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Gender differences in the association of hypertension with gamma–glutamyltransferase and alanine aminotransferase levels in Chinese adults in Qingdao, China

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Abstract

Objective

To study the associations of hypertension with gamma–glutamyltransferase (GGT) and alanine aminotransferase (ALT) levels.

Methods

Data of 3575 men and 5504 women were analyzed. Multivariable logistic regression analysis was performed to estimate the odds ratio (OR) for hypertension with GGT and ALT.

Results

Compared with the lowest quartile, the multivariate adjusted ORs for hypertension were 0.97(0.79, 1.19) in men and 0.88(0.74, 1.04) in women for ALT and 2.29(1.68, 3.14) and 1.52(1.27, 1.83) for GGT in the highest quartile group. The ORs for hypertension in the low waist circumference (WC) category were 2.61(1.56, 4.36) in men and 1.41(0.94, 2.12) in women, and in the high WC category 4.01(2.21, 7.29) and 2.26 (1.54, 3.32) for GGT.

Conclusions

The elevated GGT, but not ALT, was associated with the presence of the hypertension in men and women. The association is stronger in obese men and women than in their lean counterparts.

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Key words: Alanine aminotransferase, gamma–glutamyltransferase, hypertension

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Introduction

Serum gamma–glutamyltransferase (GGT) is commonly used as an indicator of alcohol consumption and oxidative stress [1, 2]. Another liver enzyme, alanine aminotransferase (ALT), is the most specific marker of liver pathology, and a strong bio-marker for liver fat accumulation and hepatic insulin sensitivity [3, 4]. Recently, emerging evidence suggests GGT and ALT are associated with the presence of hypertension [5-16].

However, the levels of ALT and GGT differ between men and women, with higher values observed in men [17, 18], only a few studies have compared these liver enzymes for their associations with hypertension separately by men and women [15, 18-20], and it is not entirely clear to clarify if there is a difference in this association between men and women. Moreover, both ALT and GGT are associated with obesity, it is, thus, important to check whether the associations of elevated blood pressure levels with ALT and GGT are not confounded by obesity.

In this study, first, the association of hypertension with serum GGT and ALT levels is examined separately by men and women in a Chinese adult living in Qingdao, China. Second, a stratified analysis by the waist circumference (WC) levels was, thus, performed to check whether the association between the serum GGT and ALT with hypertension depend on obesity in men and women.

Research design and methods

Study population

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Population-based cross-sectional surveys were conducted separately in 2006 and 2009 in Qingdao, China. A stratified, random cluster sampling method was used to recruit a representative sample of the general population aged 35-74 years old for all surveys. Both surveys were conducted in the same three urban districts (Shinan, Shibei and Sifang) and three rural counties (Jiaonan, Huangdao and Jimo). Five residential communities from each area with 200-250 individuals from each community were randomly selected, and a total of 6100 individuals were invited to the survey in 2006 and 6000 individuals in 2009, respectively. All participants were invited to a survey site near their resident communities. Similar approaches were applied in two surveys. The number of participants in each survey was 5355 (giving a response rate of 87.8%) in 2006 and 5165 (giving a response rate of 86.1%) in 2009.

Each survey participant completed a questionnaire and underwent a detailed medical examination by a trained doctor or nurse. Waist circumference (WC) was calculated at the umbilical level. Height and weight was measured with participants wearing light clothes and without shoes. Body mass index (BMI) was then measured by dividing weight (kg) by height (m) squared (kg/m^2). Blood pressure was measured with mercury sphygmomanometer (Yuyue, China). Three consecutive blood pressure readings, apart by at least 30 seconds, were taken from the right arm of seated subjects in a quiet room, and the average of the three readings was used in the data analysis. The alcohol-drinking was classified as heavy drinkers (with an alcohol intake of ≥ 40 gram per day)，moderate drinkers (with an alcohol intake of <40 gram per day) and

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non-drinkers (including ex-drinking or not drinking at all) [21]. The smoking status was defined as current smokers (smoking every day) and non-smokers (including ex-smoking, smoking now and then and not smoking at all). A family history of hypertension was classified as having at least one of parents, siblings or offsprings with diagnosed hypertension. Education levels was divided into two levels (≤ 9 or＞9 school years). Blood samples were collected locally and all participants were informed to be fast at least 10 hours before blood samples were collected. The lab assays were performed in the central laboratory of Qingdao Hiser Medical Center using Olympus AU analyzers in 2006 and in Qingdao Endocrinology and Diabetes Hospital using Hitachi AU analyzers in 2009. Fasting serum triglycerides (TG) and total cholesterol (TC) were determined by enzymatic method while fasting serum high-density lipoprotein cholesterol (HDL-C) by direct method. Low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald equation. Fasting plasma glucose (FPG) were determined by the glucose oxidize method. ALT and GGT were measured by using an International Federation of Clinical Chemistry (IFCC) method. The concentration of fasting insulin was measured using the chemiluminescence immunoassay method (Abbott AxSym). The index of the homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using the formula [HOMA-IR =fasting insulin (mU/L）× FPG (mmol/L)/22.5].

