Kobe J. Med. Sci., Vol. 57, No. 2, pp. E38-E48, 2011

Lipid Profile Parameters in Malaysian Dyslipidemic Patients

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Received 28 June 2010/ Accepted 20 August 2010

Key Words: Cardiovascular risk factor, Dyslipidemia, Low density lipoprotein cholesterol, Malaysia, NCEP.

ABSTRACT

Introduction

The importance of serum lipids as cardiovascular risk factors is well recognized. However, most published studies have focused on western countries. The present study aimed to describe and analyze the lipid profile parameters in Malaysian dyslipidemic patients, and to identify concomitant clinical problems and risk factors associated with cardiovascular disease (CVD) among such patients.

Methods:

A retrospective record review was carried out at Hospital Universiti Sains Malaysia.The records were reviewed for 890 dyslipidemic patients who attended the hospital in 2007. Data were collected for age at time of presentation, sex, ethnicity, smoking status, pre-treatment lipid levels, and presence of associated illnesses. The study sample was classified according to the National Cholesterol Education Program Adult Treatment Panel III risk groups.

Results:

The mean (SD) values for total cholesterol, low-density lipoprotein cholesterol, high density lipoprotein cholesterol,

and triglycerides were 6.4 (1.3), 4.1 (1.3), 1.4 (0.5) and 1.9 (1.2) mmol/l, respectively. Less than half of study sample (43.1%) had coronary heart disease and coronary heart diseases equivalents, 24.3% were at moderate risk, and 32.6% were at low risk. Hypertension was present in 79.9% of the study sample, while 27.5% were diabetics. Cardiovascular disease was reported among 17.9%. Logistic regression revealed that family history of premature cardiovascular disease, higher age risk group; ethnicity and total cholesterol were predictors for the development of cardiovascular disease.

Conclusion:

The present review showed that dyslipidemic patients had high total cholesterol levels, according to National Cholesterol Education Program Adult Treatment Panel III guidelines. They were clinically diagnosed at middle age. Hypertension and diabetes

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were the commonest associated clinical problems. A large proportion of the patients were within the coronary heart disease or coronary heart disease risk equivalent group. Family history of premature cardiovascular disease, age, ethnicity, and total cholesterol are important risk factors for the development of cardiovascular disease in Malaysian dyslipidemic patients.

INTRODUCTION

Malaysia has an area of 330,000 km² and a population of 27 million, comprising three major ethnic populations: Malay (65%), Chinese (26%) and Indian (7.7%) (1).

Cardiovascular disease (CVD) is a term that incorporates diseases affecting the heart and arterial system, and is currently the major cause of death in developed countries (2). Data from the Information and Documentation System Unit of the Ministry of Health of Malaysia showed that CVD was the principal cause of death in government hospitals; 20-25% of deaths in government hospitals between the years 2000 and 2004, were due to CVD (2).

Rapid changes in dietary habits and way of life in most Asian populations have occurred together with rapid economic growth over the last 2-3 decades. These changes mean that some diet-related chronic diseases are typically exaggerated in later adult life, possibly explaining the increased risk of coronary artery disease in south Asian populations (3) .

Clinical and epidemiological studies have clearly established a link between high lipid levels and the development of CVD (4). The relationship between low-density lipoprotein cholesterol (LDL-C) levels and CVD risk is continuous over a broad range of LDL-C levels from low to high. The National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III therefore classify LDL-C levels from optimal (<2.6 mmol/l) to very high (≥4.9 mmol/l) (5). In addition to high levels of LDL-C, low levels of high-density lipoprotein cholesterol (HDL-C) are also associated with increased CVD risk**.** Current guidelines for the prevention and treatment of CVD specify LDL-C lowering as the primary goal of lipid-related therapy (5). However, other important factors that modify the treatment of LDL-C and contribute to the development of CVD have been established by the ATP III, including smoking, hypertension, diabetes mellitus (DM) and family history of premature cardiovascular disease (PCVD) (5).

In an isolated population, low serum total cholesterol (TC) is associated with low prevalence of CVD (6), and rising TC levels, even below the normal level of 5.2 mmol/l, are associated with an increased risk of CVD. There is no evidence to suggest that there is a threshold level of TC below which there is a reduced risk of developing CHD. This was demonstrated in a study by Chen and his co-researchers in China (7).

Where rapid urbanization has occurred in Asian populations, rising lipid levels have become an increasing problem, with a consequent increase in CVD risk (7).

