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Original article

Impact of elevated aspartate and alanine aminotransferase on metabolic syndrome and its components among adult people living in Ningxia, China

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Abstract

Objective: Metabolic syndrome (MS) is a combination of medical disorders that increase the risk for cardiovascular disease and diabetes mellitus. It suggests an association between an elevated serum aminotransferase level and MS. Little data show the relationship between the levels of serum aminotransferase and the incidence of MS in Ningxia, China.

Methods: A total of 5415 subjects who received medical health checkups from 2007 to 2009 were enrolled in the study. The participants were interviewed by trained health workers under a structured questionnaire. MS was defined according to the modified ATPIII criteria for Asian Americans by the American Heart Association (AHA-ATP III).

Results: The prevalence of elevated aspartate aminotransferase (AST) and ALT (>40 U/L) were 7.1% and 22.2% in males, and 2.1% and 4.8% in females respectively. The prevalence of MS was 32.1% in males and 15.4% in females. The components of MS were significantly more in the group with elevated aminotransferase levels than in the group with normal aminotransferase levels. The odds ratios (95% *CI*) for elevated AST were 1.90 (1.49, 2.42), 2.59 (2.01, 3.39), 1.68 (1.32, 2.15), and 1.81 (1.36, 2.42) in the adults with abdominal obesity, high serum triglycerides levels, high blood pressure, and high plasma glucose levels respectively. After adjustment for age, the odds ratios (95% *CI*) for elevated ALT were 3.08 (2.63, 3.61), 4.30 (3.64, 5.08), 1.26 (1.08, 1.48), 2.16 (1.93, 2.65) and 2.38 (1.96, 2.87) in adults with abdominal obesity, high serum triglycerides levels, low serum high-density lipoproteincholesterol (HDL-C), high blood pressure, and high plasma glucose levels respectively. The odds ratios (95% *CI*) for elevated AST were 1.67 (1.06, 2.63), 2.28 (1.46, 3.63), 2.59 (1.59, 4.21) and

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for elevated ALT 2.02 (1.50, 2.73), 2.68 (1.96, 3.65), 3.94 (2.86, 5.43) for the subjects with 1, 2, and ≥3 risk factors after adjustment for age, gender, and BMI.

Conclusion: The serum aminotransferase levels were higher in males compared to females, and serum ALT level was more closely associated with MS than the AST level in adults in Ningxia, China. With an increasing the number of components of MS, the aminotransferase levels and the risks for elevated aminotransferase increase, whereas the AST/ALT ratios decrease.

Keywords: Metabolic syndrome; Serum aminotransferase; Odds ratios

Introduction

Metabolic syndrome (MS) is a combination of metabolic disorders, such as dyslipidemia, hypertension, impaired glucose tolerance, compensatory hyperinsulinemia and the tendency to develop fat around the abdomen.[1] Consequently, people with MS are at high risk of atherosclerosis and cardiovascular disease.

Liver enzymes are used most commonly in laboratory tests, and are the key to the laboratory evaluation of liver damage. Several studies reported that liver enzymes might be associated with MS through many metabolic disorders such as overweight and obesity, dyslipidemia, diabetes (DM), and hypertension, while insulin resistance was considered as the main cause.[2−4] Alanine aminotransferase (ALT), a marker of fatty liver, has been reported as an independent risk factor of MS, diabetes, and cardiovascular diseases.[5,6] Elevated serum ALT levels have a positive correlation with MS-related diseases, such as type 2-DM and cardiovascular disease.[7,8]

Although there have been many studies regarding to hypertension, obesity, diabetes, dyslipidemia, impaired glucose tolerance, and MS in China,[9−11] few studies directly examined the correlation between MS and aspartate aminotransferase (AST) or ALT in China, especially in the relatively un-developed areas such as Ningxia. Therefore, in this study, we focus on the role of elevated aspartate and alanine aminotransferases on MS and its components among adults living in Ningxia, China.

Methods

People and materials

The study population was selected from the employees of the local governments and industries who visited the General Hospital of Ningxia Medical University, Ningxia, China, for medical health checkups, during 2007 and 2009 using stratified cluster sampling. During the study period, 5415 subjects (age 20−78 years old, 3318 males and 2097 females) who did not have any clinical evidence for cardiovascular disease were randomly selected to participate in the study. The subjects had no reported chronic viral infection, cold or flu, acute respiratory infection, dental problems, or any type of surgery during the study. All participants were interviewed by trained investigators with a standard closed-ended questionnaire.