The inclusion criteria for the current study were participants who had no data missing for age, BMI, WC，alcohol status, smoking status, lipids, FPG and blood pressure.

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Finally, a total of 9079 (40% men) subjects were included in the analysis. The two surveys were approved by the Ethic Committee of Qingdao Municipal Hospital and Qingdao Municipal Center for Disease Control and Prevention, respectively. Verbal and written consent was obtained from each participant before the data collection.

Classification of hypertension

Newly diagnosed hypertension was defined as systolic blood pressure (SBP) ≥140 mm Hg and /or diastolic blood pressure (DBP) ≥90 mm Hg. Subjects who reported a history of hypertension and/or who were under treatment with oral anti-hypertensive medication were considered as previously diagnosed hypertension, regardless of their blood pressure levels. There was no difference in the mean levels of ALT and GGT between the subjects with a history of hypertension and the subjects with newly diagnosed hypertension, therefore newly and previously diagnosed hypertension were included in the data analysis.

Statistical analysis

Data were summarized as mean (± standard error) for continuous variables and proportions for categorical variables. Due to skewed distribution, values derived from logarithmically transformed means were used for GGT and ALT in data analysis. The general linear model approach for continuous variables and a chi-square test for categorical variables were used to compare differences in age-adjusted means and prevalence between hypertension and normotension in both surveys. The linear association of ALT and GGT with SBP and DBP was tested using multivariable linear

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regression model, adjusting for age, school years, family history of hypertension, *current smoking, alcohol-drinking,* BMI, HDL and TG, and the standard β coefficients and 95% confidence interval (CI) were calculated. The *multivariable logistic regression was performed to investigate the association of hypertension with serum ALT and GGT levels in both genders, adjusting for age, current smoking, alcohol-drinking, school year, family history of* hypertension, *BMI, HDL and TG. We divided the serum values of ALT and GGT into four groups based on gender-specific quartiles (25th, 50th and 75th percentiles)*. Odds ratios (ORs) (95% CI) of *hypertension were tested* for *each ALT andGGT quartiles, with the lowest quartiles as the reference*.

The participants between two surveys were not different in mean values of age, BMI, WC, blood pressure, FPG and lipids, and there might be a few variables in which the two surveys seemed to differ, such as the proportions of heavy drinkers, so we pool data from both surveys for data analysis. The distribution of BMI is normal, so a linear measure of the BMI was fitted in the model as a co-variable. To examine the quadratic association, a squared term of the BMI was added into a model together with the linear BMI, and the result showed the linear associations was significant. Moreover, the linear associations between other continuous variables with the presence of hypertension were validated also, and the results remained no changes. Thus a linear measure of the BMI and other continuous variables were fitted into the *multivariable* logistic regression model. All analyses were performed using SPSS (Version15.0; SPSS Inc, Chicago, IL, USA) or SAS 9.3 (SAS Institute, Cary, NC). A p-value less than 0.05 (two tailed) was

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considered statistically significant.

Results

The baseline characteristics of the study population in two surveys were shown in table 1. The subjects with hypertension were older, more obese, had greater levels of FPG and lipids in men and women in comparison with individuals with normotension. They also had significantly higher levels of GGT, but the mean levels of ALT were higher only in men with hypertension. The proportions of family history of hypertension, current smoker and heavy drinker were not statistically significant between hypertensive and non-hypertensive groups of either gender.

The standard beta coefficients and 95% CI were summarized in table 2. The correlation coefficients for GGT-SBP, GGT-DBP were statistically significant in men and women, whereas those for ALT were significant with DBP in men. There is no major differences in the contributions of GGT with SBP between the two surveys but slight discrepancies are identified in the standard beta coefficients of GGT with SBP between two surveys.

Compared with the lowest quartile, the multivariable adjusted ORs for hypertension was significantly higher within the top three quartiles of the GGT in men and women. The relationship of hypertension with ALT was positive merely in men, but faded significantly when BMI was adjusted into the model (table 3).