Information on the association between lipid levels and CVD risk in Western countries has been extensively investigated and widely published; however, information on Asian populations is less accessible. Such information is generally considered to be of only local importance, and is therefore only available in local Asian publications (8). Although serum lipids and lipoproteins have been well-studied in Malaysia, no studies have focused on the cardiovascular risk factors in dyslipidemic patients (9) .

The aim of this study was to describe and analyze the lipid profile parameters in Malaysian dyslipidemic patients, and to identify the concomitant clinical problems and predictive factors for CVD among these patients.

METHODS

Study design and population

The patient sample in this study was based on a computer-generated list of 2,500 dyslipidemic patients (inpatients and outpatients), which was obtained from the Record Unit, Hospital Universiti Sains Malaysia (HUSM), in the State of Kelantan, Malaysia. HUSM is a large public teaching hospital dealing with patients referred from Kota Bharu city, as well as referrals from other hospitals in Kelantan, and the nearby states of Terengganu and Pahang. Subjects were dyslipidemic patients who attended HUSM in 2007. The first lipid profile parameters recorded before starting lipid-lowering therapy were regarded as baseline values.

Sample size formulae were calculated and the largest sample size came from the single proportion formula. The prevalences of hypertension, DM, smoking and CVD were 78%, 41%, 8.4%, 28%, respectively (10,11). At 95% confidence levels and a precision of 5%, the total sample sizes for hypertension, DM, smoking and CVD were 342, 482, 153 and 412, respectively. The largest sample required was thus 482 subjects. In order to screen more patients and increase the power of the study, a random systematic sampling method was applied, by which every third patient's file was selected. Eight hundred and ninety dyslipidemic subjects who attended the HUSM during 2007 were thus recruited and reviewed.

The variables recorded were: age, sex, ethnicity, smoking status, stroke and lipid profile parameter values, and presence or absence of related clinical problems (hypertension defined as systolic blood pressure ≥ 140mm Hg or diastolic blood pressure ≥90 mm Hg (12,) and/or patient's statement about the use of antihypertensive drugs; family history of premature CVD defined as age of onset before 55 years for men and before 65 years for women in first-degree relatives (13); diabetes, diagnosed by symptoms of hyperglycemia and random plasma glucose ≥11.1 mmol/l or fasting plasma glucose ≥7.0 mmol/l and/or drug history of hypoglycemic drugs (14); clinical CVD defined as a definite myocardial infarction (new Q waves or ST elevation or new T wave inversion persisting in more than two leads with creatine kinase >400 IU/l), or having undergone coronary artery bypass grafting, percutaneous transluminal coronary angioplasty, having angina with an ischemic resting echocardiogram, or a reported angiogram showing clinically important stenosis.

Patients were grouped according to the NCEP ATP III into three categories (5): the highest risk category included patients with coronary heart disease (CHD)and/or CHD risk equivalents, which comprises other clinical forms of atherosclerotic disease and DM. The second category included patients with ≥2 other risk factors identified by the NCEP ATP III. Such patients were considered to be at moderate risk. The third category included patients with ≤1 risk factor, and was considered to represent the low-risk group. The NCEP ATP III recommended that HDL ≥1.55 mmol/l was regarded as a "negative" risk factor; its presence removes one risk factor from the total count (5).

Statistical analysis:

All numerical data were presented as mean (SD), while frequencies were used for categorical variables. One-way analysis of variance (ANOVA) was used to compare mean values of lipid profiles among the different risk groups with post hoc Bonferroni multiple comparisons.

Differences in lipid profiles between two characteristic groups were compared using unpaired Student's *t*-tests. Categorical variables were compared using $\chi 2$ tests. Stepwise multiple regression analysis was used to test the influence of various confounders on CVD.

A P value of ≤0.05 was considered to be significant in two-tailed tests. Statistical analysis was performed using SPSS version 12.0.1

RESULTS

The initial database consisted of a total of 2,500 records of dyslipidemic patients who attended the HUSM in 2007, of whom 890 patients were selected by systematic random sampling. Table I shows the baseline characteristics of the study patients. Of the selected patients, 75.5% were Malays, and 57% were females. The mean age was 54 years (range 20-90 years). Regarding medical history, 79.9% reported a history of hypertension and 27.5% were diabetics; established CHD was reported in 17.9 %, while smoking status was recognized in 6.9%.

