Differential impact of aging and gender on lipid and lipoprotein profiles in a cohort of healthy Chinese Singaporeans

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Abstract

Aim: To evaluate the impact of age and gender on lipid and lipoprotein profiles and the burden of dyslipidemia in a cohort of healthy Chinese Singaporean. Methods: A total of 1 775 healthy Chinese, 536 men and 1 239 women aged between 30 and 70 years old were involved in the present study. Results: Gender differences in all lipid and lipoprotein levels were clearly evident. Singaporean Chinese men have significantly higher levels of total cholesterol (TC), triglyceride (TG), low density lipoprotein-cholesterol (LDL-C) and total cholesterol/high density lipoprotein-cholesterol (TC/HDL-C), and lower levels of HDL-C than women. Although lipid and lipoprotein levels in men did not change in the different age groups, those in women, especially TC, LDL-C and TC/HDL-C, were significantly higher in older women (> 50 years old) than corresponding levels in younger women (30–46 years old). Furthermore, TG was significantly correlated with lipids and lipoproteins differently in men and women. If 100 mg/dL of LDL-C were to be adopted as the therapeutic cut-off level, then the burden of care will be huge as approximately 90% of both Chinese men and women have LDL-C greater than 100 mg/dL. Conclusion: In light of the findings of the present study, we suggest that preventive measures to promote the reduction in risk of coronary heart disease (CHD) must address the high proportion of men and women with high LDL-C, and that these measures should take into account both the gender and age factors. For men, reduction of high cholesterol must start early in life, whereas for women, steps must be taken earlier to mitigate the anticipated sharp increase in risk, especially after menopause. (Asian J Androl 2007 Nov; 9: 787–794)

Keywords: total cholesterol; low density lipoprotein-cholesterol; high density lipoprotein-cholesterol; triglyceride; total cholesterol/high density lipoprotein-cholesterol; cardiovascular diseases, arteriosclerosis; Asian men and women

1 Introduction

As Asian countries continue to develop and progress economically, the incidence of lifestyle diseases, such as coronary heart disease (CHD), arteriosclerosis and metabolic syndrome, is rising. To minimize the incidence of these lifestyle diseases, there is a need to identify and
address the risk factors early [1]. Today, there is evidence to show that the risks of CHD and arteriosclerosis increase with a decline in high density lipoprotein-cholesterol (HDL-C), increase in low density lipoprotein-cholesterol (LDL-C), triglyceride (TG) and total cholesterol (TC) [2]. The National Cholesterol Education Program Adult Treatment Panel III [3] identifies LDL-C as the primary target for cholesterol-lowering therapies. The therapeutic target is the reduction of LDL-C to levels below 100 mg/dL. In addition, strategies to increase HDL-C through regular exercise and to lower TG levels through proper diet and cutting down smoking and alcohol consumption are equally important lifestyle modifications that will help to mitigate the risk of CHD and arteriosclerosis as a result of dyslipidemia [3].

There is a perception that Asian diets, unlike those in developed countries, are low in fat and, hence, Asians are less likely to have high cholesterol than their developed-world counterparts. This is certainly not the case. Geographical and socioeconomic factors and diet all influence lipid and lipoprotein profiles. On top of these factors, age and gender might impact the profile of lipids and lipoproteins differently. Therefore, we evaluated the impact of age and gender on lipid and lipoprotein profiles of a cohort of generally healthy Chinese Singaporeans. We also assessed the burden of dyslipidemia and the considered challenges in tackling the increasing risks of CHD and arteriosclerosis in Asia.

2 Methods

2.1 Subjects

Institutional approval for the study was obtained and each volunteer gave written consent to participate. A total of 1 775 healthy subjects, 536 men and 1 239 women aged between 30 and 70 years old, were included in this analysis. Subjects were recruited from the general public through an open invitation to participate. All subjects included in this analysis were ethnic Chinese. They represented a wide spectrum in the society with educational background ranging from those with primary to those with tertiary educations. Subjects’ vocations ranged from non-working to clerical, technical and professional positions. Salary scales ranged from < SG$1 000/month to > SG$10 000/month. Singapore is a city-country, its population is strictly urban, and there is no rural population. Certain major illnesses, such as diabetes and hypogonadism affect lipid and lipoprotein profiles. To assess the impact of age and gender on lipid and lipoprotein profiles, only subjects with no known existing or history of major medical illnesses, such as cancer, hypertension, thyroid dysfunction, diabetes, osteoporotic fracture and cardiovascular events were recruited into the present study.

