SciMedCentral
Annals of Clinical and Experimental Hypertension

Short Communication

Prevalence and Determinants of Elevated Gamma-Glutamyl Transferase in Chinese Hypertensive Adults

Xiao-Tao Zhao[1#], Xian-Hui Qin[2#], Yan Zhang[3], Jian-Ping Li[3], Bin-Yan Wang[2], Xiao-Bin Wang[4,5], Xin Xu[6], Xi-Ping Xu[2], Xin-Chun Yang[1]* and Yong Huo[3]

[1]Department of Cardiology, Chaoyang Hospital, Capital Medical University, China
[2]Depatment of Biomedicine, Anhui Medical University, China
[3]Department of Cardiology, Peking University First Hospital, China
[4]Center on the Childhood Origins of Disease, Johns Hopkins University,
[5]Department of Population, Family and Reproductive Health, School of Public Health, USA
[6]Guangdong Institute of Nephrology, Southern Medical University, China
[#]Both authors contribute equally.

***Corresponding author**

Xin-Chun Yang, Department of Cardiology, Chaoyang Hospital, Capital, Medical University, Beijing, 10000, China, Tel: 86-10-85231937; Fax: 86-10- 65913543; Email: xinchunyangdr@sina.com

Submitted: 04 February 2016

Accepted: 16 March 2016

Published: 18 March 2016

ISSN: 2373-9258

Keywords

- Chinese hypertensive adults
- Levels of gamma-glutamyl transferase
- Diet
- Obesity
- Cigarette Smoking
- Alcohol drinking
- Gender
- Age
- Geographical profile

Abstract

Objectives: This study aims to examine the prevalence and determinants of elevated gamma-glutamyl transferase (GGT) in 11,901 Chinese hypertensive adults aged 45-75 years.

Methods: A cross-sectional investigation was carried out in the rural area of Lianyungang, China. Elevated GGT was defined as a GGT level ≥50 IU/L.

Results: The prevalence of elevated GGT was 11.2% (4.9% in women and 21.9% in men). Median GGT level was 23.0 IU/L (20.0 IU/L in women and 29.0 IU/L in men). In multivariable logistic-regression models, abdominal obesity (waist circumference ≥90 cm), obesity (body mass index ≥25 kg/m^2), current drinking, residents inland (*vs.* coastal), and greater red meat consumption were important independent risk factors for elevated GGT in both genders. For other risk factors, gender-related differences were observed. Older age in men was inversely associated with elevated GGT, and women with antihypertensive treatment had a higher prevalence of elevated GGT. Physical activity levels were negatively correlated to GGT levels in men and women. In addition, there was a positive interaction effect between current smoking and current drinking (P=0.037) or waist circumference (≥90 cm *vs.*<90 cm, P<0.001) in GGT levels between men and women.

Conclusions: In conclusion, there was a high prevalence of elevated GGT in Chinese hypertensive adults, particularly in participants from inland (*vs.* coastal) areas. A detrimentally interactive effect between current smoking and current drinking or abdominal obesity in GGT levels was also observed.

INTRODUCTION

Gamma-glutamyl transferase (GGT) is an enzymatic liver function test that has been available for several decades, and has been initially used as a sensitive indicator of alcohol ingestion, hepatic inflammation, fatty liver disease and hepatitis [1]. However, at present, growing evidence suggest that GGT is not only a marker of oxidative stress [2], but also a proatherogenic marker [3]. Furthermore, several prospective epidemiological studies have shown a robust association between higher GGT levels within the normal range [4-7] or changes in GGT [8] and the incidence of cardiovascular diseases (CVD). By contrast, current data suggests that alanine aminotransferase (ALT) levels are not significantly associated with CVD risk. In addition, in prospective studies, baseline serum GGT levels are within the normal range predicted future diabetes and hypertension [9-11].

Increased GGT level is also a strong predictor for existing hypertension in Hong Kong Chinese [12]. However, to our knowledge, no previous publication has studied the prevalence of elevated serum GGT in Chinese hypertensive adults, particularly in coastal areas. For this reason, the present study was performed to examine the prevalence and determinants of elevated serum GGT and GGT levels in Chinese hypertensive adults aged 45-75 years in Lianyungang, Jiangsu province, China.