The study protocol was approved by the Medical Ethics Review Committee of Ningxia Medical University and there were no activities in the study that violated ethical policies in China. All participants gave consent to enrollment after they received written and verbal information.

Anthropometric and biochemical measurements

Anthropometric measurements including height, weight, and waist and hip circumference were measured by well-trained examiners. Standing height was measured once to the nearest 0.5 cm using a portable ruler (made in China), body weight was also measured once to the nearest 0.1 kg using a weight scale (made in China). Body mass index (BMI) was calculated as kg/m^2. Waist circumference (WC) was measured to the nearest 0.1 cm at the midpoint between the lower borders of the rib cage and the iliac crest and the hip circumference (HC) was measured to the nearest 0.1 cm at the point about 1 cm above the navel. All measurements were performed by the study investigators. Blood pressure was also recorded after at least 10 minutes of rest in a chair, with feet on the floor, and arm supported at heart level, using a mercury sphygmomanometer. Patients with average blood pressure ≥140/90 mmHg or taking antihypertensive medication were classified as hypertensive. Blood samples of 5 ml were collected from the antecubital vein between 7 and 9 AM, after 10 hours of fasting and

avoidance of alcohol (avoidance of alcohol is already implied by fasting). Total cholesterol, triglyceride, serum glucose, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, AST, and ALT levels were measured by an auto-analyzer (Olympus AU2700, Japan).

Definition of elevated serum aminotransferase and metabolic syndrome

Both elevated AST and ALT are defined as when the enzyme activity is higher than 40 U/L, similar to thresholds that have been previously used in studies.[12–15] MS was defined according to the modified ATPIII criteria for Asian Americans by the American Heart Association (AHA-ATP III). In the present study, individuals having three or more among the five following metabolic components were defined as having the MS: waist circumference $\geq$90 cm for men or $\geq$80 cm for women, triglyceride level $\geq$1.7 mmol/L, HDL-cholesterol level <1.03 mmol/L for males or <1.3 mmol/L for females, blood pressure $\geq$130/85 mmHg or antihypertensive medication, fasting blood glucose $\geq$5.6 mmol/L or on drug treatment for elevated glucose.[16]

Statistical analysis

Data are presented as mean values with standard deviations for continuous variables and as absolute and relative frequencies or prevalence for categorical variables. Comparisons between two groups were performed with Pearson χ^2 tests for categorical variables, and Student's *t*-tests for continuous variables. The relationships among serum aminotransferase and other continuous variables were analyzed using Spearman's rank correlations. The general linear model was used to test the linear trend of serum aminotransferase levels according to the number of components of the MS. Logistic regression analysis was performed to detect the risks of elevated serum aminotransferase according to the presence of each component of the MS. The adjusted odds ratios (ORs) for elevated serum aminotransferase according to the number of components of the MS after adjustment for age, gender, and BMI are presented together with their 95%*CI*s. The linear trend in odds ratios was evaluated by using the trend test. All reported *P* values were two-sided, and a *P* value less than 0.05 was considered statistically significant. All data were input into EpiData first and then exported into SPSS version 14.0 (SPSS Corp, College Station, NX).

Results

The incidence of elevated levels of AST, elevated ALT and MS in the study population were presented in Table 1. The incidence of elevated AST, elevated ALT, and MS were 7.1%, 22.2%, and 32.1% for males and 2.1%, 4.8%, and 15.4% for females, respectively. The overall elevated AST, ALT, and MS were more in males than females. The incidence of elevated AST and ALT decreased with age in males and increased in females. The incidence of MS increased with age in both males and females.

Of the study participants, 3318 (61.3%) were males and 2097 (38.7%) were females. The levels of AST, ALT, and AST/ALT, grouped by age and gender, were

Table 1
The prevalence of elevated AST levels, elevated ALT levels, and MS in the study population.

