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Analysis of the relationship between serum alanine aminotransferase and body composition in Chinese women

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Abstract

Objective: To investigate the relationships between serum alanine aminotransferase (ALT) and body composition among postmenopausal women in China.

Methods: A cross-sectional study was conducted with 776 postmenopausal women in China from May to July 2008. Clinical information was collected using a standardized questionnaire. Measures of body composition were obtained using dual X-ray absorptiometry. Body lean mass and fat mass indices were calculated by dividing total body lean/fat weight (kg) by body height squared (kg/m^2). Blood samples were collected to assess liver and renal functions and lipid profiles. Analysis of variance, Pearson correlations, and multiple regression were used to analyze the associations between serum ALT and body composition.

Results: We found negative relationships of serum ALT with age, menopause duration, and serum HDL-C levels. Serum ALT was positively correlated with BMI, serum TG levels, and the lean mass index and fat mass index. In a multivariate model adjusted for age, menopause duration, serum TG, and HDL-C levels, a 1-unit increase in the fat mass index was associated with a 0.176 U/L increase in ALT (95% CI 0.020 to 0.050, $P < 0.001$).

Conclusion: Serum ALT was positively associated with the body fat mass index of postmenopausal women in China.

KEYWORDS
alanine aminotransferase, body composition, postmenopausal women,

1 | INTRODUCTION

Alanine aminotransferase (ALT) is an enzyme found mostly in liver cells, which is widely used as a sensitive marker of liver injury. Recent studies have related ALT with liver steatosis, oxidative stress, and insulin resistance.[1,2] In addition, new evidence has shown that a high level of serum ALT may lead to type 2 diabetes, metabolic syndrome, and cardiovascular disease (CVD).[3–5] Therefore, it is important to identify the risk factors associated with elevated levels of serum ALT.

A study of an overweight and obese population found that serum ALT was positively associated with body fat mass in men and lean mass in men and women.[6] However, there are conflicting reports about the relationship between serum ALT and body composition. For example, Messier et al.[7] reported that lower ALT was associated with lower liver fat content in obese postmenopausal women. As data on the possible associations between serum ALT and body composition among postmenopausal women in China are limited, we designed this study to investigate the relationship between serum ALT and body composition among postmenopausal women in China.

2 | METHODS

2.1 | Study population

The data were obtained from a randomly selected population-based cohort.[8] A total of 1096 potential participants who had experienced their last menstrual cycle at least 1 year before recruitment were invited to participate in the study. The exclusion criteria were: diabetes mellitus, hyperthyroidism, oligomenorrhoea, malabsorption, rheumatoid arthritis, impaired renal function (eGFR <60 ml/min/1.73 m^2), and hepatic dysfunction (ALT ≥2.0 times the upper limit of normal). Of the 1096 potential participants, 776 healthy postmenopausal women were selected for the analysis. Written consent was obtained from all of them, and the ethics committee of the Second Xiangya Hospital of Central South University approved the study. The study was conducted in accordance with the principles of the Helsinki Declaration.

2.2 | Clinical measures

The participants completed a self-report questionnaire that asked questions about their age, menopause duration, marital status, and history of chronic diseases and medical treatment. Laboratory tests were conducted to measure ALT, aspartate aminotransferase (AST), lipid profiles (triglyceride [TG], total cholesterol [TC], low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C]), renal function (blood urea nitrogen [BUN], and serum creatinine [Scr]). The 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used to calculate the estimated glomerular filtration rate (eGFR).[9]

The body weight (kg) and height (cm) of participants were measured while wearing light clothes. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Measures of body composition were assessed using dual X-ray absorptiometry (DXA; Lunar Prodigy Advance, GE Healthcare). The body lean/fat indices were calculated as total body lean and fat weight (kg) divided by body height squared (m^2).

2.3 | Statistical analysis

Log transformations were made when the distributions of the variables were skewed, e.g. BUN, Scr, eGFR, ALT, AST, TG, and HDL-C. Descriptive data are reported as mean ± standard deviation (SD), whereas skewed variables are reported as median (25% and 75% quartiles). Linear associations between ALT and the independent variables were examined using Pearson's correlation coefficient. One-way analysis of variance (ANOVA) was used to compare continuous variables across ALT quartiles. Multiple regression was used to identify the variables associated with ALT, after adjusting for possible confounders. The statistical analyses were performed using SPSS, version 26.0 (SPSS Inc.). A *P*-value <0.05 was considered statistically significant.

3 | RESULTS

The mean age of the 776 participants was 62.1 years and their mean menopause duration was 12.6 years. The mean lean mass index was 14.36 kg/m^2 and the mean fat mass index was 7.96 kg/m^2 (Table 1).