Each subject answered a detailed questionnaire with questions on medical, dietary, social, sex, and family history, and other relevant history regarding consumption of hormones or food supplements.

2.2 Serum lipid and triglyceride levels

An overnight 12-h fasting blood sample was collected and serum levels of TC and TG were measured using an automated procedure. HDL-C was determined after precipitation of apolipoprotein B with sodium phosphotungstate and MgCl2 [4]. LDL-C was computed according to the following formula: LDL-C = TC – (HDL-C + [TG × 0.45]). According to this formula, the calculated LDL-C values are not valid if TG levels are high. The ratio of TC to HDL-C (TC/HDL-C) was used as the atherogenic index [5].

2.3 Statistical analysis

Statistical analyses were performed using SPSS for windows version 12 (SPSS Inc., Chicago, IL, USA). One-way analysis of variance, χ², Fisher exact, unpaired t-test and Pearson linear regression test were used where appropriate.

3 Results

Gender differences in lipid and lipoprotein levels were clearly evident. Overall, Singaporean Chinese men have significantly higher levels of TC, TG, LDL-C and TC/HDL-C and lower levels of HDL-C than corresponding levels in women (Figure 1).

The gender difference in lipid and lipoprotein levels was further affected by age. In men, HDL-C level was positively correlated with age (r = 0.141, P = 0.001), whereas TC/HDL-C was negatively correlated with age (r = -0.11, P = 0.011). In women, however, TC (r = 0.284, P < 10⁻⁴), HDL-C (r = 0.063, P = 0.023), LDL-C (r = 0.218, P < 10⁻⁴) and TC/HDL-C (r = 0.143, P =0.000) were all positively correlated with age. A gender difference in the relationship among TG levels and other lipid and lipoprotein levels was also noted. TG
Figure 1. Comparison of all lipid and lipoprotein levels between men and women. All lipid levels in men were significantly different from corresponding levels in women ($P < 0.003$). TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol.

Figure 2. Total cholesterol levels by age groups in men and women. *Levels in men were significantly higher than corresponding levels in women ($P < 0.015$). *Levels in women were significantly higher than corresponding levels in men ($P = 0.01$). 1, Levels in women were significantly lower than corresponding levels in age groups between ages 41 and 70 years ($P = 0.025, P = 0.002, P < 10^{-4}, P < 10^{-4}, P < 10^{-4}$). 2, Levels in men were significantly lower than corresponding levels in age groups between ages 46 and 70 years ($P = 0.005, P < 10^{-4}, P < 10^{-4}, P < 10^{-4}, P < 10^{-4}$). 3, Levels in women were significantly lower than corresponding levels in age groups between 51 and 70 years ($P < 10^{-4}, P < 10^{-4}, P < 10^{-4}, P < 10^{-4}$). 4, Levels in men were significantly lower than corresponding levels in the 51–55, 61–65 and 66–70-year age groups ($P = 0.002, P < 10^{-4}, P = 0.029$).

Figure 3. Low density lipoprotein-cholesterol (LDL-C) levels by age groups in men and women. *Levels in men significantly higher than corresponding levels in women ($P < 0.005$). *Levels in women were significantly higher than corresponding levels in men ($P = 0.049$). 1, Levels in women were significantly lower than corresponding levels in age groups between ages 51 and 70 years ($P < 10^{-4}, P < 0.003, P < 10^{-4}, P < 10^{-4}$). 2, Levels in women were significantly lower than corresponding levels in age groups between ages 51 and 70 years ($P < 10^{-4}, P < 0.021, P < 10^{-4}, P < 0.001$). 3, Levels in women were significantly lower than corresponding levels in the 51–55, 61–65 and 66–70-year age groups ($P = 0.020, P < 10^{-4}, P = 0.042$). 4, Levels in women were significantly lower than corresponding levels in the 51–55 and 61–65-year age groups ($P = 0.032, P < 10^{-4}$).