Age	Elevated AST (%)		Elevated ALT (%)		MS (%)	
	Male	Female	Male	Female	Male	Female
20 ~	9.2 (38/414)[b]	1.5 (6/401)[a,b]	26.1 (108/414)[b]	3.5 (14/401)[a,b]	12.3 (51/414)[b]	3.2 (13/401)[a,b]
30 ~	8.4 (80/947)	1.2 (9/727)[a]	28.0 (265/947)	4.0 (29/727)[a]	26.0 (246/947)	7.2 (52/727)[a]
40 ~	7.4 (80/1085)	2.1 (13/622)[a]	23.9 (259/1085)	5.0 (31/622)[a]	38.9 (422/1085)	18.3 (114/622)[a]
50 ~	4.8 (27/599)	4.3 (10/230)	14.3 (80/559)	8.3 (19/230)[a]	41.3 (231/599)	33.9 (78/230)
60 ~	3.2 (10/313)	6.0 (7/117)	7.7 (24/313)	6.8 (8/117)	36.4 (114/313)	56.4 (66/117)[a]
overall	7.1 (235/3318)	2.1 (45/2097)[a]	22.2 (736/3318)	4.8 (101/2097)[a]	32.1 (1064/3318)	15.4 (323/2097)[a]

AST: aspartate aminotransferase; ALT: alanine aminotransferase; MS: metabolic syndrome. The number of subject with serum AST >40 U/L, serum ALT >40 U/L and MS versus total subject number in different age groups based on gender is displayed in brackets.

[a] Significantly different from the female group are males with elevated AST, elevated ALT and MS in different age groups, $\chi^2 = 23.540, 42.468, 21.422, 63.862; 81.707, 163.540, 100.003, 5.436, 296.520; 23.193, 99.594, 80.240, 13.981, 189.611$; respectively, all $P < 0.05$ or $P < 0.01$ (Pearson χ^2 test).

[b] Significantly different from different age groups with elevated AST, elevated ALT and MS in the male and female group, $\chi^2 = 17.084, 82.173, 138.167; 17.183, 9.655, 299.696$; respectively, all $P < 0.05$ or $P < 0.01$.

shown in Table 2. The overall mean values of AST levels were higher in males than females (25.49 ± 10.88 U/L vs. 20.84 ± 8.09 U/L, $t = 16.841$, $P < 0.001$). Similarly, the ALT levels were also higher in males (31.40 ± 22.03 vs. 18.17 ± 13.52 U/L, $t = 24.660$, $P < 0.001$). The AST/ALT ratio was lower in males (0.99 ± 0.80 vs. 1.37 ± 0.71, $t = -17.530$ $P < 0.001$). The mean values of AST and ALT decreased with age in males and increased in females.

The baseline characteristics of all subjects, with and without MS, based on gender are shown in Table 3. After adjustment for age, the mean values of BMI, WC, systolic blood pressure, diastolic blood pressure, triglycerides, AST, and ALT were higher in males than in females. Females had higher levels of HDL cholesterol and AST/ALT ratio males. Both males and females with MS were more likely to be older individuals, with a higher BMI, WC, systolic blood pressure, diastolic blood pressure, triglycerides, total cholesterol, and plasma glucose. Higher AST and ALT concentrations and lower AST/ALT ratio were found in both males and females with MS.

As shown in Table 4, 5.2% and 15.5% of the participants had elevated AST and ALT levels, respectively. The subjects with elevated AST and ALT levels had higher mean BMI, WC, systolic blood pressure, diastolic blood pressure, triglycerides, total cholesterol, and LDL cholesterol than the subjects with normal AST and ALT levels. Age, HDL cholesterol, and plasma glucose levels were not significantly different between the normal AST group and the elevated AST group. The subjects with elevated ALT levels were significantly older and had a higher plasma glucose level and significantly lower HDL cholesterol than the subjects with normal ALT levels.