In addition, a positive interaction of the GGT with the WC in men (P<0.001) and women (P<0.001) was discovered, a stratified analysis according to the quartiles of WC

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was performed to further check the association between GGT and hypertension in low and high WC categories. The ORs for hypertension in the low waist circumference (WC) category were 2.61(1.56, 4.36) in men and 1.41(0.94, 2.12) in women, and in the high WC category 4.01(2.21, 7.29) and 2.26 (1.54, 3.32) for GGT. The association between GGT and hypertension is stronger in high WC categories than in low one in both genders (table 4).

Discussions

In these population-based cross-sectional studies, we demonstrated that increased serum GGT levels were positively associated with the presence of hypertension in men and women. Such an association was, however, not observed for the ALT. The effect of elevated GGT on hypertension was significant only in obese women, but GGT was positively associated with hypertension in both lean and obese men. Specifically, the association between and hypertension appeared to be stronger in obese men and women than in their lean counterparts.

To the best of our knowledge, many cross-sectional and longitudinal studies have investigated the association between GGT and hypertension [5-10, 13-16]. However, only a few previous studies that examined sex-specific association between concentrations of GGT with hypertension demonstrated inconsistent results and none of these studies have been carried out in Chinese [15, 17, 19, 20]. A population-based prospective study including 1556 men and 1889 women aged 35-69 years old showed the positive association only in men [19]. But another prospective population-based

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study including 1171 men and 1267 women aged 20-54 years old performed in Norway showed a weak association between GGT levels and blood pressure only in women but not in men [17]. In the prospective population-based study including 1167 adults aged 33-84 years old performed in Turkey, the positive association between GGT levels and the presence of hypertension was significant in men and women [15], which consisted with our results.

The mechanisms underlying the association of the development of hypertension with the elevated levels of GGT have not been fully addressed and several possible mechanisms may explain this. First, GGT might be an early sensitive enzyme related to oxidative stress [2], and oxidative stress may play an important role in the initiation and progression of hypertension in the long run [8], which suggested that the significant association of hypertension with the elevated levels of GGT might be explained by oxidative stress. Second, prospective study indicated that increased GGT activity is significantly associated with inflammation markers, such as white blood cell (WBC) count, C–reactive protein, fibrinogen and F2-isoprostanes [8, 22, 23], so high GGT levels could be a marker of subclinical inflammation, which was a causal factor of hypertension. Finally, GGT was shown to be associated with insulin resistance [24, 25], and insulin resistance existed in subjects with hypertension [26, 27].

In our study, the effect of elevated GGT on hypertension was significant only in obese women, but GGT was positively associated with hypertension in both lean and obese men. Specifically, the association between and hypertension appeared to be

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stronger in obese men and women than in their lean counterparts. This indicated that obesity enhances the effect of GGT on blood pressure. This is partly due to the fact that obesity increases the GGT concentrations [9], and all these may explain the weak association between GGT and hypertension in women who had low waist circumference. The other reason might explain our finding that GGT was associated with hypertension only in obese women might be sex hormone levels, such as the sex hormones binding globulin (SHBG), which are lower in obese women than in lean women. So the decrease in SHBG contributes to the high GGT concentration [28]. This may largely explain the association of GGT with hypertension in obese women observed in our current study.

Our results lent support to the previous studies showing that there is not an independent association between the presence of hypertension with the elevated serum levels of ALT in men and women in this Chinese population [9, 14]. It is possible that higher serum levels of ALT is an early reflection of hepatic steatosis and considered a more liver-specific marker than GGT [29, 30], but GGT is the enzyme for the extracellular catabolism of antioxidant glutathione and commonly used as an indicator of oxidative stress [1, 2, 31]. The lack of relationship between the presence of hypertension with the elevated serum levels of ALT further showed that the association of GGT with hypertension may largely depend on oxidative stress rather than merely liver injury.

The main strengths of our study are: (1) this is a population-based study with a random

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sampling approach and represents the general population in China; (2) the collaborative analysis of two surveys can increase the statistical power, and the sample size of the study is large enough to examine sex-specific associations between the presence of hypertension with the liver enzymes; However, the cross-sectional nature of present study limits it from going further to investigate the direct causation between elevated GGT levels and hypertension. In addition, self-reported alcohol consumption was questionable because of its validity and reliability.

Conclusions

In summary, the elevated serum GGT levels, but not ALT, were independently associated with the presence of the hypertension in men and women in this Chinese population. The association is stronger in obese men and women than in their lean counterparts. Further study on the natural relationship between GGT concentration and hypertension as well as the effect of obesity on the relationship is warranted.

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Declaration of competing interests: Nothing to declare.

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Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; GGT, gamma–glutamyltransferase; GLM, general linear model; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; OR, odds ratio; SBP, systolic blood pressure; SE, standard error;; TG, triglyceride; TC, total cholesterol; WC, waist circumference.