SUBJECTS AND METHODS

Study Population

Study subjects were participants of an ongoing China Stroke Primary Prevention Trial (CSPPT). CSPPT is a multi-center randomized controlled trial designed to confirm that enalapril maleate and folic acid tablets combined is more effective in preventing stroke among patients with hypertension when compared with enalapril maleate alone. Details regarding inclusion/exclusion criteria, treatment assignment and outcome measures of the trial have been described elsewhere (http://clinicaltrials.gov/ct2/show/NCT00794885). In the current study, we included subjects from Lianyungang who participated in the screening phase of the CSPPT.

Briefly, we conducted a community-based screening in 20 townships within two counties (Ganyu, which is coastal, and Donghai, which is inland) in Lianyungang of Jiangsu province, East China, from October 2008 to September 2009. Inclusion criteria were as follows: (1) aged 45-75 years, and (2) seated systolic blood pressure (SBP) ≥140 mmHg and/or seated diastolic blood pressure (DBP) ≥90 mmHg in both of the two screening visits (with at least 24 hours between visits) or currently under anti-hypertension treatment. Participants were excluded if they reported a history of myocardial infarction, stroke, heart failure, cancer, serious mental disorders; or if they were unwilling to participate in the survey. This study was approved by the Ethics Committee of the Institute of Biomedicine, Anhui Medical University, Hefei, China. Written informed consent was obtained from each participant before data collection.

Data collection procedures

Baseline data collection was conducted by trained research staff according to standard operating procedures. Each participant was interviewed using a standardized questionnaire designed specifically for this study. The question on standard of living was phrased as, “How does your standard of living compare to others?”, and a choice of three responses (bad, medium and good) was provided. The question on physical activity was phrased as, “How do you describe your daily physical activity level?”, and a choice of three responses (low, moderate and high) was provided. The question on meat consumption was phrased as, “Do you eat meat (red meat) frequently (count the yearly averaged weekly intake times of meat consumption)?”, and a choice of four responses regarding weekly intake was provided: <1 time, 1-2 times, 3-5 times, and ≥5 times. The question on fruit and green vegetable consumption was phrased as, “How much fruit and green vegetables do you eat (count the yearly averaged weekly intake of fruits and green vegetables)?”, and a choice of three responses regarding weekly intake was provided: <1 jin (<500 g), 1-3 jin (500-1,500 g) and ≥3 jin (≥1,500 g). Finally, the question regarding family history was phrased as, “Has any of your immediate family (mother, father and/or siblings) had any of the following conditions?”, and choices of hypertension, diabetes, coronary heart disease (CHD) and stroke were given.

Anthropometric measurements including height, weight and waist circumference were taken using standard operating procedures. Height was measured without shoes to the nearest 0.1 cm on a portable stadiometer. Weight was measured in light indoor clothing without shoes to the nearest 0.1 kg. Body mass index (BMI) was calculated as weight (kilograms)/height (meters) squared. Waist circumference (WC) measurements were taken at the level of the maximum extension of the buttocks.

Seated blood pressure (BP) measurements were obtained by a trained research staff after subjects had been seated for 10 minutes using a mercury manometer with the standard method of calibration and appropriately sized cuffs, according to standard operating procedures. Triplicate measurements on the same arm were taken, with at least two minutes between readings. Each patient’s systolic and diastolic blood pressures were calculated as the mean of three independent measures. BP measured at the second visit was used for analysis.

Blood sample collection and laboratory methods

After 12-15 hours of fasting, venous blood sample was obtained from each subject. Serum or plasma samples were separated within 30 minutes of collection and stored at -70°C, which were used for measurement of GGT concentrations using a Dade Dimension Chemistry Analyzer (Siemens, Germany).

Statistical Analysis

Hypertension (HTN) was categorized into three grades: grade 1, SBP 140-159 and/or DBP 90-99 mmHg; grade 2, SBP 160-179 and/or DBP 100-109 mmHg; grade 3, SBP ≥180 and/or DBP ≥110 mmHg [9]. Treated hypertension was defined as receiving antihypertensive medication within the past two weeks. Current smoking was defined as having smoked at least one cigarette per day or ≥18 packs in the previous year. Current drinking was defined as drinking alcohol at least two times per week in the previous year. Obesity was defined as a BMI of ≥25 kg/m^2 [13]. Abdominal obesity was defined as having a waist circumference ≥90 cm. Elevated GGT was defined as a GGT level ≥50 IU/L [13].