The correlation between each metabolic component and the risk of elevated AST and ALT were shown in Table 5. The percentage based on gender, BMI, abdominal obesity, high serum triglycerides, high blood pressure, and high plasma glucose were significantly different between the normal and elevated groups for both AST and ALT, whereas age and the proportion with low serum HDL-C was only significantly different for the elevated ALT group and normal ALT group. Overall, males had a 3.48 (2.51−4.85) fold risk of developing elevated AST levels compared to females. The odds ratio for BMI (BMI 24−27.9: *OR* 1.96, 95%*CI*: 1.50−2.57; BMI ≥28: *OR* = 3.77, 95% *CI*: 2.69−5.30), abdominal obesity (*OR* = 1.90, 95% *CI*: 1.49−2.42), high triglycerides (*OR* = 2.59, 95%*CI*: 2.01−3.39), high blood pressure (*OR* = 1.68, 95%*CI*: 1.32−2.15) and high plasma glucose (*OR* = 1.81, 95% *CI*: 1.36−2.42) in the subjects were significantly associated with elevated AST, whereas only the low serum HDL-C was not significantly associated. After adjustment of age, males had a 6.23 (5.01−7.75) fold risk of developing elevated ALT levels compared to female. The odds ratio for BMI (BMI 24−27.9: *OR* = 3.63, 95%*CI*: 3.05−4.33; BMI ≥28: *OR* 6.88, 95%*CI*: 5.46−8.69), abdominal obesity (*OR* = 3.08, 95%*CI*: 2.63−3.61), high triglycerides (*OR* = 4.30, 95%*CI*: 3.64−5.08), low serum HDL-C (*OR* = 1.26, 95%*CI*: 1.08−1.48), high blood pressure (*OR* = 2.16, 95%*CI*: 1.93−2.65), and high plasma glucose (*OR* = 2.38, 95% *CI*: 1.96−2.87) in the subjects were significantly associated with elevated ALT after adjustment of age.

The relationship between the clustering of MS components and the risk of elevated AST and ALT in the participants are shown in Table 6. Consistent with the above observations, AST and ALT increased progressively with an increasing number of MS components. Levels of AST and ALT increased from 21.11 ± 9.4 U/L and 18.84 ± 17.92 U/L without any MS component to 26.15 ± 11.33 U/L and

Table 2
The levels of AST, ALT, and AST/ALT grouped by age and gender.

	AST		ALT		AST/ALT	
	Male	Female	Male	Female	Male	Female
20 ~	26.37 ± 12.36[b]	19.74 ± 6.56[a,b]	34.27 ± 28.19[b]	16.21 ± 16.34[a,b]	0.99 ± 0.54[b]	1.48 ± 0.49[a,b]
30 ~	26.19 ± 11.76	20.06 ± 7.10[a]	34.22 ± 24.21	16.85 ± 10.65[a]	0.96 ± 1.21	1.39 ± 0.58[a]
40 ~	25.66 ± 10.89	20.84 ± 8.34[a]	32.49 ± 21.71	18.84 ± 12.61[a]	0.94 ± 0.64	1.32 ± 1.03[a]
50 ~	24.42 ± 9.01	23.53 ± 10.91	27.27 ± 14.15	22.64 ± 17.09[a]	1.02 ± 0.43	1.21 ± 0.41[a]
60 ~	23.51 ± 8.39	24.19 ± 8.81	21.96 ± 13.15	20.70 ± 13.07	1.22 ± 0.40	1.32 ± 0.41[a]
overall	25.49 ± 10.88	20.84 ± 8.09	31.40 ± 22.03	18.17 ± 13.52	0.99 ± 0.80	1.37 ± 0.71

AST: aspartate aminotransferase; ALT: alanine aminotransferase.

[a] Significantly different from the female group are male AST, ALT and AST/ALT in different age groups, $t = 9.519$, 12.435, 9.549; 1.327, 18.046, 14.344, 3.631; 13.627, -8.921, -9.590, -5.988, -2.225; respectively, all $P < 0.05$ or $P < 0.01$ (Student's *t*-test).

[b] Significantly different from different age groups with AST, ALT and AST/ALT in the male and female group, $F = 5.708$, 26.752, 8.495; 15.365, 11.773, 6.341; respectively, all $P < 0.01$.

Table 3
Baseline characteristics of all subjects with and without the metabolic syndrome.

