ORIGINAL ARTICLE

Serum Lipids and their Relationship with other Coronary Risk Factors in Healthy Subjects in a City Clinic

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Summary

Over a thousand subjects who visited a city private medical clinic for health screening and advice were examined for their lipid profile and other cardiovascular risk factors. The mean TC, TG, LDL-C and HDL-C were 5.43, 1.45, 3.61 and 1.15 mmol/l. Their derived ratios viz, TC:HDL-C and LDL:HDL-C were 5.11 and 3.43 respectively. The prevalance of hyperlipidaemia was moderately high. Of the subjects studied 58.5% had elevated serum cholesterol, 14.8% had raised triglycerides, 64.9% had raised LDL-C and 20.8% had low HDL-C. Male subjects generally showed higher mean values and abnormality frequency in TC, TG, LDL-C, TC:HDL-C and LDL:HDL-C as compared to female subjects. Although significant ethnic differences were not detected for certain lipid parameters (e.g. TC, TG and HDL-C), the Indians appeared to have higher mean lipid values (except HDL-C), and higher percentage abnormality for all the lipid parameters as compared to the Chinese and the Malays. In correlation studies, the following lipid parameters:- TC versus TG, LDL-C, TC:HDL-C; TG versus TC:HDL-C and LDL:HDL-C; LDL-C versus TC:HDL-C and LDL:HDL-C; were positively correlated. On the other hand, TC versus HDL-C, TG versus HDL-C, LDL-C and HDL-C, and HDL-C versus TC:HDL-C and LDL:HDL-C were negatively correlated. The coronary risk factors which generally showed positive correlations with lipid parameters were BMI and blood pressure. Positive correlations were also recorded between fasting blood glucose and TG; uric acid with TG, TC:HDL-C and LDL:HDL-C. In contrast, risk factors of negative correlations were observed between HDL-C and the coronary risk factors of BMI, diastolic blood pressure and uric acid. Smoking showed raised per cent lipid abnormality for TG, HDL-C, TC:HDL-C and LDL:HDL-C. Alcohol consumption also increased the mean level and abnormality frequency for TG. The implication of this investigation is discussed.

Key Words: Serum lipids, Coronary risk factors, Lipid profile, Lipid abnormality, Hyperlipidaemia, Hypercholesterolaemia, Hypertriglyceridaemia, Mixed hyperlipidaemia, Correlation

Introduction

The importance of serum lipid as a cardiovascular risk factor is well recognised. In the Multiple Risk Factor Intervention Trial, MRFIT, high lipid levels were shown to be associated with an increase of heart attack[1]. Heart attack or cardiovascular mortality is now regarded as the number one cause of mortality in many parts of the world. Khoo *et al*[2] reported that cardiovascular mortality in Malaysia has increased 15 fold from 1950 to 1989. Since 1970, cardiovascular disease has been the most commonly reported cause of death in Peninsular Malaysia with coronary artery disease specifically identified as the leading cause of mortality. In view of this, it is necessary to monitor the lipid levels of Malaysians over time and at different localities and

among the different social classes, in order to evaluate the significance of this correlation between the serum lipid fractions and other cardiovascular risk factors. Further confirmation of a positive correlation would suggest that steps might have to be taken to stem this rise in cardiovascular mortality and morbidity.

In the early 1970s, a survey on lipid values of urban Malaysians was carried out by Khoo and Chong[3], Chong and Khoo[4] and Khoo[5]. The authors have estimated the normal values of some lipid parameters (total cholesterol, triglycerides and β-lipoprotein) by race and age groups. They reported that total cholesterol and triglycerides levels were comparable to those of Americans at that time. More than twenty years has elapsed during which many things have taken place, for instance, rapid economic growth, public awareness of health care, changes of social habit and lifestyle and increased incidence of cardiovascular disease and mortality, etc.

Although the levels of serum lipids and lipoproteins have been studied quite extensively in Malaysia[3-18], the relationship between these lipid parameters and other cardiovascular (coronary) risk factors, however, has been less frequently examined.