As shown in Table 2, ALT had a significant negative correlation with age, menopause duration, and HDL-C, and it had a significant positive correlation with BMI, TG, lean mass index, and the fat mass index.

The lean mass and fat mass indices increased significantly from quartile 1 to quartile 4 of serum ALT in the sample (Table 3). Furthermore, a 1-unit increase in the fat mass index was associated with a 0.176 U/L increase in ALT, after adjusting for age, menopause duration, TG, and HDL-C. However, the lean mass index was not associated with ALT levels, after controlling for these variables (Table 4).

TABLE 1 Characteristics of the study participants

Variable	Total
Age (years)	62.1 ± 6.1
Menopause duration (years)	12.6 ± 7.1
Height (cm)	153.8 ± 5.1
Weight (kg)	55.4 ± 7.8
BMI (kg/m^2)	23.4 ± 3.0
BUN (mmol/L)	5.28 (4.38, 6.18)
Scr (μmol/L)	58.30 (49.43, 66.10)
eGFR (ml/min/1.73^2)[a]	94.75 (85.33, 101.50)
ALT (U/L)	17.10 (13.50, 22.00)
AST (U/L)	22.00 (19.33, 26.10)
TG (mmol/L)	1.45 (1.08, 2.02)
TC (mmol/L)	5.33 ± 0.90
HDL-C (mmol/L)	1.54 (1.34, 1.76)
LDL-C (mmol/L)	3.14 ± 0.75
Body lean mass (kg)	34.00 ± 3.36
Body fat mass (kg)	18.86 ± 5.23
Lean mass index (kg/m^2)	14.36 ± 1.19
Fat mass index (kg/m^2)	7.96 ± 2.16

Note: Data are presented as mean ± SD or median (25% and 75% quartiles).

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Scr, serum creatinine; TC, total cholesterol; TG, triglyceride.

[a]eGFR calculated using the 2009 CKD Epidemiology Collaboration equation.

4 | DISCUSSION

Alanine aminotransferase is an enzyme that is located primarily in the cytosol of hepatocytes, and thus, it is a specific marker for liver injury.[10] Many studies have confirmed the association between ALT and body composition.[6,11] However, some research has found no association between serum ALT and fat mass in women,[6] and the relationship between ALT and the body composition of postmenopausal women in China has not been reported, to date. The current study found that ALT was positively associated with the fat mass index in this sample. After adjusting for age, menopause duration, TG, and HDL-C, BMI was independently associated with ALT among the postmenopausal Chinese women in this study.

Study results of the relationship between ALT and body composition in different populations are controversial. Ruhl et al.[12] found that higher ALT was associated with higher levels of fat and lean mass among Hispanic and African Americans. In this study, we found positive relationships between serum ALT levels and both fat and lean mass indices among postmenopausal women in China. However, after adjusting for age, menopause duration, TG, and HDL-C, the lean mass index was not significantly associated with ALT. Previous studies have found that the association of body fat mass with serum ALT levels differ between premenopausal and postmenopausal women. A cross-sectional study of premenopausal and postmenopausal women found no association between serum ALT levels and body fat mass.[6] These findings suggest that the association between serum ALT levels and fat mass may be due to confounding factors. Postmenopausal women are more susceptible to weight gain, loss in body lean mass, and fat redistribution from the gluteofemoral to the abdominal region.[13,14] Furthermore, a previous study showed that women of Chinese origin have a lower fat mass and a higher lean mass than women of South Asian origin.[15] Finally, significant race difference exists in serum ALT levels.[16] These differences may explain, in part, why our results differ from those of previous research.[6]

One of the most important physiological changes in postmenopausal women is a dramatic reduction in estrogen. Estrogen deficiency promotes metabolic dysfunction that predisposes women to obesity, type 2 diabetes, and liver fat accumulation.[17–19] In our study, after adjusting for age, menopause duration, TG, and HDL-C, a 1-unit increase in the fat mass index was associated with a 0.176 U/L increase in ALT. The association between serum ALT levels and the fat mass index is postulated to be caused by insulin resistance and inflammation. Hepatic fat accumulation, known as nonalcoholic fatty liver disease (NAFLD), is closely related to insulin resistance.[20] Previous studies have reported a positive association between insulin resistance and serum ALT levels.[1,21] It is well known that inflammation induces the progression of NAFLD and increases serum ALT levels.[22] Moreover, body fat mass is positively related to high-sensitive C-reactive protein, a general indicator of inflammation.[23]