Table I. Baseline clinical characteristics and lipid profile parameters of recorded patients, n= 890

Characteristics	Mean (SD)/n (%)
Age (years)	54.6(16.7)
Sex	
Male	384(43.1)
Female	506 (56.9)
Ethnicity	
Malays	672(75.5)
Non Malays	218(24.5)
Cardiovascular risk factors	
Diabetes mellitus	245(27.5)
Hypertension	711(79.9)
Family history of premature heart disease	82(9.2)
Cerebrovascular accident	63(7.1)
Age risk (men≥ 45 or women ≥55	526(59.1)
Smoking	61(6.9)
Coronary heart disease	159(17.9)
TC mmol/l (n=890)	6.4(1.3)
LDL-C mmol/l (n=843)	4.1(1.2)
HDL-C mmol/l (n=857)	1.4 (0.5)
TG mmol/l (n=890)	1.9(1.2)

The status of the associated risk factor groups are given in Table II. Three hundred and eighty-four (43.1%) had CHD or CHD risk equivalents, while 216 (24.3%) had multiple risk factors, and only 290 (32.6%) had one or no risk factor. The mean TC and HDL-C values, but not the LDL-C values, differed significantly among the risk groups, as demonstrated by ANOVA. Post-hoc tests confirmed that patients with no or one risk factor presented with significantly higher TC levels than the CHD or CHD risk equivalent group (P=0.006), while significant differences were observed among the three risk groups in terms of HDL-C (P<0.001).

Table II. Baseline lipid profile among the different risk categories

	Risk categories						
Variables	0-1 Risk factor Mean(SD)	≥2 risk factors Mean(SD)	CHD or CHD risk equivalent Mean(SD)	*P-value	**P-value 0-1 Risk Factor Vs ≥2 risk factors	**P-value 0-1 Risk Factor Vs CHD or CHD risk equivalent	**≥2 risk factors Vs CHD or CHD risk equivalent
TC (mmol/l)	6.5(1.2)	6.4(1.2)	6.2(1.4)	0.006	1.0	0.006	0.1
LDL-C	4.2(1.2)	4.2(1.1)	3.9(1.3)	0.06	1.0	0.1	0.2
HDL-C	1.6(0.4)	1.2(0.3) **	1.3(0.6) **	<0.001	<0.001	<0.001	<0.001

* One-way analysis of variance (ANOVA)
** Post hoc test: Bonferroni

CVD was reported in 159 patients (17.9%). The clinical characteristics of the CVD-positive and CVD-negative patients are shown in Table III. The frequency of CVD among Malays was significantly higher than among non-Malays (P=0.005).

A significantly higher proportion of CVD patients were classified within the higher age risk group (men ≥45 years; women ≥55 years) (15). A significantly higher proportion of CVD patients also had a family history of PCVD. TC, LDL-C and TC:HDL ratio were significantly higher in patients with CVD than in those without CVD (P=0.006, 0.02 and 0.04, respectively).

Predictors of cardiovascular disease by multivariate analyses

Stepwise multiple regression analysis was used to identify independent predictors of CVD among the 890 patients. Significant correlations were found for family history of PCVD (OR=1.9, CI95%: 1.1-3.6), ethnicity (non-Malays were at lower risk of developing CVD than Malays; OR=0.5, CI95%: 0.3-0.8), higher age (OR=1.7, CI95%: 1.0-1.3), and basal TC (OR=1.2, C 95%: 1.0-1.3) (Table IV).

Table V shows the mean lipid profile parameter values according to personal characteristics of the study subjects. Females had significantly higher levels of TC, LDL-C and HDL-C **(**P=<0.001, 0.02 and <0.001, respectively).

Malays had significantly higher values of TC and HDL-C than non-Malays (both P=0.03). Although Malays also had higher mean LDL-C values than non-Malays, this difference was not statistically significant. People with higher ages had significantly higher TC levels (P=0.05), while HDL-C levels were similar, and there was a nonsignificant difference in lipid parameters between patients with and without a family history of PCVD.

