

*Full Length Research Paper*

## **The effect of sex, age and weight on blood lipids in a Chinese population over 45 years old and related factors**

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**Blood lipids are a major risk factor for coronary heart disease (CHD), and they change distinctly after the fourth decade in humans. In order to understand the relationships between blood lipids and sex, age, and weight in individuals over 45 years old, we recruited 362 healthy males aged 45-87 years (mean  $\pm$  SD, 62.9  $\pm$  11.3) and 297 healthy females aged 45-107 years (mean  $\pm$  SD, 61.0  $\pm$  11.6); all were of Chinese ancestry. We measured total cholesterol (CH), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C) and triglycerides (TG). After adjustment for age and /or weight, significant differences in CH, HDL-C and LDL-C among male-female groups were observed. There were significant differences in CH in males ( $P = 0.001$ ), HDL-C in Chinese females ( $P < 0.001$ ), and TG in both females and males among age-stratified groups. In weight- stratified groups, significant differences in CH ( $P = 0.012$ ) and LDL-C ( $P = 0.037$ ), were identified only in Chinese males. Regression analysis suggested that age tended to show a negative correlation with blood lipids variations compared to positive correlations with weight. The proportion of CH variation related to age in males, HDL-C variation related to age in females, and CH related to weight in females were 5.4, 5.0 and 1.4%, respectively. These results suggest that there is a difference in blood lipids based on sex, and that age and weight may have different effects on blood lipids in Chinese individuals over 45 years old.**

**Key words:** Blood lipid, sex, age, weight, Chinese.

### **INTRODUCTION**

Coronary heart disease (CHD) is the leading cause of deaths worldwide (Murray and Lopez, 1997; Bernard, 2002), and it is an increasingly serious public health problem in the Chinese population (Zhao et al., 1999; Critchley et al., 2004; Liu et al., 2004). Plasma

concentrations of total cholesterol (CH), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C) and triglycerides (TG) are among the most important risk factors for CHD and are targets for therapeutic intervention of CHD (Kathiresan et al., 2007).

Over the past decade, a variety of studies have attempted to quantify the contribution of genetic and environmental components to blood lipid content and CHD susceptibility (Keavney, 2002; Teslovich et al., 2010).

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For example, age, gender, diabetes mellitus, high blood pressure, smoking, drinking, obesity and physical inactivity all have a great impact on blood lipids (Wilson et al., 1998; Keavney, 2002; Roeters et al., 2002; Zhou et al., 2002). A meta analysis of 46 lipid genomewide association studies (GWASs) involving up to 100,000 individuals of European ancestry and three non-European populations (East Asians, South Asians and African Americans) have identified 95 genetic loci associated with plasma TC, LDL-C, HDL-C and TG concentrations (Teslovich et al., 2010). The effects of both common variants and non-genetic factors are important for establishing CH, LDL-C, HDL-C and TG as targets for diagnostic and therapeutic procedures of CHD.

Blood lipids appear to change after the fourth decade (Kuhn and Rackley, 1993; Tremollieres et al., 1999; Brown et al., 1993). A large number of studies have explored the blood cholesterol level changes in Caucasians, but, much less is known about Chinese populations, especially in elderly Chinese (Zhou et al., 2002; Critchley et al., 2004). Some researchers have proposed that sex has different effects on blood lipids and is related to the lifetime risk and body mass index, with the risk of developing CHD at age 40 years being 50% for men compared to 33% for women (Roeters et al., 2002). Sex and age have been introduced as composite covariates for blood cholesterol levels in Caucasians (Roeters et al., 2002). Weight is another important factor related to lipids level variation, and several studies reported that weight reduction was associated with an improvement in risk factor and favorable changes in TG, HDL-C and LDL-C and blood pressure (Van et al. 1997; Wood et al., 1991; Willett et al., 1995). The question remains, are these measurements appropriate for adjusting blood lipids in Chinese after the fourth decade as well? Here, we report our study of the effects of age, sex, weight on blood lipids in Chinese over 45 years old. This study was carried out with three major aims: (1) to examine the differences in blood lipids; (2) to explore the relationship between sex-, age- and weight- and blood lipid distributions and (3) to determine the relative contribution of these variables in accounting for blood lipid variation in Chinese individuals over 45 years old.