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Table1. Baseline characteristics of participants in two surveys.

	Men		Women	
	Normotension	Hypertension	Normotension	Hypertension
Number (%)	1668(46.6%)	1907(53.4%)	2918(53.0%)	2586(47.0%)
Age (years)	49.5(49.3,49.7)	53.4(53.1,53.7)*	47.8(47.6,48.0)	55.0(54.8,55.2)*
School years> 9 (yes, %)	23.6	19.9*	26.6	8.5*
Current smoking (yes, %)	21.3	19.6	1.0	0.5
Current drinking (%)				
non-drinkers	72.7	72.5	99.1	99.3
Moderate-drinkers	12.1	14.0	0.9	0.7
heavy-drinkers	15.2	13.5	0	0
Family history of hypertension (yes, %)	12.1	12.9	11.6	13.1
Body mass index (kg/m^2)	24.2(23.5,24.9)	25.9(25.1,26.7)*	24.5(23.9,25.1)	26.7(26.1,27.2)*
Waist circumference (cm)	83.5(83.2,83.8)	87.2(86.9,87.5)*	79.6(79.7,79.8)	85.2(85.0,85.4)*
Fasting plasma glucose(mmol/L)	5.77(5.72,5.62)	6.17(6.11,6.23)*	5.65(5.62,5.68)	6.25(6.14,6.36)*
Haemoglobin A1c ‖	5.50(5.47,5.53)	5.65(5.62,5.67)*	5.44(5.37,5.51)	5.76(5.68,5.84)*
HOMA-IR ‖	10.9(9.7,12.1)	12.4(10.5,14.3)	12.1(11.2,13.0)	16.7(14.8,18.6)*
Low density lipoprotein cholesterol (mmol/L)	2.84(2.77,2.91)	3.02(2.94,3.10)*	2.89(2.85,2.93)	3.13(3.06,3.20)*
High density lipoprotein cholesterol (mmol/L)	1.61(1.58,1.64)	1.62(1.59,1.65)	1.67(1.62,1.72)	1.61(1.57,1.65)
Total cholesterol (mmol/L)	5.15(5.11,5.19)	5.35(5.30,5.40)*	5.09(5.07,5.11)	5.49(5.42,5.56)*
Triglyceride (mmol/L)	1.40(1.36,1.44)	1.59(1.56,1.62)*	1.21(1.15,1.27)	1.56(1.47,1.65)*
Alanine aminotransferase (U/L)§	20.4(19.7,21.1)	22.1(21.2,23.0)*	17.5(16.3,18.7)	18.7(17.4,19.1)
Gamma–glutamyltransferase (U/L) §	23.9(22.6,25.2)	29.5(27.8,31.2)*	14.6(13.2,16.0)	17.9(16.4,19.4)*

Data are age-adjusted mean (95% confidence interval) or number (percentages) indicated. *P＜0.05, hypertension vs. normotension by the same survey within the same gender. §Geometric mean (95% CI). ‖ With missing data. HOMA-IR, homeostasis model assessment of insulin resistance.

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Table2. Multiple linear regression analysis for alanine aminotransferase (ALT) and gamma–glutamyltransferase (GGT) in association with diastolic blood pressure and systolic blood pressure.

	Diastolic blood pressure		Systolic blood pressure	
	Standard β coefficients	95%CI	Standard β coefficients	95%CI
Men				
ALT**(**U/L)	0.09*	(0.08, 0.11)	0.03	(0.01, 0.05)
GGT**(**U/L)	0.07*	(0.05, 0.08)	0.11*	(0.10, 0.13)
Women				
ALT**(**U/L)	0.04	(0.03, 0.05)	0.05	(0.04, 0.06)
GGT**(**U/L)	0.07*	(0.06, 0.08)	0.09*	(0.07, 0.10)

Adjusted for age, school years, family history of hypertension, *current smoking*, *alcohol-drinking*, body mass index, triglycerides and high density lipoprotein cholesterol. ALT and GGT are logarithmic transformed. * P<0.01.

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Table3. Odds ratio (95% confidence interval) for hypertension in relation to quartiles of alanine aminotransferase (ALT) and gamma–glutamyltransferase (GGT) concentrations.