Means and proportions were calculated for population characteristics by gender. The difference in population characteristics were compared using Student’s *t*-test or chi-square test. The adjusted odds ratios and 95% confidence interval (CI) of having elevated serum GGT levels was determined from multivariable logistic-regression models that included age group, gender, obesity, abdominal obesity, cigarette smoking, alcohol drinking, antihypertensive treatment status, HTN grades, geographic region (coastal and inland), standard of living, meat consumption, fruit and green vegetable consumption, education level, physical activity levels and family history of HTN, diabetes, CHD or stroke. A multivariable regression model was also applied to evaluate the relation between ln-transformed GGT levels and the above factors. All statistical analyses were performed in SAS 8.2 (SAS Institute, Cary, NC, USA).

RESULTS

Overall, 13,335 participants aged 45-75 years with hypertension had valid measurements of serum GGT levels. In this report, participants with CVD (*n*=380), cancer (*n*=32), diabetes (n=469), dyslipidemia (n=344), known hepatic disease (n=144), or with any missing data (*n*=65) on antihypertensive treatment status, age, gender, height, weight, WC, smoking status, drinking status, standard of living, meat consumption, fruit and green vegetable consumption, education and physical activity levels, and family history of hypertension, coronary heart disease, diabetes and stroke, were excluded. Our final analysis included 11,901 participants.

Population characteristics by gender are listed in (Table 1). Men had significantly higher age, DBP, cigarette smoking, alcohol drinking, standard of living, meat consumption and education levels, and lower SBP, BMI, antihypertensive treatment and family history of HTN, compared with women.

Table 1: Characteristics of study participants, *n* (%).

	Total	Men	Women	P value
N	11901	4403	7498	
Age ,yrs[1]	59.5 (7.5)	60.3 (7.6)	59.1 (7.4)	<0.001
Age group (y)				
45-54	3581 (30.1)	1190 (27.0)	2391 (31.9)	<0.001
55-64	5168 (43.4)	1860 (42.2)	3308 (44.1)	
65-75	3152 (26.5)	1353 (30.7)	1799 (24.0)	
GGT ,IU/L[2]	23.0 (17.0-34.0)	29.0 (20.0-46.0)	20.0 (15.0-28.5)	<0.001
Antihypertensive Treatment, Treated	5547 (46.6)	1884 (42.8)	3663 (48.9)	<0.001
SBP, mm Hg[1]	169.0 (20.6)	167.7 (20.6)	169.8 (20.6)	<0.001
DBP, mm Hg[1]	95.7 (11.8)	97.6 (12.2)	94.5 (11.3)	<0.001
HTN Grades				
Normal BP or Grade 1[3]	3177 (26.7)	1154 (26.2)	2023 (27.0)	0.175
Grade 2	4880 (41.0)	1781 (40.4)	3099 (41.3)	
Grade 3	3844 (32.3)	1468 (33.3)	2376 (31.7)	
BMI (kg/m^2)				
Mean[1]	25.7 (3.6)	25.0 (3.3)	26.1 (3.7)	<0.001
Obesity[4]	6560 (55.1)	2057 (46.7)	4503 (60.1)	<0.001
Waist Circumference				
Mean, cm[1]	85.2 (9.5)	85.4 (9.6)	85.1 (9.4)	0.098
Abdominal Obesity[5]	3898 (32.8)	1508 (34.2)	2390 (31.9)	0.008
Current Smoking	2685 (22.6)	2372 (53.9)	313 (4.2)	<0.001
Current Drinking	2629 (22.1)	2387 (54.2)	242 (3.2)	<0.001
Family history of HTN	4660 (39.2)	1645 (37.4)	3015 (40.2)	0.002
Family history of diabetes	538 (4.5)	188 (4.3)	350 (4.7)	0.313
Family history of CHD	490 (4.1)	172 (3.9)	318 (4.2)	0.375
Family history of stroke	1650 (13.9)	619 (14.1)	1031 (13.8)	0.638
Counties				
Ganyu(coastal)	5139 (43.2)	1968 (44.7)	3171 (42.3)	0.011
Donghai(inland)	6762 (56.8)	2435 (55.3)	4327 (57.7)	
Living Standards				
Bad	1217 (10.2)	389 (8.8)	828 (11.0)	<0.001
Medium	9288 (78.0)	3406 (77.4)	5882 (78.4)	
Good	1396 (11.7)	608 (13.8)	788 (10.5)	
Red Meat Consumption				
<1 time/week	7456 (62.7)	2241 (50.9)	5215 (69.6)	<0.001
1-2 times/week	3268 (27.5)	1549 (35.2)	1719 (22.9)	
≥3 times/week	1177 (9.9)	613 (13.9)	564 (7.5)	
Fruits and vegetables Consumption				
<500 g/week	186 (1.6)	78 (1.8)	108 (1.4)	0.329
500-1500g/week	2450 (20.6)	915 (20.8)	1535 (20.5)	
≥ 1500g/week	9265 (77.9)	3410 (77.4)	5855 (78.1)	
Education				
Illiterate	7823 (65.7)	1660 (37.7)	6163 (82.2)	<0.001
Primary level	1758 (14.8)	1048 (23.8)	710 (9.5)	
Elementary or higher levels	2320 (19.5)	1695 (38.5)	625 (8.3)	
Physical Activity				
Low	4920 (41.3)	1766 (40.1)	3154 (42.1)	0.112
Moderate	4578 (38.5)	1729 (39.3)	2849 (38.0)	
High	2403 (20.2)	908 (20.6)	1495 (19.9)	