Chong and Ng[14] reported positive correlations between the levels of total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C) and body mass index (BMI). They also reported an inverse correlation between high density lipoprotein cholesterol (HDL-C), particularly the % HDL-C and the obesity index, BMI.

Another study by Teo, Chong *et al*[15] reported a high prevalence of hyperlipidaemia and their associations with other risk factors in a group of Malaysian executives; they also reported that Malays had a significantly higher prevalence for hyperlipidaemia, obesity and hyperuricaemia compared to Chinese.

This paper attempts to provide an insight into the serum lipid profile of a segment of urban Malaysians visiting a private medical clinic between January 1989 and August 1991. In addition, the relationships between their serum lipids and other risk factors of coronary heart disease, such as, levels of blood glucose, blood pressure, uric acid and BMI were also examined and reported.

Materials and Methods

The subjects of the study comprised individuals of different ethnic groups who came for routine medical check-up in a city clinic in Kuala Lumpur from January 1989 to August 1991. These individuals were regarded as "healthy" because they had no medical complaints and no previous known major illnesses such as cancer, hypertension, heart disease, liver or renal disorders. Both males and non-pregnant females were included in the study.

The majority of the subjects belonged to the middle and upper income class who could afford private medical care. They consisted of executives in corporate companies, sole proprietors of small businesses such as fish mongers, owners of car repair shops, sundry shops, hardware shops and some senior civil servants.

Lipid Measurements

Blood was collected venaepuncture after a 12 hr overnight fast. The serum was separated from the clotted blood and stored at 4 degree Celsius. The following lipid parameters were studied:1) Total Cholesterol (TC), 2) Triglycerides (TG), 3) HDL-Cholesterol (HDL-C), 4) LDL-Cholesterol (LDL-C), 5) TC:HDL-C Ratio and 6) LDL:HDL-C Ratio.

The first three parameters (TC, TG and HDL-C) were estimated using the photometric system 4010 Boehringer Mannheim machine according to the methods described in the manual[19] (Boehringer Mannheim Co.). LDL-C was estimated by using the Friedewald[20] Formula as follows: LDL-C = (TC - HDL-C) - TG /2.19 mmol/l.

For TC and HDL-C measurements, the enzymatic CHOD PAP method as outlined by Siedet *et al*[21] and Lopes-Virella *et al*[22] was employed. For TG measurement, the method which involved the enzymatic hydrolysis of triglycerides with subsequent determination of liberated glycerol by colorimetry as described by Wahlefeld[23] was used.

Quality control of the lipid determinations was maintained by regular determination of reference sera

(freeze dried commercial standards) in order to monitor and ensure the accuracy. In general the coefficient of variation for the lipid determination for the commercial sera was about 5%. The above lipid profile determinations were carried out in one laboratory.

Other Measurements

In addition to the above lipid measurements, other biochemical parameters such as uric acid and fasting blood glucose and a physical examination were done routinely. The weight and height measurements (expressed as body mass index, BMI=weight in kg/height in meter^2), hip and waist circumference measurements (expressed as hip/waist ratio, a central obesity index), chest X-ray, lung, liver and renal function tests, resting and exercise ECG (treadmill test), ultrasound and urine test and blood counts were also carried out. The personal and family history, exercise habits and lifestyle of individuals were also recorded.

The levels of exercise, smoking and alcohol consumption were obtained from answers to questions put to the subjects during the medical examination.

a) Exercise – Subjects who performed physical activities such as walking, jogging, cycling, martial art, 'qi gong' and other sports at least 3 days a week for a minimum of 1/2 hour per session were considered to have regular physical exercise.

b) Smoking – Subjects who smoked cigarettes or cigars more than 5 sticks per day for at least 3 days per week were regarded as smokers.

c) Alcohol Consumption – Subjects who had one drink or more (beer, stout, whisky, brandy or wine) per day for at least 3 days per week were regarded as drinkers.