Variables	Metabolic syndrome		Non metabolic syndrome	
	Male (n = 1064)	Female (n = 323)	Male (n = 2254)	Female (n = 1774)
Age (years)	45.88 ± 10.78[a,c]	48.85 ± 11.63[c]	41.70 ± 12.02[a]	37.80 ± 9.59
BMI (kg·m^{-2})	26.59 ± 2.68[b,d]	24.73 ± 2.72[d]	23.74 ± 2.81[b]	21.28 ± 2.58
WC (cm)	94.08 ± 6.21[b,d]	84.18 ± 7.84[d]	84.70 ± 7.82[b]	72.71 ± 7.05
WHR	0.95 ± 0.05[b,d]	0.87 ± 0.06[d]	0.89 ± 0.06[b]	0.80 ± 0.06
SBP (mmHg)	133.42 ± 17.79[b,d]	129.64 ± 17.93[d]	116.22 ± 15.97[b]	108.01 ± 14.66
DBP (mmHg)	89.82 ± 12.42[b,d]	85.29 ± 11.70[d]	77.75 ± 10.86[b]	72.13 ± 9.60
TG (mmol/L)	3.34 ± 2.23[b,d]	2.49 ± 1.27[d]	1.92 ± 1.30[b]	1.19 ± 0.68
TC (mmol/L)	4.90 ± 0.97[d]	4.95 ± 1.00[d]	4.58 ± 0.90[b]	4.28 ± 0.85
HDL-C (mmol/L)	1.08 ± 0.27[b,d]	1.21 ± 0.26[d]	1.30 ± 0.32[b]	1.49 ± 0.33
LDL-C (mmol/L)	2.56 ± 0.90[b]	2.69 ± 0.91[d]	2.50 ± 0.80[b]	2.29 ± 0.72
FPG (mmol/L)	5.61 ± 1.70[d]	5.64 ± 2.01[d]	4.86 ± 1.23[b]	4.69 ± 0.71
AST (U/L)	26.92 ± 11.40[b,d]	23.62 ± 10.86[d]	24.81 ± 10.57[b]	20.33 ± 7.37
ALT (U/L)	35.98 ± 21.69[b,d]	24.81 ± 17.82[d]	29.19 ± 21.86[b]	16.96 ± 12.20
AST/ALT ratio	0.92 ± 1.24[b,d]	1.12 ± 0.40[d]	1.03 ± 0.46[b]	1.41 ± 0.75

BMI: body mass index; WC: waist circumference; WHR: waist-hip ratio; SBP: systolic blood pressure; DBP: diastolic blood pressure; TG: triglycerides; TC: total cholesterol; HDL: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; FPG: fasting plasma glucose.

[a] Significantly different from the female group is the male group with metabolic syndrome or no metabolic syndrome, all $P < 0.05$ or $P < 0.01$.

[b] Significantly different from the male group is the female group with metabolic syndrome or without metabolic syndrome after adjustment for age, all $P < 0.05$ or $P < 0.01$.

[c] Significantly different from the male group or the female group with metabolic syndrome and without metabolic syndrome, all $P < 0.05$ or $P < 0.01$.

[d] Significantly different from the male group or the female group with metabolic syndrome and without metabolic syndrome after adjustment for age, all $P < 0.05$ or $P < 0.01$.

33.38 ± 21.37 U/L with three MS components or more ($P = 0.002$ and 0.002 for the trend). In contrast, the AST/ALT ratio decreased progressively with an increasing number of MS components ($P = 0.017$ for trend). The incidence rates of elevated AST were 2.2%, 4.2%, 6.6%, and 8.0%, and were 5.1%, 12.1%, 18.5%, and 26.8% for elevated rates of ALT in the subjects with 0, 1, 2, and ≥3 risk factors, respectively. The adjusted odds ratios for subjects with 1, 2, and ≥3 risk factors were 1.67 (95%*CI*: 1.06–2.63), 2.28 (95%*CI*:

Table 4
Metabolic variables in the study population with normal and elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT).