Abbreviations: BMI: Body Mass Index; CHD: Coronary Heart Disease; DBP: Diastolic Blood Pressure; GGT: Gamma-glutamyl transferase; HTN: Hypertension; SBP: Systolic Blood Pressure
[1]Means (SD); [2]Median (25th-75th); [3]296 subjects with antihypertensive treatment and normal blood pressure were included; [4]Obesity was defined as a BMI of ≥25kg/m^2; [5]Abdominal obesity was defined as a waist circumference ≥90 cm.

The prevalence of elevated GGT was 11.2% (4.9% in women and 21.9% in men).Median GGT level was 23.0 IU/L (20.0 IU/L in women and 29.0 IU/L in men).

In multivariable logistic-regression models, abdominal obesity, obesity, current drinking, inland (*vs.* coastal) residents and greater red meat consumption were important independent risk factors for elevated GGT in both genders. For other risk factors, gender-related differences were observed. Older age in men was inversely associated with elevated GGT, and women with antihypertensive treatment had a higher prevalence of elevated GGT (Table 2).

Consistently, odds ratios (95% CIs) that have elevated GGT for men and women were 1.68 (1.38-2.06) and 1.49 (1.16-1.91) for abdominal obesity, 1.21 (0.99-1.48) and 1.34 (1.02-1.76) for obesity, 3.36 (2.82-1.48) and 1.74 (1.00-3.03) for current alcohol drinkers (*vs.* non-current drinkers), 1.43 (1.22-1.68) and 2.30 (1.79-2.96) for inland *vs.* coastal residents, 1.45 (1.16-1.82) and 1.57 (1.09-2.27) for participants with red meat consumption ≥3 times/week *vs.*<1 time/week, 0.47 (0.39-0.57), and 0.90 (0.65-1.24) for participants aged 65-75 years *vs.* 45-55 years, 0.98 (0.83-1.15) and 1.30 (1.04-1.62) for participants with *vs.* without antihypertensive treatment (Table 2).

Table 2: Adjusted[1] odds ratios (95% Confidence Intervals) of having elevated serum gamma-glutamyl transferase (GGT) in Different Subgroups.