Statistical Analysis

Basic statistics for serum lipids were estimated from the data according to ethnic groups, sex and age groups. Abnormalities for the various lipid components were mainly based on cut-off values according to criteria given by the expert panel of the National Cholesterol Education Program (NCEP) Adult Panel II[24]. The abnormality status and cut-off values used in this paper were as follows:-

		Abnormality Status	
Trait	Unit	I	II
TC	m mol/l	≥ 5.2	≥ 6.2
TG	m mol/l	≥ 2.3	–
HDL-C	m mol/l	< 0.9	–
LDL-C	m mol/l	≥ 3.3	≥ 4.1
TC:HDL-C	–	≥ 6.0	–
LDL:HDL-C	–	≥ 4.0	–

In addition, classification of lipid abnormalities into hypercholesterolaemia, hypertriglyceridaemia and mixed (or combined) hyperlipidaemia was based on the guidelines of the European Atherosclerosis Society (EAS)[25].

The relationship studies between serum lipids and other measurements such as BMI, blood pressure, fasting blood glucose and uric acid were done by simple correlation analysis. Contingency Chi-square was used to test the dependency between lipids and lifestyles or habits. In the above statistical analysis, the computer software SAS/BASE[26] and SAS/STAT[27] of SAS Institute Inc, USA, were employed.

Results

The Population Studied

The population studied during the period from January 1989 to August 1991 consisted of 1116 subjects of which 74.2% (N=828) were males and 25.8% (N=288) were females. There were 819 (73.4%) Chinese, 282 (25.3%) Malays, 36 (3%) Indians and 29 (2.6%) other ethnic groups. The mean age of the population was 43.6 year-old ranging from 12 to 87 year-old. Majority of the subjects (85.5%) fall between 30 - 59 age group. Some of the relevant health parameters associated with this study are given below:

Character	Unit	Mean	SD
Body Mass Index	kg/m^2	23.49	3.50
Waist/Hip Ratio	–	0.87	0.08
Systolic Blood Pressure	mmHg	121.08	15.54
Diastolic Blood Pressure	mmHg	83.25	8.99
Fasting Blood Sugar	mmol/l	5.21	1.08
Blood Urea	mmol/l	4.50	1.24
Blood Uric Acid	mmol/l	0.33	0.18

The means of all these parameters generally fall within the accepted normal ranges, suggesting the sample studied on the whole appears normal and healthy, besides having normal chest X-ray, ECG and treadmill test.

Lipid Profile

The serum lipid profiles of the healthy subjects in a city clinic studied are summarized in Table I. The mean LDL-C of 3.61 mmol/l is considered to be borderline according to the NCEP Adult Panel II. This is reflected in the marginally raised TC (5.43 mmol/l) which is the surrogate of the LDL cholesterol. The mean TG (1.45 mmol/l) and HDL-C (1.15 mmol/l) are within normal ranges.

There was a tendency of these serum lipid levels (except HDL-C) to increase with age. Males generally had higher means for TC, TG, LDL-C, TC:HDL-C and LDL:HDL-C ratios than females. These differences are

Table I
Serum lipid profile of healthy subjects in a city clinic by sex and age group