## MATERIALS AND METHODS

### Subjects

The sample population came from parents of the nuclear families in a CHD linkage and association study, which was approved by the Ethical Committee of Hunan Normal University and the Ethical Committee Guangzhou General Hospital of Guangzhou Military Command. We recruited more than 400 nuclear families composed of both parents and at least one healthy offspring. Of the original sample further selection was performed to minimize any potential confounding effects on blood lipids. Thus, individuals with chronic diseases/conditions that may potentially affect blood lipids were

excluded. These diseases/conditions included chronic disorders involving vital organs (heart, lung, liver, kidney, and brain), serious metabolic diseases (diabetes, hypoparathyroidism, hypothyroidism and hyperthyroidism), chronic use of drugs and malnutrition conditions (chronic diarrhea and chronic ulcerative colitis). Finally, 362 healthy males aged 45-87 years (mean  $\pm$  SD, 62.9  $\pm$  11.3) and 297 healthy females aged 45 to 107 years (mean  $\pm$  SD, 61.0  $\pm$  11.6) were used in the present study. All the subjects came from a local population of Guangzhou city, which is located on the southern part of the south coast of the People's Republic of China. Before entering the project, all the subjects signed informed-consent documents. For each study subject, we obtained information on age, sex, weight, medical history, and family history at the time of blood lipids measurement. All the study subjects belong to the Chinese Han ethnic group, which comprises about 90% of the total population of the People's Republic of China.

### Blood lipids measurement

We used a HITACHI 7600 automatic biochemical analyzer (HITACHI, Japan) to measure CH, LDL-C, HDL-C and TG. All the measurements were carried out with 3 ml venous blood after 12 hours of fasting. The machine was calibrated daily, and the coefficient of variation values was obtained from five repeated measures from seven individuals.

### Statistical analyses

The SPSS program (version 12.0) was used to perform statistical analyses. Differences between males and females were analyzed using a Student's *t*-test. To analyze the effect of weight and sex on blood lipids, we performed an analysis of covariance (ANCOVA) after adjustment either for age or both age and weight. To examine the pattern of blood lipids change in different age or weight groups in our study, we divided the subjects into eight groups, with a 5-unit (year or kg) span in each group, and we evaluated the differences in blood lipids, by analysis of variance (ANOVA), among the different groups. Then, we described the proportion of blood lipids variation as explained by age and weight in males and females through regression analysis, with blood lipids as a dependent variable and age or weight as an independent variable. A regression coefficient was used to assess the significance of differences in blood lipids distribution. All the analyses did not violate the assumptions of normal distribution and homogeneity of variance for ANOVA; the assumptions of normal distribution, homogeneity of variance, and interaction between variables for ANCOVA; the assumptions of normal distribution of dependent variable and colinearity for regression analysis. The significance level was set at  $P < 0.05$ .

## RESULTS

### Subject characteristics

Basic characteristics of the subjects and a comparison between the males and females are given in Table 1. The average age and weight values were higher in males than in females, but the average CH, LDL-C, HDL-C and TG values were higher in females than in males. Significant differences ( $P < 0.05$ ) in age, weight, total cholesterol, high and low-density lipoprotein levels were found

**Table 1.** Basic characteristics of the subjects.

Variable	Males (n = 362)		Females (n = 297)		P - value
	Mean	SD	Mean	SD	
Age (years)	62.9	11.3	61.0	10.6	0.028
Weight (kg)	67.3	9.4	62.6	8.8	< 0.001
Total cholesterol	4.72	1.10	5.39	1.08	< 0.001
Low-density lipoprotein cholesterol	3.14	1.09	3.50	0.99	< 0.001
High-density lipoprotein cholesterol	1.06	0.33	1.35	0.34	< 0.001
Triglycerides	1.86	1.33	1.93	1.34	0.527

P value is result of student's t-test between males and females.

**Table 2.** Blood lipids in male and female before and after adjustment for weight.

Variable	Adjusted for age				Adjusted for age and weight			
	Mean		Percent difference female vs. male	P value	Mean		Percent difference female vs. male	P value
	Males	Females			Males	Females		
Total cholesterol	4.74	5.37	13.3	< 0.001	4.73	5.39	13.9	< 0.001
Low-density lipoprotein cholesterol	3.15	3.49	10.8	< 0.001	3.14	3.50	11.5	< 0.001
High-density lipoprotein cholesterol	1.06	1.34	26.4	< 0.001	1.07	1.34	25.2	< 0.001
Triglycerides	1.87	1.92	2.7	0.682	1.85	1.94	4.9	0.371

The adjusted mean is the least square mean. Percent difference (female vs. Male) was calculated as: (female mean–male mean)/ male mean\*100%. P values are the result of analysis of covariance (ANOVA).

between the males and females. No significant difference was observed for TG ( $P = 0.527$ ). This suggested a sex-based difference in CH, LDL-C and HDL-C levels in a Chinese population over 45 years old.