	Total		Men		Women	
	Prevalene, n (%)	Adjusted OR (95% CI)	Prevalene, n (%)	Adjusted OR (95% CI)	Prevalene, n (%)	Adjusted OR (95% CI)
Total	1330(11.2)		963(21.9)		367(4.9)	
Sex						
Men	963(21.9)	1.00(ref)				
Women	367(4.9)	0.32(0.27-0.39)				
Age (y)						
45-55	513(14.3)	1.00(ref)	391(32.9)	1.00(ref)	122(5.1)	1.00(ref)
55-65	558(10.8)	0.70(0.60-0.81)	396(21.3)	0.60(0.50-0.72)	162(4.9)	0.90(0.70-1.17)
65-75	259(8.2)	0.47(0.39-0.56)	176(13.0)	0.35(0.28-0.44)	83(4.6)	0.90(0.65-1.24)
Antihypertensive Treatment						
Untreated	739(11.6)	1.00(ref)	581(23.1)	1.00(ref)	158(4.1)	1.00(ref)
Treated	591(10.7)	1.09(0.96-1.24)	382(20.3)	0.98(0.83-1.15)	209(5.7)	1.30(1.04-1.62)
HTN Grades						
Controlled BP or Grade 1[2]	318(10.0)	1.00(ref)	224(19.4)	1.00(ref)	94(4.6)	1.00(ref)
Grade 2	556(11.4)	1.15(0.98-1.35)	407(22.9)	1.16(0.95-1.41)	149(4.8)	1.06(0.81-1.39)
Grade 3	456(11.9)	1.21(1.03-1.43)	332(22.6)	1.23(1.00-1.51)	124(5.2)	1.11(0.84-1.47)
Obesity[3]						
No	518(9.7)	1.00(ref)	413(17.6)	1.00(ref)	105(3.5)	1.00(ref)
Yes	812(12.4)	1.24(1.06-1.45)	550(26.7)	1.21(0.99-1.48)	262(5.8)	1.34(1.02-1.76)
Abdominal Obesity [4]						
No	708(8.8)	1.00(ref)	507(17.5)	1.00(ref)	201(3.9)	1.00(ref)
Yes	622(16.0)	1.63(1.39-1.90)	456(30.2)	1.68(1.38-2.06)	166(6.9)	1.49(1.16-1.91)
Current smoking						
No	770(8.4)	1.00(ref)	416(20.5)	1.00(ref)	354(4.9)	1.00(ref)
Yes	560(20.9)	0.98(0.84-1.40)	547(23.1)	0.96(0.82-1.13)	13(4.2)	0.74(0.64-0.86)
Current drinking						
No	590(6.4)	1.00(ref)	239(11.9)	1.00(ref)	351(4.8)	1.00(ref)
Yes	740(28.1)	3.19(2.72-3.75)	724(30.3)	3.36(2.82-4.01)	16(6.6)	1.74(1.00-3.03)
FHH						
No	824(11.4)	1.00(ref)	603(21.9)	1.00(ref)	221(4.9)	1.00(ref)
Yes	506(10.9)	0.84(0.73-0.97)	360(21.9)	0.79(0.67-0.95)	146(4.8)	0.92(0.73-1.16)
FHD						
No	1266(11.1)	1.00(ref)	920(21.8)	1.00(ref)	346(4.8)	1.00(ref)
Yes	64(11.9)	1.06(0.79-1.42)	43(22.9)	0.95(0.66-1.38)	21(6.0)	1.24(0.78-1.98)
FHC						
No	1278(11.2)	1.00(ref)	924(21.8)	1.00(ref)	354(4.9)	1.00(ref)
Yes	52(10.6)	0.86(0.62-1.18)	39(22.7)	0.91(0.61-1.34)	13(4.1)	0.79(0.44-1.40)
FHS						
No	1134(11.1)	1.00(ref)	822(21.7)	1.00(ref)	312(4.8)	1.00(ref)
Yes	196(11.9)	1.04(0.87-1.25)	141(22.8)	1.01(0.80-1.27)	55(5.3)	0.85(0.74-0.99)
Counties						