Age Group	Sample Size			TC			TG			LDL-C			HDL-C			TC:HDL-C			LDL-C:HDL-C		
	M	F	C	M	F	C	M	F	C	M	F	C	M	F	C	M	F	C	M	F	C
19 & below	4	2	6	4.10	4.15	4.12	0.72	0.95	0.80	2.53	2.60	2.55	1.28	1.05	1.20	3.22	3.94	3.46	1.98	2.47	2.14
20 - 29	42	19	61	5.21	4.78	5.08	1.43	0.76	1.22	3.57	3.05	3.41	0.97	1.37	1.09	5.57	3.62	4.99	3.80	2.32	3.36
30 - 39	268	73	341	5.37	5.05	5.30	1.51	0.83	1.37	3.59	3.17	3.50	1.07	1.41	1.15	5.36	3.76	5.02	3.63	2.38	3.36
40 - 49	316	78	394	5.49	5.11	5.42	1.65	1.05	1.54	3.68	3.38	3.62	1.07	1.33	1.12	5.54	4.07	5.25	3.75	2.70	3.54
50 - 59	142	77	219	5.61	5.70	5.65	1.68	1.21	1.52	3.75	3.76	3.76	1.12	1.37	1.21	5.33	4.49	5.04	3.58	3.00	3.37
60 - 69	37	25	62	5.58	6.10	5.79	1.48	1.63	1.54	3.75	4.12	3.90	1.12	1.20	1.15	5.42	5.27	5.36	3.69	3.55	3.64
70 & above	19	14	33	5.68	5.51	5.60	1.34	1.51	1.42	3.67	3.64	3.66	1.39	1.16	1.30	4.81	5.07	4.92	3.23	3.41	3.31
Overall	828	288	1116	5.46[a]	5.33[a]	5.43	1.58[a]	1.09[b]	1.45	3.65[a]	3.48[b]	3.61	1.09[b]	1.34[a]	1.15	5.42[a]	4.22[b]	5.11	3.66[a]	2.78[b]	3.43
S.D.	-	-	-	1.05	1.00	1.04	0.99	0.67	0.94	1.01	0.92	0.99	0.43	0.36	0.43	1.65	1.32	1.65	1.35	1.10	1.34

Footnotes : Means with the same alphabet are not significantly different in each lipid component
M: Males F: Females C: Males and females
Units for TC, TG, LDL-C, HDL-C were in mmol/l

Table II
Means and standard deviations of serum lipid values (mmol/l) for healthy subjects in a city clinic by race

Race	TC	TG	LDL-C	HDL-C	TC:HDL-C	LDL:HDL-C
Chinese (819)	5.36 ± 1.04[a]	1.45 ± 0.96[a]	3.53 ± 0.98[ab]	1.17 ± 0.42[a]	4.97 ± 1.57[a]	3.31 ± 1.27[a]
Malay (232)	5.59 ± 1.08[a]	1.42 ± 0.83[a]	3.85 ± 0.98[bc]	1.09 ± 0.29[a]	5.46 ± 1.78[a]	3.77 ± 1.42[b]
Indian (36)	5.73 ± 0.82[a]	1.68 ± 0.83[a]	3.93 ± 0.97[c]	1.02 ± 0.61[a]	6.28 ± 1.69[b]	4.39 ± 1.47[c]
Others (29)	5.63 ± 0.90[a]	1.68 ± 1.27[a]	3.46 ± 1.07[a]	1.37 ± 0.94[b]	4.94 ± 1.95[a]	3.04 ± 1.54[a]

Bracketed figures refer to sample size. Means with the same alphabet are not significantly different.

statistically significant except for TC. The HDL-C was statistically higher in females compared to males. It is interesting to note that the mean lipid values except HDL-C were generally shown to be higher in females than in males in the age group of 50 - 59 or greater.

The mean lipid values of different ethnic group – Chinese, Malays, Indians and Others are given in Table II. Although there were no statistical differences in the means of TC, TG and HDL-C for the three major ethnic groups, some differences in terms of ranking order in their means were observed. The Indians appeared to have the highest mean TC (5.73 mmol/l) followed by the Malays (5.59 mmol/l) and the Chinese (5.36 mmol/l). The highest TG was recorded for the Indians (1.68 mmol/l) followed by the Chinese (1.45 mmol/l) and the Malays (1.42 mmol/l). In the case of HDL-C, the Chinese have the highest mean (1.17 mmol/l), followed by the Malays (1.09 mmol/l) and the Indians (1.02 mmol/l) being the lowest. There was, however, a statistical significance in the ranking of means for LDL-C and the ratios of TC:HDL-C and LDL:HDL-C for the three major ethnic groups with the Indians having the highest means followed by the Malays and then the Chinese.