was significantly correlated to TC ($r = 0.283, P < 10^{-4}$) in men, but not in women. In addition, the degrees of negative correlation of TG with HDL-C (men, $r = -0.351, P < 10^{-4}$; women, $r = -0.095, P = 0.001$) and positive correlation with TC/HDL-C (men, $r = 0.582, P < 10^{-4}$; women, $r = 0.107, P < 10^{-4}$) were much higher in men than in women.

Although TC and LDL-C levels in men were not affected by age, those in women showed progressive and significant increases. Both TC and LDL-C levels increased in age groups of women from 30 to 50 years, and thereafter the concentrations did not change. The levels of TC in the age groups between 30 to 45 years in men were significantly higher than corresponding levels in women, whereas those of LDL-C in the age groups between 30 and 50 years in men were significantly higher than corresponding levels in women (Figures 2 and 3). Interestingly, in the 61–65 year age group, the gender differences for TC and LDL-C seen in the younger age groups were reversed: both TC and LDL-C levels were significantly higher in women than corresponding levels in men (Figures 2 and 3).

A clear gender difference in HDL-C levels was also noted: levels in women in age groups from 30 to 65 years were significantly higher than corresponding levels in men. However, HDL-C levels in men and women in the 66–70 year age group were not significantly different (Figure 4).

Triglyceride levels in men and women were not affected by age. The TG levels in men were significantly
higher than corresponding levels in women for age groups from 36 to 60 years, and thereafter, no gender difference in levels was noted (Figure 5).

The gender differences, with higher TC and lower HDL-C in men, respectively, than in women, have accentuated the gender differences in TC/HDL-C ratios (Figure 6). The ratio remained significantly higher in men than in women up to 60-year age. In the higher age groups, however, a moderation of the TC/HDL-C ratio was noted in men. The TC/HDL-C ratio in women in the 61–65-year age group was significantly higher than corresponding levels in the 30–35-year age group. In men, a reduction in the TC/HDL-C levels was noted in the 61–65-year age group when compared to the 41–45-year age group (Figure 6).

Although the effects of gender and age on the lipid and lipoprotein profiles are clearly seen in Figures 1–6, the burden of dyslipidemia is best assessed by tabulating the various lipid levels according to the recommendations of the National Cholesterol Education Program Adult Treatment Panel III [2].

Although the proportions of men and women with TC above 200 mg/dL were not significantly different, there were significantly more men with high TC (> 240 mg/dL) than women ($\chi^2$-test, $P = 0.005$, Table 1). In addition, although the distribution of men (32%) with high TC in the age groups between 30 and 70 years was not age-dependent, those in women were. Significantly more women in the older age groups (above 50 years) have high TC compared to women in the younger age groups (Table 1).