Table III. characteristics dyslipidemic patients with and without CVD

Variables	**CVD positive n (%) 159(17.9)**	**CVD negative n (%) 731 (82.1)**	**P value**
Age*[a]	55.5(10.8)	54.5(17.7)	0.4
Age at risk[b]	108(67.9)	418(57.2)	0.01
Sex[b]			0.07
Male	79(49.7)	305(41.7)	
Female	80(50.3)	426(58.3)	
Ethnicity[b]			
Malays	134(84.3)	538(73.6)	0.005
Non Malays	25(15.7)	193(26.4)	
Diabetes[b]	45(28.3)	200(27.4)	0.8
Hypertension[b]	129(81.1)	582(79.6)	0.6
Smoking[b]	12(7.5)	49(6.7)	
Family history of PCVD[b]	24(15.1)	58(7.90)	0.005
Lipid profile parameters mmol/l*[a]			
TC	6.6(1.7)	6.3(1.2)	0.006
TG	2.0(1.4)	1.8(1.1)	0.06
LDL-C	4.3(1.5)	4.0(1.1)	0.02
HDL-C	1.3(0.4)	1.4(0.5)	0.6
TC:HDL ratio	5.2(2.0)	4.8(1.7)	0.04

* Data are expressed as mean (SD)
[a] Independent t-test was used
[b] Chi square test was used

Table IV. Predictors of cardiovascular disease by multivariate analyses

Variables	Adjusted OR (95% CI)	P-value
Family history of PCVD		
No family history	1*	
Positive family history	1.9(1.1-3.6)	0.013
Ethnicity		
Malays	1*	
Non Malays	0.5(0.3-0.8)	0.005
Age at risk	1*	
Low risk group	1.7(1.0-1.3)	0.003
High risk group		
Basal TC	1.2(1.0-1.3)	0.016

*Reference group

Table V. Lipid profile parameters' mean values by personal characteristics of study subjects

Lipid profile mmol/l Mean(SD)	Groups		*P* value*
	Male	Female	
TC (n=890)	6.2(1.3)	6.5(1.3)	<0.001
LDL-C(n=843)	4.0(1.2)	4.2(1.3)	0.02
HDL-C(n=857)	1.3(0.4)	1.5(0.5)	<0.001
	Malays	Non -Malays	
TC(n=890)	6.4(1.3)	6.2(1.3)	0.03
LDL-C(n=843)	4.2(1.3)	3.9(1.2)	0.07
HDL-C(n=857)	1.35(0.5)	1.4(0.5)	0.03
	Age at higher risk	Age at lower risk	
TC(n=890)	6.5(1.3)	6.3(1.3)	0.05
LDL-C(n=843)	4.2(1.3)	4.1(1.2)	0.4
HDL-C(n=857)	1.4(0.5)	1.4(0.5)	0.4
	Family history of Premature CHD	None	
TC(n=890)	6.6(1.6)	6.4(1.3)	0.17
LDL-C(n=843)	4.3(1.7)	4.1(1.2)	0.16
HDL-C(n=857)	1.3(0.5)	1.4(0.5)	0.1

*Independent t test was used

DISSCUSSION

High lipid levels in Asian people are related to age, ethnicity, sex, economic development, urbanization, fatty food intake, and other risk factors, such as DM (8).

The current analysis was the first survey conducted in dyslipidemic patients from the northeast state of Malaysia, Kelantan.

The mean TC level at baseline was 6.4 mmol/l, which is high according to the NCEP ATP III guidelines. The LDL-C level was 4.1 mmol/l, and regarded as borderline high (5). In comparison to the healthy Malaysian population examined by Khoo and his colleagues in 1997, our study subjects showed significantly higher lipid profile parameters, except for HDL-C, which showed a significantly lower value (9).

However, the present study found similar TC, TG, LDL-C and HDL-C levels to those reported in another study of Malaysian hyperlipidemic patients (10). The TC and LDL-C levels were higher, and the HDL-C levels lower than in hypercholesterolemic patients in Korea (16) and Europe (17). Lipid levels generally vary with age, sex, body weight, lifestyle, hereditary background, and associated illnesses (such as DM, and liver, kidney and thyroid diseases). However, certain factors should be considered when comparing or evaluating TC assessments, such as the type of blood sample (plasma or serum), and methods of blood collection and analysis (8).