Lipid Abnormality

The percentage abnormality of serum lipid values in the sample studied (all ethnic groups) is given in Table III. Based on the cut-off values of the NCEP Adult Panel II[24], the frequencies for elevated lipids (under Abnormality Status I) were 58.6%, 14.8%, 20.8%, 64.9%, 26.6% and 30.6% for TC, TG, HDL-C, LDL-C, TC:HDL-C and LDL:HDL-C, respectively.

Table III
Abnormality of serum lipid levels (mmol/l) of a healthy subjects in a city clinic by age group

Age Group	Percent abnormality							
	TC		TG	HDL-C	LDL-C		TC:HDL-C	LDL:HDL-C
	(I)	(II)			(I)	(II)		
19& Below (6)	0.0	0.0	0.0	0.0	16.7	0.0	0.0	0.0
20 - 29 (61)	42.6	9.8	10.0	23.3	55.7	21.3	25.0	26.7
30 - 39 (341)	51.7	16.7	12.3	22.2	60.5	25.1	28.1	30.4
40 - 49 (394)	60.2	16.8	17.3	23.9	65.8	26.0	28.2	33.4
50 - 59 (187)	62.3	33.9	16.0	15.7	72.2	30.1	22.6	26.6
60 - 69 (62)	67.7	33.9	14.5	16.1	69.4	45.2	25.8	35.5
70 & Above (33)	69.7	27.3	15.2	12.1	69.7	30.3	27.3	27.3
Combined (1116)	58.6	19.0	14.8	20.8	64.9	27.3	26.6	30.6
Abnormal criteria	≥ 5.2	≥ 6.2	≥ 2.3	< 0.9	≥ 3.3	≥ 4.1	≥ 6.0	≥ 4.0

Bracketed figures refer to sample size involved in the respective age groups

Under Abnormality Status II, which considered only high risk category, the abnormality was 19.0% for TC and 27.3% for LDL-C.

There was an increased percentage of the abnormality in TC, TG, LDL-C, TC:HDL-C and LDL:HDL-C with increasing age. The percentage of abnormality in HDL-C remained the same till the age of 50 years, after which the percentage of abnormality fell. Males showed a higher percentage of abnormality than females for all the lipid components studied (Table IV).

Among the ethnic groups, Malays generally had a higher abnormality than Chinese for all the lipid

Table IV
Abnormality for serum lipid levels (mmol/l) of healthy subjects in a city clinic

Serum lipid	Abnormality Status	Cut-off value	Abnormality (%) Male	Female
TC	I	≥5.2	59.8	55.2
	II	≥6.2	19.6	17.0
TG	I	≥2.3	17.8	6.3
HDL-C	I	<0.9	26.1	5.6
LDL-C	I	≥3.3	67.2	58.5
	II	≥4.1	28.2	24.7
TC:HDL-C	I	≥6.0	32.2	10.2
LDL:HDL-C	I	≥4.0	36.4	13.7

Bracketed figures refer to sample size

Table V
Abnormality of serum lipid levels (mmol/l) for healthy subjects in a city clinic by ethnic groups

Serum lipid	Abnormality Status	Cut-off value	Abnormality (%) Chinese (819)	Malays (232)	Indians (36)	Others (29)	Combined (1116)
TC	I	≥5.2	55.4	65.5	77.8	69.0	58.5
	II	≥6.2	16.0	28.0	22.2	27.6	19.0
TG	I	≥2.3	14.3	14.7	16.7	27.6	14.8
LDL-C	I	≥3.3	61.9	71.9	83.3	72.4	64.9
	II	≥4.1	24.0	38.1	36.1	24.1	27.3
HDL-C	I	<0.9	18.4	24.8	58.3	10.3	20.8
TC:HDL-C	1	≥6.0	22.8	34.4	66.7	20.7	26.6
LDL:HDL-C	I	≥4.0	26.6	39.7	66.7	24.1	30.6

Bracketed figures refer to sample size

Table VI
Frequency of lipid abnormality according to European Atherosclerosis Society classification (1992)