Variables	Normal AST (n = 5135)	Elevated AST (n = 280)	t	P	Normal ALT (n = 4578)	Elevated ALT (n = 837)	t	P
Percentage (%)	94.8	5.2			84.5	15.5		
Age (years)	41.71 ± 11.60	40.86 ± 10.74	1.195	0.232	41.98 ± 11.86	39.97 ± 9.54[a]	5.372	<0.001
BMI (kg·m^{-2})	23.46 ± 3.27	25.17 ± 3.40[a]	−8.494	<0.001	23.17 ± 3.20	25.62 ± 3.11[a]	−20.793	<0.001
WC (cm)	82.26 ± 10.56	88.48 ± 10.12[a]	−9.996	<0.001	81.34 ± 10.43	89.37 ± 9.01[a]	−23.104	<0.001
WHR	0.87 ± 0.08	0.91 ± 0.07[a]	−9.842	<0.001	0.86 ± 0.08	0.91 ± 0.06[a]	−20.292	<0.001
SBP (mmHg)	117.44 ± 18.54	122.69 ± 19.39[a]	−4.608	<0.001	116.82 ± 18.44	122.59 ± 18.82[a]	−8.296	<0.001
DBP (mmHg)	78.55 ± 12.57	82.06 ± 12.93[a]	−4.544	<0.001	78.01 ± 12.45	82.68 ± 12.77[a]	−9.944	<0.001
TG (mmol/L)	1.95 ± 1.53	2.84 ± 2.26[a]	−6.538	<0.001	1.85 ± 1.48	2.81 ± 1.88[a]	−13.969	<0.001
TC (mmol/L)	4.55 ± 0.93	4.92 ± 1.03[a]	−5.891	<0.001	4.51 ± 0.92	4.89 ± 0.98[a]	−11.024	<0.001
HDL-C (mmol/L)	1.32 ± 0.33	1.27 ± 0.47	1.920	0.055	1.33 ± 0.34	1.20 ± 0.35[a]	10.356	<0.001
LDL-C (mmol/L)	2.44 ± 0.80	2.62 ± 0.91[a]	−3.274	0.001	2.42 ± 0.79	2.61 ± 0.89[a]	−5.636	<0.001
FPG (mmol/L)	4.99 ± 1.32	5.15 ± 1.25	−1.897	0.058	4.96 ± 1.19	5.25 ± 1.86[a]	−4.433	<0.001

BMI: body mass index; WC: Waist circumference; WHR: Waist-hip ratio; SBP: Systolic blood pressure; DBP: Diastolic bloodpressure; TG: Triglycerides; TC: Total cholesterol; HDL: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; FPG: Fasting plasma glucose.

[a] Significantly different from the elevated group with normal AST and ALT, all $P < 0.05$ or $P < 0.01$ (Student's t-test).

Table 5
The associations between each metabolic variable and the risk of elevated AST and ALT.

Items	Overall	Normal AST	Elevated AST	*OR* (95%*CI*)	*P*-value	Normal ALT	Elevated ALT	*OR* (95%*CI*)	*P*-value
	$n = 5415$	$n = 5135$	$n = 280$			$n = 4578$	$n = 837$		
Age	41.67 ± 11.56	41.71 ± 11.60	40.86 ± 10.74			41.98 ± 11.86	39.97 ± 9.54[d]		
Gender[d]									
Female	2097 (38.7)	2052 (40.0)	45 (16.1)	1		1996 (43.6)	101 (12.1)	1	
Male	3318 (61.3)	3083 (60.0)	235 (83.9)	3.48 (2.51−4.85)	<0.001	2582 (56.4)	736 (87.9)	6.23 (5.01−7.75)	<0.001
BMI[d]									
<24	3009 (55.6)	2908 (56.6)	101 (36.1)	1		2762 (60.3)	247 (29.5)	1	
24−27.9	1914 (35.3)	1792 (34.9)	122 (43.6)	1.96 (1.50−2.57)	<0.001	1495 (32.7)	419 (50.1)	3.63 (3.05−4.33)	<0.001
≥28	492 (9.1)	435 (8.5)	57 (20.4)	3.77 (2.69−5.30)	<0.001	321 (7.0)	171 (20.4)	6.88 (5.46−8.69)	<0.001
Abdominal obesity[a]	1965 (36.3)	1822 (35.5)	143 (51.5)[d]	1.90 (1.49−2.42)	<0.001	1503 (32.8)	462 (55.2)[d]	3.08 (2.63−3.61)	<0.001
Serum triglycerides ≥1.70 mmol/L	2408 (44.5)	2222 (43.3)	186 (66.4)[d]	2.59 (2.01−3.35)	<0.001	1814 (39.6)	594 (71.0)[d]	4.30 (3.64−5.08)	<0.001
Low serum HDL-C[b]	1599 (29.5)	1517 (29.5)	82 (29.3)	0.99 (0.76−1.29)	0.927	1317 (28.8)	282 (33.7)[d]	1.26 (1.08−1.48)	0.004
High blood pressure[c]	1823 (33.7)	1696 (33.0)	127 (45.4)[d]	1.68 (1.32−2.15)	<0.001	1441 (31.5)	382 (45.6)[d]	2.26 (1.93−2.65)	<0.001
FPG ≥5.6 mmol/L	785 (14.5)	721 (14.0)	64 (22.9)[d]	1.81 (1.36−2.42)	<0.001	592 (12.9)	193 (23.1)[d]	2.38 (1.96−2.87)	<0.001

OR: odds ratio; CI: confidence interval; BMI: body mass index; HDL: high-density lipoprotein cholesterol; FPG: fasting plasma glucose; AST: aspartate aminotransferase; ALT: alanine aminotransferase.