Currently, serum ALT is widely used not only to assess the development and prognosis of liver disease, but also as a reference with screening overall health status during health check-ups.[24] Hernaez et al.[25] reported that individuals with elevated ALT had an increased risk for all-cause and cardiovascular mortality. Furthermore, an increase in serum ALT is considered to be an important risk factor for type 2 diabetes and metabolic syndromes.[3,4] As found in the present study, higher values of the fat mass index were related to higher ALT levels, adjusting for confounding factors. Therefore,

TABLE 2 Correlations of ALT with body composition, and potential confounders

	r	*p*
Age (years)	−0.108	0.003
Menopause duration (years)	−0.119	0.001
BMI (kg/m^2)	0.280	<0.001
eGFR (ml/min/1.73^2)	0.068	0.057
TG (mmol/L)	0.233	<0.001
TC (mmol/L)	0.067	0.063
HDL-C (mmol/L)	−0.155	<0.001
LDL-C (mmol/L)	0.063	0.079
Lean mass index (kg/m^2)	0.207	<0.001
Fat mass index (kg/m^2)	0.258	<0.001

Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

TABLE 3 Lean mass index, fat mass index, and confounders by quartiles of serum ALT

ALT quartiles	Q1	Q2	Q3	Q4	*p*
Q-intervals (U/L)	≤13.50	13.50–17.10	17.10–22.00	≥22.00	
Age (years)	62.9 ± 6.0	62.2 ± 6.4	62.4 ± 6.3	60.8 ± 5.5	0.007
Menopause duration (years)	13.6 ± 7.1	12.7 ± 7.3	12.8 ± 7.1	11.1 ± 6.9	0.006
BMI (kg/m^2)	22.31 ± 2.82	23.21 ± 2.88	23.65 ± 2.66	24.48 ± 3.17	<0.001
TG (mmol/l)	1.45 ± 0.80	1.59 ± 0.85	1.70 ± 0.87	1.99 ± 1.15	<0.001
HDL-C (mmol/l)	1.60 ± 0.33	1.60 ± 0.31	1.54 ± 0.29	1.49 ± 0.30	<0.001
Lean mass index (kg/m^2)	14.03 ± 1.12	14.29 ± 1.14	14.42 ± 1.14	14.71 ± 1.26	<0.001
Fat mass index (kg/m^2)	7.26 ± 2.08	7.86 ± 2.15	8.08 ± 1.84	8.64 ± 2.32	<0.001

Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; Q1, first quartile; Q2, second quartile; Q3, third quartile; Q4, fourth quartile; TG, triglyceride.

TABLE 4 Associations of ALT with the body composition of the participants

	ALT (U/L) as dependent variable		
	β[a]	95% CI	*p*
Age (years)	−0.059	−0.013 to 0.005	0.379
Menopause duration (years)	−0.029	−0.010 to 0.006	0.659
TG (mmol/L)	0.166	0.182 to 0.506	<0.001
HDL-C (mmol/L)	−0.044	−0.607 to 0.174	0.276
Lean mass index (kg/m^2)	0.076	0.000 to 0.055	0.052
Fat mass index (kg/m^2)	0.176	0.020 to 0.050	<0.001

Abbreviations: ALT, alanine aminotransferase; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride.

[a]Values are the regression coefficients (95% CI) expressed in ALT U/L for a 1-unit change in the independent variables.

postmenopausal women should monitor their body composition, exercise, and eat appropriately to maintain proper body fat mass, all of which may eventually reduce the risk of all-cause and cardiovascular disease death.

This study has notable strengths, including its sample size and the fact that the study collected data on a population that has rarely been investigated. In addition, we assessed body composition with DXA, which has been shown to be more accurate than other methods of measuring total body fat mass.[26] Finally, we focused on Chinese women, as serum ALT levels are higher in Chinese women than in Western women.[16] Our study also has some limitations. First, the participants may be healthier than average women. Thus, further studies are needed to explore the relationships between ALT and body composition in the general population. Another limitation of the present study is the lack of measures of partial body composition, such as visceral fat mass and the waist–hip ratio. Finally, some clinical data were collected in the form of a questionnaire, whose accuracy may be questionable.

In conclusion, our study indicated that participants with increased body fat mass have significantly increased levels of serum ALT. The government and physicians should implement strategies to screen body composition in postmenopausal women and give them appropriate recommendations about how to maintain an optimize their body fat mass.

AUTHOR CONTRIBUTIONS

Conceptualization: Shuang Li, Junkun Zhan, Yanjiao Wang. Data curation: Yi Wang, Wu Huang. Data analysis: Shuang Li, Jieyu He. Funding acquisition: Shuang Li, Junkun Zhan, Youshuo Liu. Project administration: Eryuan Liao, Youshuo Liu. Writing - original: Shuang Li, Junkun Zhan, Yanjiao Wang. Writing - review and editing: all authors.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest regarding the conduct or publication of this paper.

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