The results of the present study showed that the most frequent health problem among the study subjects was hypertension (79.9%), followed by DM (27.5%), and ischemic heart disease (17.9%). Smoking as an example of an unhealthy lifestyle practice was present in only 6.9%. The reported prevalence of hypertension was identical to that reported among Asians with atherothrombosis (79.9%), while the prevalences of DM and smoking were lower (11). However, the present study population had higher prevalences of hypertension and diabetes (59.6, 22.1 %, respectively) compared to European dyslipidemic patients, (17). Cardiovascular risk factors were common and occurred either alone or combined; 24.3% of subjects had more than one risk factor, and 32.6% had one or no risk factor. Among the study patients, 43.1% had established CHD or CHD risk equivalent, and this high prevalence of CHD and its associated risk factors may be explained by the socioeconomic development and westernization in Malaysia. Although this prevalence is lower than that among dyslipidemic patients in Thailand (18), it is still high compared to the results of another study by Laforest et al. (39.05%) (17). The clustering of these risk factors is an important consideration during lipid-lowering therapy. Based on these risk determinants, ATP III identifies three categories of risk that modify the goals and modalities of LDL-C-lowering therapy: these include CHD and CHD risk equivalents, multiple (2+) risk factors, and 0-1 risk factor, associated with LDL-C goals of <2.6, <3.6 and <4.1 mmol/l, respectively (19).

The high prevalences of these risk factors coupled with unhealthy lifestyle practices may account for the early development of CHD, which has increased rapidly in Malaysia to become the major cause of morbidity and mortality in the country (20).

In the present study, subjects with 0-1 risk factors had the highest cholesterol levels, compared to those with CHD or CHD risk equivalent (6.5 mmol/l versus 6.2 mmol/l, P=0.006). CHD risk equivalents included DM, symptomatic carotid artery disease and/or aortic aneurysm, and high-risk subjects were defined as having ≥2 CHD risk factors (i.e., age, family history of premature CHD, smoking, hypertension, and low levels of HDL-C (5)). Even in the absence of lipid-lowering therapy, these patients may be more worried about their lifestyles and may be under strict dietary control, especially in the case of diabetics who represented 27.5% of the study group. This could explain the lower TC levels compared with subjects with 0-1 risk factors, and is supported by the higher TC and LDL-C levels in the

CVD group (17.9%) compared to the non-CVD group (82.1%). Logistic regression also showed that other factors in addition to TC level were risk factors that contributed to the development of CVD, including ethnicity, family history of PCVD, and age risk group.

The present analysis showed that women had higher lipid levels than men, which could be explained by the postmenopausal status, when the decline in female hormones causes an increase in lipid levels, as shown by Pang et al. (21). The present study showed that Malays had significantly higher TC and lower HDL-C levels than non-Malays, which was in agreement with the results of Khoo et al. (9). This observation may be explained by differences in dietary habits or lifestyles, or by genetic factors, or may be associated with the higher prevalence of CVD among the Malays than non-Malays, together with the strong prediction of CVD by TC.

Overall, the results of this study suggest the need to treat risk factors other than dyslipidemia that play a role in the development of atherothrombosis and CHD.

Data from hospital records are an important source of information for epidemiological studies. Such studies can help to identify health problems in the community and provide inferences to be explored in future work. Moreover, claims information, combined with other clinical data such as laboratory data, can provide a powerful tool for understanding the real-world impacts of therapy on patient health (22).

However, retrospective hospital database analysis is subject to some problems, including limitations caused by selectivity, misdiagnosis or inaccurate data coding, and admissions policies. The problem of selectivity was reduced in the current study, because the sample included both inpatients and outpatients. In addition, the current data were collected from a single centre that may therefore not be representative of the whole Malaysian community; it may, however, represent the northeast Malaysian population, as the hospital concerned acted as a referral centre for three states. A further potential limitation was that patient compliance and the level of physical activity could not be investigated.

CONCLUSION

The present study demonstrated that dyslipidemic subjects had high TC levels, according to the NCEP ATP III, and borderline high LDL-C levels. Hypertension and DM were the commonest associated clinical problems. A large proportion of the subjects fell within the CHD or CHD risk equivalent groups. A family history of PCVD, higher age, ethnicity, and TC levels were important risk factors for the development of CVD in Malaysian dyslipidemic patients.

ACKNOWLEDGEMENTS

We would like to acknowledge the Ministry of Science, Technology and Innovation of Malaysia (MOSTI) e Science Fund grant No 305/PPSP/6113212, Universiti Sains Malaysia short term grant No 304/PPSP/6139013, Institute for Postgraduate Studies, Universiti Sains Malaysia for their Fellowship support and the Record unit of the Universiti Sains Malaysia for their assistance in the development of this article.

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