Ganyu(coastal)	485(9.4)	1.00(ref)	393(20.0)	1.00(ref)	92(2.9)	1.00(ref)
Donghai(inland)	845(12.5)	1.65(1.45-1.88)	570(23.4)	1.43(1.22-1.68)	275(6.4)	2.30(1.79-2.96)
Living Standards						
Bad	106(8.7)	1.00(ref)	69(17.7)	1.00(ref)	37(4.5)	1.00(ref)
Medium	1025(11.0)	1.03(0.82-1.29)	734(21.6)	0.96(0.71-1.28)	291(4.9)	1.17(0.82-1.67)
Good	199(14.3)	1.01(0.76-1.34)	160(26.3)	0.94(0.66-1.35)	39(4.9)	1.07(0.66-1.73)
Red Meat Consumption						
<1 time/week	650(8.7)	1.00(ref)	397(17.7)	1.00(ref)	253(4.9)	1.00(ref)
1-2 times/week	440(13.5)	1.11(0.96-1.28)	364(23.5)	1.18(0.99-1.40)	76(4.4)	0.95(0.73-1.25)
≥3 times/week	240(20.4)	1.47(1.21-1.78)	202(33.0)	1.45(1.16-1.82)	38(6.7)	1.57(1.09-2.27)
Fruit and vegetable consumption						
<500 g/week	23(12.4)	1.00(ref)	18(23.1)	1.00(ref)	5(4.6)	1.00(ref)
500-1500g/week	258(10.5)	0.84(0.51-1.37)	196(21.4)	0.89(0.50-1.60)	62(4.0)	0.77(0.30-1.99)
≥ 1500g/week	1049(11.3)	0.86(0.53-1.39)	749(22.0)	0.89(0.50-1.57)	300(5.1)	0.86(0.34-2.16)
Education						
Illiterate	611(7.8)	1.00(ref)	306(18.4)	1.00(ref)	305(4.9)	1.00(ref)
Primary level	226(12.9)	0.83(0.69-0.99)	191(18.2)	0.83(0.67-1.03)	35(4.9)	0.90(0.62-1.29)
Elementary or higher levels	493(21.3)	1.03(0.87-1.22)	466(27.5)	1.04(0.86-1.27)	27(4.3)	0.75(0.49-1.14)
Physical Activity						
Low	542(11.0)	1.00(ref)	389(22.0)	1.00(ref)	153(4.9)	1.00(ref)
Moderate	533(11.6)	0.98(0.85-1.13)	391(22.6)	0.94(0.79-1.12)	142(5.0)	1.12(0.88-1.43)
High	255(10.6)	0.84(0.71-1.01)	183(20.2)	0.79(0.64-0.99)	72(4.8)	0.98(0.72-1.33)

Abbreviations: BMI: Body Mass Index; FHC: Family History of Coronary Heart Disease; FHD: Family History of Diabetes; FHH: Family History of Hypertension; FHS= Family History of Stroke; HTN: Hypertension

[1]All variables were included in the same models; [2]296 subjects with antihypertensive treatment and controlled blood pressure were included; [3]Obesity was defined as a BMI of ≥25kg/m^2; [4]Abdominal obesity was defined as a waist circumference ≥90 cm.

Multivariable regression models revealed similar trends as the multivariable logistic-regression model (Supplemental Table). Furthermore, physical activity levels were negatively related to GGT levels in men and women. Moreover, there was a detrimental interactive effect between current smoking and current drinking (P=0.037) or waist circumference (≥90 cm *vs.*<90 cm, P<0.001) on GGT levels in men and women.

DISCUSSION

This is the first study to examine the prevalence of elevated GGT and simultaneously explore the effect of socioeconomic status, lifestyle, diet and family history on the prevalence of elevated GGT and GGT levels in Chinese hypertensive adults. In our present study, median GGT level was 23.0 IU/L (29.0 IU/L in men and 20.0 IU/L in women). Consistently, median GGT level (n=5,385) [14] was 29 IU/L for men and 18 IU/L for women in an ethnic She Chinese population. In addition, median GGT level (n=5404) [15] was 27 IU/L for men and 21 IU/L for women in two urban communities in Shanghai, China.

Consistent with previous studies [13,16], men and low physical activity levels were important determinants for higher GGT levels. At the same time, our study was the first to prove that even in fully adjusted models, abdominal obesity, obesity and greater red meat consumption were independent risk factors for elevated GGT and higher GGT levels, which suggests that both obesity and abdominal obesity control and red meat consumption restriction are necessary to decrease GGT levels. Furthermore, though the positive association between age and GGT levels in previous studies [13], older age was inversely associated with elevated GGT in men in our study, which was consistent with a report [17] in Germany.

Breitling LP *et al.* reported [18] that there was a positive interaction effect between smoking and alcohol, and a negative interaction effect between smoking and BMI with regards to GGT levels in men, without adjustment for waist circumference, socioeconomic status and diet. However, there was a detrimentally interactive effect between current smoking and current drinking (P=0.037) or waist circumference (≥90 cm *vs.*<90 cm, P<0.001) in GGT levels in men and women in our study, even in fully adjusted models. Considering the high prevalence of these avoidable risk factors, our findings have important clinical and public health implications, which suggest the importance of taking effective measures to reduce the above combinations in Chinese population, and decrease GGT levels and related diseases.