### Sex differences in blood lipids

Significant differences ( $P < 0.05$ ) in age and weight were observed between males and females in this study. We compared the blood lipids differences between males and females before and after the adjustment for weight and /or age (Table 2). Before the adjustment for weight, the male and female difference in age-adjusted CH, LDL-C and HDL-C were significant ( $P < 0.001$ ), with female lipid levels being over 10% higher than the male level. After adjustment for weight, the magnitude of the sex difference in HDL-C was reduced, but the magnitudes of the sex difference in the other blood lipids were elevated. The sex difference of TG was not significant either before or after adjustment for weight. These results indicate that age and weight may have different effects on CH, LDL-C and

HDL-C in Chinese males and females over 45 years old.

### Blood lipids distributions among different age and weight groups

To investigate the blood lipid distributions related to age and weight in Chinese over 45 years old, we compared the blood lipids in age- and weight- stratified groups of males and/or females. Table 3 showed comparisons for blood cholesterol levels in different age-stratified groups of males and/or females. Significant differences in CH in Chinese males ( $P = 0.001$ ) and HDL-C in Chinese females ( $P < 0.001$ ), were identified among the different age-stratified groups. The highest values and the lowest values of CH in Chinese males were observed in 45 to 49 years group and 70 to 74 years group, respectively. And also, the highest values of HDL-C in Chinese females were in 45 to 49 years group and the lowest values in 70 to 74 years group. The differences in TG levels were significant in age-stratified groups ( $P < 0.001$ ). Table 4 shows comparisons for blood lipids in different weight-stratified groups of males and/or females. The only

**Table 3.** Comparisons of total cholesterol (CH), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) age-stratified groups in female and/or male.

Variable		45-49 years (n =46 )	50-54 years (n =45 )	55-59 years (n =67 )	60-64 years (n =30 )	65-69 years (n = 39)	70-74 years (n = 34)	75-79 years (n =22 )	≥ 80 years (n =14 )	P value
Female	CH	5.31 ± 0.85	5.49±1.06	5.68 ± 1.00	5.39 ± 1.20	4.93 ± 1.05	5.36 ± 1.27	5.25 ± 1.16	5.52 ± 1.23	0.071
	LDL-C	3.47 ± 0.91	3.66 ± 0.92	3.66 ± 0.93	3.30 ± 0.96	3.13 ± 1.04	3.60 ± 1.05	3.50 ± 1.14	3.60 ± 1.22	0.190
	HDL-C	1.57 ± 0.39	1.34 ± 0.28	1.32 ± 0.39	1.31 ± 0.31	1.28 ± 0.31	0.26 ± 0.04	1.24 ± 0.28	1.25 ± 0.22	< 0.001
Male		45-49 years (n = 52)	50-54 years (n = 55)	55-59 years (n = 49)	60-64 years (n =44 )	65-69 years (n =50 )	70-74 years (n =36 )	75-79 years (n =45 )	≥ 80 years (n =31 )	
	CH	5.05 ± 1.02	5.04 ± 1.15	4.98 ± 1.03	4.73 ± 1.13	4.38 ± 1.07	4.32 ± 1.23	4.63 ± 0.89	4.35 ± 1.07	0.001
	LDL-C	3.44 ± 0.94	3.35 ± 1.07	3.27 ± 0.87	3.04 ± 0.89	2.84 ± 0.83	2.85 ± 1.06	3.07 ± 0.82	3.12 ± 2.09	0.057
Female and male		45-49 years (n = 98)	50-54 years (n = 100)	55-59 years (n = 116)	60-64 years (n =74 )	65-69 years (n =89 )	70-74 years (n =70 )	75-79 years (n =67 )	≥ 80 years (n =45 )	
	TG	1.75 ± 1.23	2.10 ± 1.24	2.20 ± 1.66	2.26 ± 1.77	1.62 ± 1.18	1.58 ± 0.75	1.78 ± 1.13	1.48 ± 0.82	< 0.001

The data are presented as the means and its standard deviation (mean ± SD). The P values for comparisons among age-stratified groups are generated by one-way analysis of variance (one-way ANOVA).

significant differences were identified among the different weight-stratified Chinese males and these differences were in the levels of CH ( $P = 0.012$ ) and LDL-C ( $P = 0.037$ ). The highest values of both CH and LDL-C were in 55-59 kg group and the lowest were in the  $\leq 49$  kg group.