Note: continuous variables are means ± SD and categorical variables are numbers (%).

[a] Waist circumference ≥90 cm in males and ≥80 cm in females.

[b] Serum HDL-C <1.03 mmol/L in males and <1.30 mmol/L in females.

[c] Systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg.

[d] Significantly different from the elevated group with normal AST and ALT, all $P < 0.05$ or $P < 0.01$ (Student's *t*-test or Pearson χ^2 test).

Table 6
The relationship between the clustering of metabolic syndrome components and the risk of elevated AST and ALT in the participants.[a]

Number of components	No. of subjects *n* (%)	AST (U/L)	ALT (U/L)	AST/ALT	Elevated AST (AST >40 U/L)		Elevated ALT (ALT >40 U/L)	
					No. of subjects *n* (%)	*OR* (95%*CI*)	No. of subjects *n* (%)	*OR* (95%*CI*)
0	1395 (25.8%)	21.11 ± 9.44[d]	18.84 ± 17.92[d]	1.35 ± 0.61[d]	30 (2.2%)	1	71 (5.1%)	1
1	1447 (26.7%)	22.94 ± 8.85	24.15 ± 18.80	1.19 ± 0.74	61 (4.2%)	1.67 (1.06–2.63)	175 (12.1%)	2.02 (1.50–2.73)
2	1186 (21.9%)	24.75 ± 10.14	29.23 ± 19.72	1.02 ± 0.50	78 (6.6%)	2.28 (1.46–3.63)	219 (18.5%)	2.68 (1.96–3.65)
≥3[b]	1387 (25.6%)	26.15 ± 11.33	33.38 ± 21.37	0.96 ± 1.11	111 (8.0%)	2.59 (1.59–4.21)	372 (26.8%)	3.94 (2.86–5.43)
P for trend[c]		0.002	0.002	0.017		0.012		0.007

AST: aspartate aminotransferase; ALT: alanine aminotransferase.
Continuous variables are means ± SD and categorical variables are numbers (%).
[a] The adjusted ORs and 95%CIs were calculated by logistic regression analysis to determine the risk of elevated AST and ALT according to the number of components of the metabolic syndrome after adjustment for age, gender and BMI.
[b] Participants having ≥3 of the following 5 risk factors were defined as having the metabolic syndrome: abdominal obesity, high triglycerides, low HDL cholesterol, high blood pressure or high plasma glucose.
[c] Trend test to show linear increase or decrease in AST, ALT, AST/ALT ratio and ORs for AST and ALT according to the number of components of metabolic syndrome.
[d] Significantly different from the groups who has different numbers of components of metabolic syndrome.

1.46–3.63), and 2.59 (95%*CI*: 1.59–4.21) for elevated AST and 2.02 (95%*CI*: 1.50–2.73), 2.68 (95%*CI*: 1.96–3.65), and 3.94 (95%*CI*: 2.86–5.43) for elevated ALT. We observed a direct relationship between the adjusted *OR*s of elevated AST and ALT and the proportion of MS, and the linear trend was significant ($P = 0.012$, and 0.007 for trend).

Discussion

Recently, some studies have demonstrated that liver enzymes are associated with risks of type 2 diabetes mellitus, nonalcoholic fatty liver disease (NAFLD), and MS in Western countries and developing countries.[17,18] However, very little progress has been made evaluating the adult population in China, especially in the relatively undeveloped areas like Ningxia. The purpose of our study was to investigate the impact of elevated aspartate and alanine aminotransferase on MS and its components among adults living in Ningxia, China.