Most interestingly, inland (*vs.* coastal) residents had a higher prevalence of elevated GGT and GGT levels. Increasing evidence has shown that altered methionine/folate metabolism may contribute to the development of hepatic injury [19]. We suggest that a higher betaine [20] and vitamin B-12 [21] (high in seafood) intake in coastal areas may possibly explain these results. Our previous study [22] also revealed that folic acid treatment may be beneficial in lowering serum ALT concentration. However, we did not collect detailed information on seafood intake in this study. However, data available in the literature suggest that the high vitamin E contents together with high levels of PUFA present in sea food confer an additional intake of antioxidants as well as other dietary components that benefit the coastal population examined. A further understanding of these regional differences would provide us with some new strategies for the control of elevated GGT levels.

In the current study, although participants with antihypertensive treatment had lower SBP (mean [SD]: 168.3 (22.3) *vs.* 169.6 (18.9) mmHg, *P*=0.001) and DBP (95.2 [12.2] *vs.* 96.0 (11.4) mmHg, *P*<0.001) than participants without antihypertensive treatment, female participants with antihypertensive treatment still had significantly higher GGT levels. These results revealed that blood pressure lowering alone would not solve the problem of high GGT levels. Concomitant lifestyle changes including cigarette smoking and alcohol drinking cessation, as well as obesity and abdominal obesity control, may be necessary to decrease GGT levels in Chinese hypertensive adults.

Family history is a surrogate marker not only for genetic susceptibility to the corresponding disease, but also environmental factors that cluster in families. Through the robust association between higher GGT levels within the normal range and incident of CVD or diabetes, we found no significant relationship between family history of diabetes, CHD or stroke with the GGT levels. Furthermore, participants with a family history of HTN had significantly lower GGT levels in both genders. Future prospective studies are needed to further confirm our results.

We excluded participants with known CVD, hepatic diseases, diabetes and dyslipidemia from our analyses to permit us to exclude the possibility of confounding our results due to concomitant diseases or medications. However, our study population was not a representative sample. Caution is needed in generalizing our findings from this hypertensive Chinese population to other populations. Furthermore, we did not have direct liver fat measurements.

In conclusion, there was a high prevalence of elevated GGT in Chinese hypertensive adults, particularly in participants from inland (*vs.* coastal) areas. A detrimental interactive effect between current smoking and current drinking or waist circumference on the GGT levels was also observed.

ACKNOWLEDGEMENT

Funding: The study was supported by The Ministry of Science and Technology of the People's Republic of China (2012zx09101-105); Department of Development and Reform, Shenzhen (2010)1744; Department of Science, industry, Trade and Information Technology, Shenzhen. The sponsors did not participate in the design or conduct of the study; collection, management, analysis, and interpretation of the data; or preparation, review, and approval of the manuscript.