Approximately 90% of normal healthy men and women in our population have LDL-C greater than 100 mg/dL, the therapeutic target level of the NECP ATP III (Table 2). Significantly more men than women have high LDL-C (> 130 mg/dL and > 160 mg/dL) (Table 2). The proportions of men with LDL-C greater than 160 mg/dL were not significantly different among the various age groups. However, more older women
Table 1. Percent of men and women in various groups of total cholesterol (TC) by age groups. aSignificantly fewer men have TC < 200 mg/dL in the 41–45-year than in the 30–35-year age group (P = 0.02). bSignificantly more men have TC between 200 mg/dL and 240 mg/dL in the 51–55 than in the 30–35 and 36–40-year age groups (P = 0.045, P = 0.024). cSignificantly more women in the 30–35–year age group have TC < 200 mg/dL than in women in age groups between 30 and 70 years (P = 0.025, P = 0.0004, P < 10^{-4}, P < 10^{-4}, P < 10^{-4}, P < 10^{-4}, P < 10^{-4}). dSignificantly more women in the 36–40 year age group have TC < 200 mg/dL than in women in age groups between 46 and 70 years (P = 0.002, P < 10^{-4}, P = 0.002, P < 10^{-4}, P < 10^{-4}). eSignificantly more women in the 41–45-year age group have TC < 200 mg/dL than women in the 51–55, 61–65 and 66–70-year age groups (P = 0.001, P < 10^{-4}, P < 10^{-4}). fSignificantly more women in the 46–50 year age group have TC > 200 mg/dL than in women in the 51–55, 61–65 and 66–70 age groups (P = 0.043, P = 0.0008, P = 0.001). gSignificantly more women in the 51–55-year age group have TC < 200 mg/dL than in women in the 61–65 and 66–70-year age groups (P = 0.046, P = 0.02). hSignificantly more women in the 56–60-year age group have TC < 200 mg/dL than in women in the 61–70 year age groups (P = 0.009, P = 0.002). iSignificantly more women in the 46–50 year age group have TC between 200 mg/dL and 240 mg/dL than in women in the 30–35 year age group (P = 0.007). jSignificantly more women in the 66–70-year age group have TC between 200 mg/dL and 240 mg/dL than in women in age groups between 30–45 and 51–70 (P < 10^{-4}, P = 0.006, P = 0.017, P = 0.007, P = 0.002, P = 0.032). kSignificantly less women in the 30–35 year age group have TC > 240 mg/dL than in women in age groups between 46–70 (P = 0.035, P = 0.03, P < 10^{-4}, P < 10^{-4}, P < 10^{-4}, P = 0.005). lSignificantly less women in the 36–40 year age group have TC > 240 mg/dL than in women in age groups between 51–70 (P < 10^{-4}, P < 10^{-4}, P < 10^{-4}, P = 0.022). mSignificantly less women in the 41–45 year age group have TC > 240 mg/dL than in women in age groups between 51–65 (P = 0.003, P < 10^{-4}). nSignificantly less women in the 46–50 year age group have TC > 240 mg/dL than in women in age groups between 51–65 (P < 10^{-4}, P < 0.001, P < 10^{-4}).

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<th>Age groups (years)</th>
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(> 50 years old) have high LDL-C (> 160 mg/dL) than younger women (< 50 years old) (Table 2).

4 Discussion

Our data showed that being male is one of the most important determinants of lipids and lipoproteins as risk factors for CHD and arteriosclerosis. Singaporean Chinese men have higher risks arising from TC, LDL-C, HDL-C, TC/HDL-C and TG, than Chinese women. In general, although age was not a determinant for lipids and lipoproteins in Singaporean Chinese men, it was an important determinant in Singaporean Chinese women. Except for HDL-C, all other lipid and lipoprotein levels (TC, LDL-C, TC/HDL-C and TG) were significantly higher in older women, especially those over 55 years, when compared to younger women in their thirties. Therefore, being of the male sex was disadvantageous with respect to all the lipid and lipoprotein risk factors. However, menopause in woman was an important risk factor. These observations reflect similar trends shown in other populations, including those in developed countries [6].

The data also showed a gender difference in the metabolism of triglyceride in Singaporean Chinese men and women. In men, higher triglyceride levels were associated with higher TC and TC/HDL-C and lower HDL-C levels. This relationship was not as acute in women. This observation implies that the high carbohydrates in the Asian diet is reflected in high triglyceride, which, in turn, is associated with high TC and TC/HDL-C and lower HDL-C levels in men.