		Model1	Model2	Model3	Model4	Model5	Model6
Men	**Number**						
ALT							
Q1 (<=10 U/l)	820	1	1	1	1	1	1
Q2 (10-15 U/l)	871	0.97(0.79, 1.20)	1.01(0.83,1.27)	1.06(0.85,1.32)	1.04(0.83,1.29)	1.04(0.83,1.30)	1.02(0.82,1.27)
Q3 (15-22 U/l)	962	0.90(0.74,1.12)	0.99(0.80,1.22)	0.97(0.78,1.22)	0.94(0.75,1.17)	0.94(0.75,1.17)	0.89(0.71,1.11)
Q4 (>22 U/l)	922	1.36(1.15, 1.64)	1.31(1.08,1.57)	1.17(0.98,1.52)	1.10(0.90,1.34)	1.10(0.91,1.35)	0.97(0.79,1.19)
P for trend		P=0.003	P=0.005	P=0.243	P=0.442	P=0.436	P=0.667
GGT							
Q1 (<=16U/l)	844	1	1	1	1	1	1
Q2 (16-24 U/l)	883	1.47(1.07, 2.10)	1.50(1.07,2.10)	1.55(1.09,2.10)	1.55(1.09,2.20)	1.50(1.05,2.13)	1.50(1.05,2.13)
Q3 (24-38 U/l)	938	2.13(1.55, 2.93)	2.13(1.55,2.93)	2.04(1.47,2.84)	1.99(1.43,2.47)	1.95(1.40,2.71)	1.95(1.40,2.71)
Q4 (>38 U/l)	910	3.59(2.68, 4.83)	3,41(2.54,4.60)	2.48(1.82,3.38)	2.33(1.70, 3.181)	2.29(1.68,3.14)	2.29(1.68,3.14)
P for trend		P＜0.001	P＜0.001	P＜0.001	P＜0.001	P＜0.001	P＜0.001
Women							
ALT							
Q1 (<=8 U/l)	1322	1	1	1	1	1	1
Q2 (8-12 U/l)	1376	0.86(0.74, 1.01)	0.87(0.74,1.02)	0.87(0.75,1.03)	0.87(0.73,1.02)	0.87(0.74,1.02)	0.87(0.74,1.02)
Q3 (12-18 U/l)	1455	0.82(0.69, 1.02)	0.83(0.71,1.03)	0.88(0.74,1.04)	0.86(0.72,1.02)	0.86(0.73,1.02)	0.86(0.73,1.02)
Q4 (>18 U/l)	1351	1.02(0.87, 1.18)	1.02(0.87,1.19)	0.98(0.83,1.16)	0.93(0.79,1.10)	0.93(0.79,1.10)	0.88(0.74,1.04)
P for trend		P=0.066	P=0.034	P=0.121	P=0.234	P=0.242	P=0.235
GGT							
Q1 (<=11U/l)	1343	1	1	1	1	1	1
Q2 (11-14 U/l)	1458	1.35(1.15, 1.59)	1.34(1.14,1.58)	1.20(1.02,1.41)	1.17(0.99,1.40)	1.17(0.98,1.38)	1.16(0.98,1.38)
Q3 (14-20 U/l)	1376	2.06(1.75, 2.45)	2.05(1.72,2.44)	1.56(1.30,1.88)	1.50(1.25,1.80)	1.47(1.22,1.77)	1.47(1.22,1.77)
Q4 (>20 U/l)	1327	2.42(2.04, 2.85)	2.39(2.02,2.83)	1.67(1.40,2.00)	1.57(1.32,1.88).	1.52(1.27,1.83)	1.52(1.27,1.83)
P for trend		P＜0.001	P＜0.001	P＜0.001	P＜0.001	P＜0.001	P＜0.001

Model1: Adjusted for age.

Model2: Adjusted for age, school years, alcohol-drinking, current smoking, family history of hypertension and survey years.

Model3: Model2+ body mass index.

Model4: Model3+ triglycerides + high-density lipoprotein cholesterol.

Model5: Model4+ fasting plasma glucose.

Model6: GGT and ALT fitted simultaneously into the Model5.

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Table 4. Odds ratio (95% confidence interval) for hypertension in relation to quartiles of gamma–glutamyltransferase (GGT) concentrations stratified by waist circumference categories.