In this study, we report that the age-adjusted prevalence of MS is 23.2% in the study population according to the modified ATPIII criteria for Asian Americans by AHA-ATP III. The MS prevalence obtained in our study is remarkably higher than what was reported previously in a survey of rural adults in Ningxia using the criteria of the International Diabetes Federation IDF (2005).[19] These findings showed that the MS had become a serious public health challenge in Ningxia. The prevalence of elevated AST and ALT were higher in males (7.1% and 22.2%) compared with females (2.1% and 4.8%), and our findings agree with the results of previous studies.[14,18]

The association of aminotransferase levels with MS or its constituents has already been reported. These studies showed that hepatic enzyme levels in subjects with MS were significantly higher than those in subjects without the MS.[2,13,17,20] Particularly, insulin resistance studies showed not only the ALT level but also the aminotransferase ratio might be used as a marker for MS.[21] Nevertheless, an ATTICA study has reported an association of MS only with the AST/ALT ratio.[22] Our study demonstrates associations of MS with AST, ALT, and the AST/ALT ratio. AST and ALT concentrations were higher and the AST/ALT ratio lower in those with MS in both males and females.

A few earlier studies have reported that the prevalence of elevated (abnormal) ALT or ALT levels decreases with increasing age in both genders.[14,23,24] There are some reports of this association being found in males but not in females.[25,26] However, other

reports suggest that there is no correlation between ALT and age.[27,28] In our study, we found that the AST and ALT levels and the prevalence of elevated (abnormal) AST and ALT decreased with age in males and increased in females. The mechanisms are still unclear. A Rancho Bernardo Study reported that ALT levels decreased with increased age in both men and women independent of MS components, adiposity signaling biomarkers, and other commonly used liver function tests.[23] They proposed that further studies were needed to understand the mechanisms responsible for a decline in ALT with age, and to establish the optimal cut-point of normal ALT in the elderly. In the present study, the serum ALT level is more closely related to MS than AST level. So, our finding agrees with the results of previous studies.[29] The reason may be that ALT has only low levels in skeletal muscle and kidneys, so it is more specific for liver damage than AST that is diffusely represented in the heart, skeletal muscle, kidneys, brain, and red blood cells.[22]

We found a significant relationship between elevated AST and ALT levels and the number of components of MS after adjustment for age, gender and BMI, although the odds ratio does not represent the exact change of biological function. A Korean study on adolescents revealed that the risks for elevated ALT increased with the number of components of MS after adjustment for age and body mass index.[13] Our results also showed that the AST and ALT levels increase with the number of components of MS, whereas the AST/ALT ratio decreases. However, the mean ALT activities in subjects with 2 or 3 metabolic risk factors were not particularly high, tending only to be close to the upper limit. Screening for serum ALT levels may facilitate identifying the potential risk for MS-related diseases in the general population, in addition to detection of liver disease, even within the reference interval.[30] Although this relationship between AST, ALT and MS is not clearly understood, some mechanisms, including the presence of oxidative stress and/or NAFLD, can explain.

We are aware that the present data have some limitations and should be interpreted with caution. Our study used a cross-sectional design, so it could not establish causal relationships, but our finding agreed with hypotheses about the link between liver enzymes and aminotransferase ratio and MS.[22] Our conclusions are based solely on liver enzymes levels, whereas serum ALT and AST levels alone cannot be used as a marker for histological diagnosis. The population sample was selected from employees of the local governments and industries of Ningxia, and might not be represented the whole populations of Ningxia. Furthermore, the threshold for defining elevated hepatic enzymes in adults remains unclear. Some studies reported that increased concentrations of hepatic enzyme in serum, even within the reference interval, may be related to an increased risk of MS.[3,29]

In conclusion, our study demonstrated that the serum aminotransferases levels were higher in both genders with MS and they were higher in males than in females in adult groups from Ningxia, China, whereas serum ALT level was more closely associated with the MS than AST levels. The mean values of serum aminotransferases decreased with increasing age in males and increased in females. Our results revealed that the risks for elevated aminotransferase levels increased with the number of components of MS after adjustment for age, gender, and BMI. Moreover, our study also showed that with the increased number of components of MS, the aminotransferases level increases and the aminotransferases ratio decreases.

Conflicts of interest

The authors declare that they have no competing interests.

Authors' contributions

Chuan Zhao and Kunpeng He performed analyzed data and wrote the paper. Herong Liu performed the lab work. Nan Chen and Xiujuan Tao performed field and lab work. Yan Qiang and Lili Chen performed field work. Hui Song designed research, wrote paper, analyzed data and performed field work.

All authors read and approved the final manuscript.

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