Coronary heart disease is becoming a serious health problem as Singapore becomes more affluent [7, 8]. In 2000, it was the second leading cause of death in Singapore, accounting for 24.5% of all deaths [9].
Table 2. Percent of men and women in various low density lipoprotein-cholesterol (LDL-C) groups by age groups. *Significantly more women in the 56–60 year age group have LDL-C between 130 mg/dL and 160 mg/dL than women in the 41–45 and 51–55 age groups ($P = 0.002$, $P = 0.042$). **Significantly more women in the 51–55 year age group have LDL-C between 130 mg/dL and 160 mg/dL than in the 36–40 and 56–60 age groups ($P < 10^{-4}$, $P = 0.049$). ***Significantly more women in the 30–35 year age group have LDL-C < 100 mg/dL than in the 51–55, 60–65 and 69–70 age groups ($P = 0.018$, $P < 10^{-4}$, $P = 0.014$). ****Significantly more women in the 36–40 year age group have LDL-C < 100 mg/dL than in age groups between the age of 41–70 year age group ($P = 0.014$, $P=0.048$, $P < 10^{-4}$, $P = 0.035$). *****Significantly more women in the 41–45 year age group have LDL-C < 100 mg/dL than women in the 61–65 year age group ($P = 0.014$). ******Significantly more women in the 46–50 year age group have LDL-C < 100 mg/dL than in women in the 61–65 and 66–70 age groups ($P = 0.0002$, $P = 0.042$). *******Significantly more women in the 30–35 year age group have LDL-C between 130 mg/dL and 160 mg/dL than women in age groups between 51–70 ($P = 0.05$, $P = 0.035$, $P = 0.005$, $P < 10^{-4}$). ********Significantly more women in the 36–40 year age group have LDL-C between 130 mg/dL and 160 mg/dL than women in the 51–65 and 66–70 age groups ($P = 0.05$, $P = 0.008$). **********Significantly more women in the 41–45 year age group have LDL-C between 100 mg/dL and 130 mg/dL than women in the 61–65 and 66–70 age groups ($P = 0.047$, $P = 0.007$). ***********Significantly more women in the 46–50 year age group have LDL-C between 100 mg/dL and 130 mg/dL than women in the 66–70 year age group ($P = 0.009$). ************Significantly more women in the 51–55 year age group have LDL-C between 100 mg/dL and 130 mg/dL than women in the 66–70 year age group ($P = 0.019$). *************Significantly more women in the 61–65 year age group have LDL-C between 130 mg/dL and 160 mg/dL than women in the 36–40 year age group ($P = 0.043$). **************Significantly more women in the 66–70 year age group have LDL-C between 130 mg/dL and 160 mg/dL than women in age groups between 30 and 65 years ($P < 10^{-4}$, $P < 10^{-4}$, $P < 10^{-4}$, $P < 10^{-4}$, $P = 0.016$). ***************Significantly less women in the 30–35 year age group have LDL-C > 160 mg/dL than in age groups between ages 46 and 70 years ($P = 0.03$, $P = 0.002$, $P < 10^{-4}$, $P < 10^{-4}$, $P = 0.041$). ******************Significantly less women in the 36–40 year age group have LDL-C > 160 mg/dL than in age groups between ages 51–65 years ($P = 0.001$, $P = 0.01$, $P = 0.006$). *******************Significantly less women in the 41–45 year age group have LDL-C > 160 mg/dL than in age groups between ages 51–65 years ($P = 0.015$, $P = 0.015$, $P = 0.008$). *********************Significantly less women in the 46–50 year age group have LDL-C > 160 mg/dL than in age groups between ages 51–65 years ($P = 0.026$, $P = 0.028$, $P = 0.0014$).

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increasing trend of CHD is not confined to Singapore, but also to countries in Asia that have become more affluent.

To mitigate risks of CHD and arteriosclerosis in the huge population bases in Asia, preventive measures must be formulated and applied to the general public. In other words, a public health approach must be adopted [10]. The results shown in the current study imply that any management modality to address dyslipidemia must take into account gender and age factors. We suggest that strategies to reduce TC, LDL-C, TG and to increase HDL-C levels should be instituted as early as possible. However, for men, the urgency to start early is more acute as high TC, LDL-C and TG levels were noted here as early as 30 years, whereas in women, they tend to occur in the menopausal years.