	Odds ratio (95% CI)	P value
Men		
Waist circumference (<79cm) (n=892)		
GGT		
Q1 (<15U/l)	1	
Q2 (15-19 U/l)	1.33(0.76,2.35)	0.314
Q3 (19-26 U/l)	1.75(1.03,2.99)	0.037
Q4（≥26U/l)	2.61(1.56,4.36)	＜0.001
Waist circumference (79-87cm) (n=893)		
GGT		
Q1 (<16U/l)	1	
Q2 (16-22 U/l)	1.55(0.84, 2.87)	0.109
Q3 (22-34 U/l)	2.72(1.25,4.10)	0.009
Q4（≥34 U/l)	2.68(1.54,4.65)	0.001
Waist circumference（87−94cm) (n=930)		
GGT		
Q1 (<19U/l)	1	
Q2 (19-28U/l)	1.86(0.87, 3.98)	0.020
Q3 (28-45 U/l)	2.58(1.26, 5.28)	0.001
Q4（≥45U/l)	3.10(1.62, 5.96)	＜0.001
Waist circumference（≥94cm) (n=860)		
GGT		
Q1 (<23U/l)	1	
Q2 (23-33 U/l)	2.25(1.14, 4.46)	0.001
Q3 (33-53 U/l)	3.12(1.64, 5.94)	＜0.001
Q4（≥53 U/l)	4.01(2.21, 7.29)	＜0.001
Women		
Waist circumference (<76cm) (n=1363)		
GGT		
Q1 (<10U/l)	1	
Q2 (10-14 U/l)	1.20(0.88,1.65)	0.243
Q3 (14-17U/l)	1.27(0.92,1.89)	0.177
Q4（≥17U/l)	1.41(0.94,2.12)	0.096
Waist circumference (76-83cm) (n=1414)		
GGT		
Q1 (<12U/l)	1	
Q2 (12-15 U/l)	0.96(0.69, 1.32)	0.800

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Q3 (15-21U/l)	1.25(0.88,1.78)	0.199
Q4（≥21U/l)	1.16(0.82,1.64)	0.409
Waist circumference（83-90cm) (n=1332)		
GGT		
Q1 (<12U/l)	1	
Q2 (12-17U/l)	1.32(0.94, 1.85)	0.107
Q3 (17-22 U/l)	1.87(1.32, 2.64)	＜0.001
Q4（≥22U/l)	2.07(1.48, 2.91)	＜0.001
Waist circumference（≥90cm) (n=1395)		
GGT		
Q1 (<14U/l)	1	
Q2 (14-19U/l)	1.57(1.05, 2.35)	0.028
Q3 (20-26U/l)	1.89(1.27, 2.83)	＜0.001
Q4（≥26U/l)	2.26(1.54, 3.32)	＜0.001

Adjusted for age, school years, family history of hypertension, *current smoking*, *alcohol-drinking*, body mass index, triglycerides, high density lipoprotein cholesterol and alanine aminotransferase.

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Table1. Baseline characteristics of participants in two surveys.

Data are age-adjusted mean (95% confidence interval) or number (percentages) indicated. *P＜0.05, hypertension vs. normotension by the same survey within the same gender. §Geometric mean (95% CI). ‖ With missing data. HOMA-IR, homeostasis model assessment of insulin resistance.

	Men		Women	
	Normotension	Hypertension	Normotension	Hypertension
Number (%)	1668(46.6%)	1907(53.4%)	2918(53.0%)	2586(47.0%)
Age (years)	49.5(49.3,49.7)	53.4(53.1,53.7)*	47.8(47.6,48.0)	55.0(54.8,55.2)*
School years> 9 (yes, %)	23.6	19.9*	26.6	8.5*
Current smoking (yes, %)	21.3	19.6	1.0	0.5
Current drinking (%)				
non-drinkers	72.7	72.5	99.1	99.3
Moderate-drinkers	12.1	14.0	0.9	0.7
heavy-drinkers	15.2	13.5	0	0
Family history of hypertension (yes, %)	12.1	12.9	11.6	13.1
Body mass index (kg/m^2)	24.2(23.5,24.9)	25.9(25.1,26.7)*	24.5(23.9,25.1)	26.7(26.1,27.2)*
Waist circumference (cm)	83.5(83.2,83.8)	87.2(86.9,87.5)*	79.6(79.7,79.8)	85.2(85.0,85.4)*
Fasting plasma glucose(mmol/L)	5.77(5.72,5.62)	6.17(6.11,6.23)*	5.65(5.62,5.68)	6.25(6.14,6.36)*
Haemoglobin A1c ‖	5.50(5.47,5.53)	5.65(5.62,5.67)*	5.44(5.37,5.51)	5.76(5.68,5.84)*
HOMA-IR ‖	10.9(9.7,12.1)	12.4(10.5,14.3)	12.1(11.2,13.0)	16.7(14.8,18.6)*
Low density lipoprotein cholesterol (mmol/L)	2.84(2.77,2.91)	3.02(2.94,3.10)*	2.89(2.85,2.93)	3.13(3.06,3.20)*
High density lipoprotein cholesterol (mmol/L)	1.61(1.58,1.64)	1.62(1.59,1.65)	1.67(1.62,1.72)	1.61(1.57,1.65)
Total cholesterol (mmol/L)	5.15(5.11,5.19)	5.35(5.30,5.40)*	5.09(5.07,5.11)	5.49(5.42,5.56)*
Triglyceride (mmol/L)	1.40(1.36,1.44)	1.59(1.56,1.62)*	1.21(1.15,1.27)	1.56(1.47,1.65)*
Alanine aminotransferase (U/L)§	20.4(19.7,21.1)	22.1(21.2,23.0)*	17.5(16.3,18.7)	18.7(17.4,19.1)
Gamma–glutamyltransferase (U/L) §	23.9(22.6,25.2)	29.5(27.8,31.2)*	14.6(13.2,16.0)	17.9(16.4,19.4)*

