In China, people's eating habits are quite different in different area. Regrettably, diet habit was not evaluated in our study. This is a limitation of our study.

In conclusion, the prevalence of metabolic syndrome was low in Han young adults. AST/ALT ratio was related with metabolic syndrome in Han young adults.

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