#### The effects of age and weight on blood lipids variations in males and females

The proportions of blood lipids variation explained by age and weight in Chinese males and females over 45 years old are shown in Table 5. Chinese over 45 years old tended to show greater differences in blood lipids as a function of age compared to weight. Differences in age and weight-related blood lipids variation in males as

compared to female, for example, the blood lipids were negative regressions to age and positive regressions to weight, the significant regressions in CH ( $P < 0.001$ ) and in LDL-C ( $P = 0.01$ ) for age in males; with no significant regressions in all blood lipids for weight in females. The proportion of CH variation related to age in males, HDL-C variation related to age in females, and CH related to weight in females were 5.4, 5.0 and 1.4%, respectively. Thus, age may be a more important factor contributing to CH variation and HDL-C variation in Chinese over 45 years old.

#### DISCUSSION

The risk of CHD is directly related to blood lipid content. It is estimated that 45% of deaths from

CHD in men and 47% in women are due to blood lipids variations (Roeters et al., 2002). For example, elevated CH, LDL-C and TG levels are major risk factors in CHD for both man and women (Manolio et al., 1992; Stamler et al., 1993; LaRosa, 1997), and HDL-C levels are reported to correlate closely and inversely with the risk of CHD (Jacobs et al., 1990; Stensvold et al., 1992; Antonio, 2001). However, the atherogenicity of CH, LDL-C, HDL-C and TG seems to be influenced by an array of factors such as sex, age, obesity, smoking and family history (Wenger, 2002; Roeters et al., 2002; Julia et al., 2003), which are usually important for using blood lipids as the predictors for CHD in clinical guidelines, especially in elder population. In the present study, we report the effects of sex, age and weight on blood lipids in a Han population over 45 years old from Southern China.

**Table 4.** Comparisons of total cholesterol (CH), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) weight-stratified groups in female and/or male.

Variable		≤ 49 kg (n =18 )	50-54 kg (n =47 )	55-59 kg (n =45 )	60-64 kg (n =58 )	65-69 kg (n = 63)	70-74 kg (n = 38)	75-79 kg (n =22 )	≥ 80 kg (n =6 )	P value
Female	CH	4.82 ± 1.05	5.14 ± 0.98	5.65 ± 1.13	5.43 ± 1.20	5.38 ± 0.93	5.71 ± 1.01	5.23 ± 1.01	5.49 ± 1.93	0.055
	LDL-C	2.93 ± 1.07	3.33 ± 0.91	3.73 ± 0.94	3.52 ± 1.01	3.49 ± 0.94	3.72 ± 0.98	3.41 ± 1.07	3.68 ± 1.61	0.103
	HDL-C	1.29 ± 0.29	1.26 ± 0.30	1.45 ± 0.33	1.35 ± 0.41	1.36 ± 0.33	1.38 ± 0.32	1.24 ± 0.30	1.45 ± 0.41	0.144
		≤ 49 kg (n = 10)	50-54 kg (n = 25)	55-59 kg (n = 27)	60-64 kg (n =71 )	65-69 kg (n =78 )	70-74 kg (n =76 )	75-79 kg (n =34 )	≥ 80 kg (n =41 )	
Male	CH	4.22 ± 0.85	4.43 ± 0.93	5.43 ± 0.94	4.59 ± 1.12	4.79 ± 1.14	4.78 ± 1.06	4.54 ± 1.16	4.74 ± 1.11	0.012
	LDL-C	2.70 ± 0.64	2.87 ± 0.85	3.77 ± 0.88	3.03 ± 0.93	3.23 ± 1.46	3.20 ± 0.97	2.98 ± 1.10	3.04 ± 0.92	0.037
	HDL-C	1.04 ± 0.39	1.09 ± 0.38	1.08 ± 0.29	1.11 ± 0.36	1.08 ± 0.28	1.03 ± 0.32	1.02 ± 0.42	1.00 ± 0.26	0.689
		≤ 49 kg (n = 28)	50-54 kg (n = 72)	55-59 kg (n = 72)	60-64 kg (n =129 )	65-69 kg (n =141)	70-74 kg (n =114)	75-79 kg (n =56)	≥ 80 kg (n =47)	
Female and male	TG	1.48 ± 1.48	1.86 ± 1.60	1.97 ± 1.30	1.89 ± 1.32	1.83 ± 1.24	1.88 ± 1.15	1.88 ± 1.00	2.26 ± 1.83	0.459

The data are presented as the means and its standard deviation (mean ± SD). The *p*-values for comparisons among weight-stratified groups are generated by one-way analysis of variance (one-way ANOVA).

Several studies have reported the existence of a gender difference in the use of blood lipids as the diagnostic and therapeutic procedures for CHD (Roeters et al., 2002). We found sex-based difference in blood lipids both before and after adjustment for weight and /or age in this study, which is similar to results reported previously for other populations (Wenger 2002; Roeters et al., 2002). Many studies showed that elevated CH, LDL-C, TG levels and lowered HDL-C are major risk factors for CHD and seem to be stronger in men than in women (Wenger 2002; Roeters et al., 2002; Manolio et al., 1992; Stamler et al., 1993;

LaRosa, 1997; Jacobs et al., 1990; Stensvold et al., 1992; Antonio, 2001).