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Table2. Multiple linear regression analysis for alanine aminotransferase (ALT) and gamma–glutamyltransferase (GGT) in association with diastolic blood pressure and systolic blood pressure.

	Diastolic blood pressure		Systolic blood pressure	
	Standard β coefficients	95%CI	Standard β coefficients	95%CI
Men				
ALT**(**U/L)	0.09*	(0.08, 0.11)	0.03	(0.01, 0.05)
GGT**(**U/L)	0.07*	(0.05, 0.08)	0.11*	(0.10, 0.13)
Women				
ALT**(**U/L)	0.04	(0.03, 0.05)	0.05	(0.04, 0.06)
GGT**(**U/L)	0.07*	(0.06, 0.08)	0.09*	(0.07, 0.10)

Adjusted for age, school years, family history of hypertension, *current smoking*, *alcohol-drinking*, body mass index, triglycerides and high density lipoprotein cholesterol. ALT and GGT are logarithmic transformed. * P<0.01.

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Table3. Odds ratio (95% confidence interval) for hypertension in relation to quartiles of alanine aminotransferase (ALT) and gamma–glutamyltransferase (GGT) concentrations.

Model1: Adjusted for age.

		Model1	Model2	Model3	Model4	Model5	Model6
Men	**Number**						
ALT							
Q1 (<=10 U/l)	820	1	1	1	1	1	1
Q2 (10-15 U/l)	871	0.97(0.79, 1.20)	1.01(0.83,1.27)	1.06(0.85,1.32)	1.04(0.83,1.29)	1.04(0.83,1.30)	1.02(0.82,1.27)
Q3 (15-22 U/l)	962	0.90(0.74,1.12)	0.99(0.80,1.22)	0.97(0.78,1.22)	0.94(0.75,1.17)	0.94(0.75,1.17)	0.89(0.71,1.11)
Q4 (>22 U/l)	922	1.36(1.15, 1.64)	1.31(1.08,1.57)	1.17(0.98,1.52)	1.10(0.90,1.34)	1.10(0.91,1.35)	0.97(0.79,1.19)
P for trend		P=0.003	P=0.005	P=0.243	P=0.442	P=0.436	P=0.667
GGT							
Q1 (<=16U/l)	844	1	1	1	1	1	1
Q2 (16-24 U/l)	883	1.47(1.07, 2.10)	1.50(1.07,2.10)	1.55(1.09,2.10)	1.55(1.09,2.20)	1.50(1.05,2.13)	1.50(1.05,2.13)
Q3 (24-38 U/l)	938	2.13(1.55, 2.93)	2.13(1.55,2.93)	2.04(1.47,2.84)	1.99(1.43,2.47)	1.95(1.40,2.71)	1.95(1.40,2.71)
Q4 (>38 U/l)	910	3.59(2.68, 4.83)	3,41(2.54,4.60)	2.48(1.82,3.38)	2.33(1.70, 3.181)	2.29(1.68,3.14)	2.29(1.68,3.14)
P for trend		P＜0.001	P＜0.001	P＜0.001	P＜0.001	P＜0.001	P＜0.001
Women							
ALT							
Q1 (<=8 U/l)	1322		1	1	1	1	1
Q2 (8-12 U/l)	1376	0.86(0.74, 1.01)	0.87(0.74,1.02)	0.87(0.75,1.03)	0.87(0.73,1.02)	0.87(0.74,1.02)	0.87(0.74,1.02)
Q3 (12-18 U/l)	1455	0.82(0.69, 1.02)	0.83(0.71,1.03)	0.88(0.74,1.04)	0.86(0.72,1.02)	0.86(0.73,1.02)	0.86(0.73,1.02)
Q4 (>18 U/l)	1351	1.02(0.87, 1.18)	1.02(0.87,1.19)	0.98(0.83,1.16)	0.93(0.79,1.10)	0.93(0.79,1.10)	0.88(0.74,1.04)
P for trend		P=0.066	P=0.034	P=0.121	P=0.234	P=0.242	P=0.235
GGT							
Q1 (<=11U/l)	1343		1	1	1	1	1
Q2 (11-14 U/l)	1458	1.35(1.15, 1.59)	1.34(1.14,1.58)	1.20(1.02,1.41)	1.17(0.99,1.40)	1.17(0.98,1.38)	1.16(0.98,1.38)
Q3 (14-20 U/l)	1376	2.06(1.75, 2.45)	2.05(1.72,2.44)	1.56(1.30,1.88)	1.50(1.25,1.80)	1.47(1.22,1.77)	1.47(1.22,1.77)
Q4 (>20 U/l)	1327	2.42(2.04, 2.85)	2.39(2.02,2.83)	1.67(1.40,2.00)	1.57(1.32,1.88).	1.52(1.27,1.83)	1.52(1.27,1.83)
P for trend		P＜0.001	P＜0.001	P＜0.001	P＜0.001	P＜0.001	P＜0.001