Studies have shown that lowering LDL-C and TC levels can mitigate cardiovascular risks [11]. To reduce the burden of coronary atherosclerosis, the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) recommends that the concentrations of LDL-C and other CHD risk factors be maintained at their optimal levels [3]. Results from the present study showed the extent of the problem of dyslipidemia in our general population and clarify the challenges ahead if the NCEP’s strategy of lowering the lipid and lipoprotein risk factors for CHD is to be adopted. Although the NCEP-ATP III recommendation is for those with CHD or with high risks of developing CHD, it is not unrealistic to use the same recommendation as a target for a preventive management strategy. According to the lipid and lipoprotein profiles shown for Singaporean Chinese men and women, the magnitude of this task varies according to the indices and cut-off target levels one uses as well as whether the target group is men or women. To bring total cholesterol below the upper limit of normal (200 mg/dL), the targeted groups include 71.6% of men and 68.7% of women. However, if one were to use the TC/HDL-C of < 4.5, then fewer men (50.0%) and especially women (15.5%) would be targeted.

The NCEP ATP–III’s recommendation of lowering LDL-C is a key strategic approach to reducing the risk of CHD. In Singapore, the current cut-off value for LDL-C remains at 130 mg/dL. Even if this cut-off is used, almost equal proportions of apparently healthy men (66.4%) and women (53.4%) would be targeted for LDL-C lowering modalities. However, if, as recommended by the NCEP ATP III, LDL-C was lowered below 100 mg/dL in our local population, then approximately 90% of both men and women in the general population would have to be targeted. This represents a huge burden of care. It is, however, for the government and the medical fraternity to decide which cut-off level to adopt as the target for any preventive strategy.

Triglyceride is an independent risk factor for CHD [12], and significantly more men (14.9%) than women (4.4%) should be targeted for inclusion in a TG lowering strategy to help to reduce the risk of CHD in our local population.

Most men (87.1%) and women (97.1%), regardless of age in our cohort, have HDL-C levels > 39 mg/dL. However, significantly more women (53.8%) than men (17.7%) have levels of HDL-C higher than 62 mg/dL. Hence, more men than women need to increase their HDL-C levels to benefit from its cardio-protective effect.

Various preventive measures must be adopted to reduce the high lipids and lipoproteins among the Chinese Singaporean men and women. Among these, public educational and advocacy strategies must be adopted for long-term effectiveness. The key to success is to educate the general public and to get individuals to take ownership of their own health. Past experience has shown that soft public awareness programs do not seem to work effectively. More aggressive and sustained educational and promotional programs, involving the health promotion authority together with family physicians as well as civic interest groups, will, more likely, be effective.

For those with lower levels of LDL-C, between 100 mg/dL and 130 mg/dL, low HDL-C and high TG levels, advocacy for lifestyle modifications, including proper diet and adequate exercise, would be the first line of action. Lifestyle and diet significantly influence the lipid risk factor levels of Singaporean Chinese [13]. However, for subjects with higher levels of LDL-C (> 160 mg/dL) or when lifestyle changes are not effective, the use of various types of statins that have been shown to be effective should be considered [14].

Dyslipidemia and obesity are risk factors for coronary arteriosclerosis [15, 16]. Therefore, strategies for lowering LDL-C and TG as well as increasing HDL-C [17] to mitigate their effect on CHD must also be carried out in conjunction with the drive to curb the increasing trend of obesity in the population. As shown in an earlier study, the incidences of obesity in Singaporean men and women were 7% and 13.9%, respectively [18]. These incidences are somewhat higher than those reported for
Taiwanese Chinese men (3.2%) and women (6.4%), but are lower than incidences in more developed countries [19]. Therefore, strategies for reduction of obesity should be intimately tied to those for reduction of bad cholesterol.

In the light of the current findings, preventive measures to promote the reduction in risk of CHD must address the high proportion of men and women with dyslipidemia, and any measure adopted should take into account gender and age factors. For men, reduction of high cholesterol must start early in life, whereas for women, the higher risk after menopause must be considered. In all, promotion of a healthy lifestyle, including proper and appropriate diet, adequate exercise, especially among women and men in the middle age group, is critical in the battle to reduce the cardiovascular risk arising from dyslipidemia and high triglyceride levels.

Acknowledgment

We would like to thank staff in the Endocrine Laboratory, Department of Obstetrics and Gynaecology, National University of Singapore for their invaluable assistance in carrying out the study. This project was supported by funds given by the National University of Singapore, Academic Research Fund (R-174-000-067-112).

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