We examined sex differences in CH, LDL-C and HDL-C after adjustment for age and/or weight, however, the sex difference in TG levels was not found. This may be caused by many factors. First, there may be different genetic determinants in TG as a risk for CHD in Chinese Han population. Second, there are methodological differences in measuring TG levels because of high biological intra- and inter-individual variability. Third, there are interactions between TG and the other lipid factors (Roeters et al., 2002). For example,

elevated TG levels are often accompanied by lower HDL levels, a combination that has been associated with increased CHD risk (Gaziano et al., 1997).

The present results suggest that the clinical procedures establishing CH, LDL-C and HDL-C as the targets for CHD should be different from using TG as the target for therapeutic intervention of CHD in Chinese females and males over 45 years old.

Age shows a strong correlation with blood lipids distributions. A number of publications have addressed differences in blood lipids changes in

**Table 5.** Simple linear regression analysis for blood cholesterol levels with age and weight as regressors in Chinese males and females over 45 years old.

Variable		Males			Females		
		$\beta$	<i>P</i>	R <sup>2</sup> (%)	$\beta$	<i>P</i>	R <sup>2</sup> (%)
Age	CH	-0.233	< 0.001	5.4	-0.064	0.269	0.4
	LDL-C	-0.135	0.01	1.8	-0.052	0.374	0.3
	HDL-C	-0.054	0.305	0.3	-0.223	< 0.001	5.0
Weight	CH	0.03	0.565	0.1	0.118	0.042	1.4
	LDL-C	0.006	0.912	< 0.1	0.114	0.050	1.3
	HDL-C	-0.065	0.216	0.4	0.034	0.559	0.1

$\beta$ , regression coefficient; *P*, *P* value of the regression coefficient test; R<sup>2</sup>, proportion of the variance of total cholesterol (CH), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) predicted by age.

longitudinal studies in different ethnic groups (Antonio, 2001; Jousilahti et al., 1999; Julia et al., 2003; Liu et al., 2004). Despite the differences in populations, research designs, and sampling methods, these studies have reported consistent results in that blood lipids change in both sexes with age, for example, blood cholesterol levels in men and women are similar up to 20 years of age, and increase more in men than in women in the third and fourth decades, then increase more sharply in women than in men following menopause. Jean and Christopher (1990) investigated serum lipid profile in a Chinese population from a Hong Kong community near to Guangzhou. They found that no significant variation attributable to age. In this study, significant differences in CH in Chinese males, HDL-C in Chinese females, were identified among the age-stratified groups. Importantly, the highest values of CH in Chinese males were in the 45-49 years old group and the lowest values of HDL-C in Chinese females were in and 70-74 year old group. The blood lipids were negatively correlated with age, and the proportion of HDL-C variation related to age in females was 5.0%. These results suggest we should consider different therapeutic procedures when using CH in elderly Chinese males and HDL-C in elderly Chinese females as CHD indicators.

Weight, height, BMI, waist-hip ratio and waist circumference are highly related to the risk of CHD (Van et al., 1997; wood et al., 1991; Willett et al., 1995). In the present study, significant differences in CH and LDL-C were found among the different weight-stratified groups in Chinese males. More interestingly, the highest values of both CH and LDL-C in Chinese males were in 55-59 kg group, and the proportions of both CH and LDL-C variations related to weight in males was about 1.4%. This result indicates that Chinese males over 45 years old in the 55-59 kg weight group may have a higher risks for CHD. CH levels showed a positive regression to weight in

this study and support the idea that weight loss reduces the risk of CHD. The potential limitation of this study is that height was not measured so we could not analyze obesity as an independent factor.

## Conclusion

The present study analyzed the effect of sex, age, and weight on serum lipids in a Chinese population over 45 years old. The identification of factors that influence blood lipids has important implications for the design of appropriate clinical strategies to prevent CHD in elder Chinese males and females. Our analysis showed that a sex difference in blood lipid composition exists, and age and weight may have different effects on CH, LDL-C, HDL-C and TG levels in Chinese over 45 years old, which suggests establishing CH, LDL-C and HDL-C as the clinical identifiers for CHD in Chinese elderly females should be different from those for Chinese elderly males. The results from studies of various ethnic groups and populations may reveal ethnic peculiarities, and may also complement and confirm common factors that are important for CHD in various ethnic groups.

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