Model2: Adjusted for age, school years, alcohol-drinking, current smoking, family history of hypertension and survey years.

Model3: Model2+ body mass index.

Model4: Model3+ triglycerides + high-density lipoprotein cholesterol.

Model5: Model4+ fasting plasma glucose.

Model6: GGT and ALT fitted simultaneously into the Model5.

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Table 4. Odds ratio (95% confidence interval) for hypertension in relation to quartiles of gamma−glutamyltransferase (GGT) concentrations stratified by waist circumference categories.

	Odds ratio (95% CI)	P value
Men		
Waist circumference (<79cm) (n=892)		
GGT		
Q1 (<15U/l)	1	
Q2 (15-19 U/l)	1.33(0.76,2.35)	0.314
Q3 (19-26 U/l)	1.75(1.03,2.99)	0.037
Q4（≥26U/l)	2.61(1.56,4.36)	＜0.001
Waist circumference (79-87cm) (n=893)		
GGT		
Q1 (<16U/l)	1	
Q2 (16-22 U/l)	1.55(0.84, 2.87)	0.109
Q3 (22-34 U/l)	2.72(1.25,4.10)	0.009
Q4（≥34 U/l)	2.68(1.54,4.65)	0.001
Waist circumference（87−94cm) (n=930)		
GGT		
Q1 (<19U/l)	1	
Q2 (19-28U/l)	1.86(0.87, 3.98)	0.020
Q3 (28-45 U/l)	2.58(1.26, 5.28)	0.001
Q4（≥45U/l)	3.10(1.62, 5.96)	＜0.001
Waist circumference（≥94cm) (n=860)		
GGT		
Q1 (<23U/l)	1	
Q2 (23-33 U/l)	2.25(1.14, 4.46)	0.001
Q3 (33-53 U/l)	3.12(1.64, 5.94)	＜0.001
Q4（≥53 U/l)	4.01(2.21, 7.29)	＜0.001
Women		
Waist circumference (<76cm) (n=1363)		
GGT		
Q1 (<10U/l)	1	
Q2 (10-14 U/l)	1.20(0.88,1.65)	0.243
Q3 (14-17U/l)	1.27(0.92,1.89)	0.177
Q4（≥17U/l)	1.41(0.94,2.12)	0.096
Waist circumference (76-83cm) (n=1414)		
GGT		
Q1 (<12U/l)	1	
Q2 (12-15 U/l)	0.96(0.69, 1.32)	0.800

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Q3 (15-21U/l)	1.25(0.88,1.78)	0.199
Q4（≥21U/l)	1.16(0.82,1.64)	0.409
Waist circumference（83-90cm) (n=1332)		
GGT		
Q1 (<12U/l)	1	
Q2 (12-17U/l)	1.32(0.94, 1.85)	0.107
Q3 (17-22 U/l)	1.87(1.32, 2.64)	＜0.001
Q4（≥22U/l)	2.07(1.48, 2.91)	＜0.001
Waist circumference（≥90cm) (n=1395)		
GGT		
Q1 (<14U/l)	1	
Q2 (14-19U/l)	1.57(1.05, 2.35)	0.028
Q3 (20-26U/l)	1.89(1.27, 2.83)	＜0.001
Q4（≥26U/l)	2.26(1.54, 3.32)	＜0.001

Adjusted for age, school years, family history of hypertension, *current smoking*, *alcohol-drinking*, body mass index, triglycerides, high density lipoprotein cholesterol and alanine aminotransferase.

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The elevated GGT was independently associated with the presence of hypertension.

The elevated ALT was not associated with the presence of hypertension.

The effect of elevated GGT on hypertension was significant only in obese women.

The effect of GGT was associated with hypertension in both lean and obese men.

The association appeared to be stronger in obese than in lean counterparts.

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