REFERENCES

1. Mason JE, Starke RD, Van Kirk JE. Gamma-glutamyl transferase: a novel cardiovascular risk biomarker. Prev Cardiol. 2010; 13: 36-41.
2. Yamada J, Tomiyama H, Yambe M, Koji Y, Motobe K, Shiina K, et al. Elevated serum levels of alanine aminotransferase and gamma glutamyltransferase are markers of inflammation and oxidative stress independent of the metabolic syndrome. Atherosclerosis. 2006; 189: 198-205.
3. Paolicchi A, Emdin M, Ghliozeni E, Ciancia E, Passino C, Popoff G, et al. Images in cardiovascular medicine. Human atherosclerotic plaques contain gamma-glutamyl transpeptidase enzyme activity. Circulation. 2004; 109: 1440.
4. Fraser A, Harris R, Sattar N, Ebrahim S, Smith GD, Lawlor DA. Gamma-glutamyltransferase is associated with incident vascular events independently of alcohol intake: analysis of the British Women's Heart and Health Study and Meta-Analysis. Arterioscler Thromb Vasc Biol. 2007; 27: 2729-2735.
5. Wannamethee SG, Lennon L, Shaper AG. The value of gamma-glutamyltransferase in cardiovascular risk prediction in men without diagnosed cardiovascular disease or diabetes. Atherosclerosis. 2008; 201: 168-175.
6. Fraser A, Thinggaard M, Christensen K, Lawlor DA. Alanine aminotransferase, gamma-glutamyltransferase (GGT) and all-cause mortality: results from a population-based Danish twins study alanine aminotransferase, GGT and mortality in elderly twins. Liver Int. 2009; 29: 1494-1499.
7. Lee DH, Buijsse B, Steffen L, Holtzman J, Luepker R, Jacobs DR Jr. Association between serum gamma-glutamyltransferase and cardiovascular mortality varies by age: the Minnesota Heart Survey. Eur J Cardiovasc Prev Rehabil. 2009; 16: 16-20.
8. Strasak AM, Kelleher CC, Klenk J, Brant LJ, Ruttmann E, Rapp K, et al. Longitudinal change in serum gamma-glutamyltransferase and cardiovascular disease mortality: a prospective population-based study in 76,113 Austrian adults. Arterioscler Thromb Vasc Biol. 2008; 28: 1857-1865.
9. Lee DH, Jacobs DR Jr, Gross M, Kiefe CI, Roseman J, Lewis CE, Steffes M. Gamma-glutamyltransferase is a predictor of incident diabetes and hypertension: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Clin Chem. 2003; 49: 1358-1366.
10. Fraser A, Harris R, Sattar N, Ebrahim S, Davey Smith G, Lawlor DA. Alanine aminotransferase, gamma-glutamyltransferase, and incident diabetes: the British Women's Heart and Health Study and meta-analysis. Diabetes Care. 2009; 32:741-750.
11. Ford ES, Schulze MB, Bergmann MM, Thamer C, Joost HG, Boeing H. Liver enzymes and incident diabetes: findings from the European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam Study. Diabetes Care. 2008; 31:1138-1143.
12. Cheung BM, Ong KL, Tso AW, Cherny SS, Sham PC, Lam TH, et al. Gamma-glutamyl transferase level predicts the development of hypertension in Hong Kong Chinese. Clin Chim Acta. 2011; 412: 1326-1331.
13. Poikolainen K, Vartiainen E. Determinants of gamma-glutamyltransferase: positive interaction with alcohol and body mass index, negative association with coffee. Am J Epidemiol. 1997; 146: 1019-1024.
14. Lin Y, Xu Y, Chen G, Huang B, Yao J, Chen Z, Yao L. Serum Î³-glutamyltransferase and associated damage among a She Chinese population. Diabet Med. 2011; 28: 924-931.
15. Xu Y, Bi YF, Xu M, Huang Y, Lu WY, Gu YF, et al. Cross-sectional and longitudinal association of serum alanine aminotransaminase and ?-glutamyltransferase with metabolic syndrome in middle-aged and elderly Chinese people. J Diabetes. 2011; 3: 38-47.
16. Ruttmann E, Brant LJ, Concin H, Diem G, Rapp K, Ulmer H. Vorarlberg Health Monitoring and Promotion Program Study Group,. Gamma-glutamyltransferase as a risk factor for cardiovascular disease mortality: an epidemiological investigation in a cohort of 163,944 Austrian adults. Circulation. 2005; 112: 2130-2137.
17. Breitling LP, Raum E, Müller H, Rothenbacher D, Brenner H. Synergism

between smoking and alcohol consumption with respect to serum gamma-glutamyltransferase. Hepatology. 2009; 49: 802-808.

18. Breitling LP, Arndt V, Drath C, Rothenbacher D, Brenner H. Smoking and Î³-glutamyltransferase: opposite interactions with alcohol consumption and body mass index. PLoS One. 2010; 5.

19. Purohit V, Abdelmalek MF, Barve S, Benevenga NJ, Halsted CH, Kaplowitz N, et al. Role of S-adenosylmethionine, folate, and betaine in the treatment of alcoholic liver disease: summary of a symposium. Am J Clin Nutr. 2007; 86: 14-24.

20. Craig SA. Betaine in human nutrition. Am J Clin Nutr. 2004; 80: 539-549.

21. Vogiatzoglou A, Smith AD, Nurk E, Berstad P, Drevon CA, Ueland PM, et al. Dietary sources of vitamin B-12 and their association with plasma vitamin B-12 concentrations in the general population: the Hordaland Homocysteine Study. Am J Clin Nutr. 2009; 89: 1078-1087.

22. Qin X, Li J, Cui Y, Liu Z, Zhao Z, Ge J, et al. Effect of folic acid intervention on ALT concentration in hypertensives without known hepatic disease: a randomized, double-blind, controlled trial. Eur J Clin Nutr. 2012; 66: 541-548.

Cite this article

Zhao XT, Qin XH, Zhang Y, Li JP, Wang BY, et al. (2016) Prevalence and Determinants of Elevated Gamma-Glutamyl Transferase in Chinese Hypertensive Adults. Ann Clin Exp Hypertension 4(1): 1034.