Lipid abnormality	Criteria (mmol/l)	Status	Abnormality N	Abnormality %
Hypercholesterolaemia	TC ≥ 5.2	Elevated	535	47.9
	TC = 5.2–6.5	Mild	444	39.8
	TC = 6.6–7.8	Moderate	82	7.3
	TC > 7.8	Severe	9	0.8
Hypertriglyceridaemia	TG > 2.3	Elevated	47	4.2
	TC = 2.3–4.6	Mild	44	3.9
	TG > 4.6	Moderate	3	0.3
Mixed hyperlipidaemia	TC ≥ 5.2 TG ≥ 2.3	Elevated	118	10.6
	TC = 5.2–7.8 TG = 2.3–4.6	Mild	117	10.5
	TC > 7.8 TG > 4.6	Moderate	1	0.1

Total Sample = 1116

parameters. Indian and other ethnic groups had small sample sizes and may not be reliable for comparison. Nevertheless, it is interesting to note that the percent of abnormality for all the serum lipid components under Abnormality Status I were higher for Indians than compared to Chinese and Malays (Table V).

An alternative classification, which may be simpler to use in clinical practice, especially with regard to the choice of drugs in management, has been proposed by the European Atherosclerosis Society (EAS)[25] in 1992. The lipid abnormalities are classified as hypercholesterolaemia, hypertriglyceridaemia or mixed hyperlipidaemia of varying degrees of severity as shown in Table VI.

Although the sample studied was considered "healthy", there was a fairly high proportion (62.7%) of the subjects considered to have elevated serum lipids but only 1% was classified as a severe form of hyperlipidaemia (hypercholesterolaemia). Majority of the lipid abnormalities were hypercholesterolaemia (47.9%) and mixed hyperlipidaemia (10.6%).

Relationships Between Serum Lipid and Other Parameters

With few exceptions, significant correlations were observed between the serum lipid parameters of the urban Malaysian sample (n=1116) studied (Table VII). Highly positive correlations were found between TC and LDL-C (r=0.87***)and between TC and the derived ratios, namely TC:HDL-C (r=0.55***) and LDL:HDL-C (r=0.58***). There was also moderate and positive correlation between TC and TG (r=0.24***). However, HDL-C was negatively correlated to TC (r=-0.06*) and TG (r=-0.23***). Similarly, LDL-C and HDL-C were negatively correlated (r=-0.19***). LDL-C was positively and highly correlated with the two derived lipid ratios, TC:HDL-C (r=0.61***) and LDL:HDL-C (r=0.76***). HDL-C, on the other hand, was negatively and highly correlated with TC:HDL-C (r=-0.65***) and LDL: HDL-C (r= -0.60***). The two lipid ratios were highly correlated (r=0.95***).

As shown in Table VIII, BMI was negatively

Table VII
Correlation coefficients among serum lipid parameters of healthy subjects in a city clinic

	TC	TG	LDL-C	HDL-C	TC:HDL-C	LDL:HDL-C
TC		0.24***	0.87***	-0.06*	0.55***	0.58***
TG			0.04 NS	-0.23***	0.47***	0.30***
LDL-C				-0.19***	0.61***	0.76***
HDL-C					-0.65***	-0.60***
TC:HDL-C						0.95***
LDL:HDL-C						

N = 1116
NS: Not significant at P < 0.05
, *: Significant at P ≤ 0.05 and 0.001 respectively.*

Table VIII
Correlation coefficients between serum lipid components and other characters of healthy subjects in a city clinic

Character	TC	TG	HDL-C	LDL-C	TC:HDL-C	LDL:HDL-C
Body mass index	0.14***	0.23***	-0.24***	0.13***	0.32***	0.27***
Systolic blood pressure	0.12***	0.17***	-0.01 NS	0.06*	0.09**	0.07*
Diastolic blood pressure	0.16***	0.21***	-0.09**	0.12***	0.20***	0.17***
Fasting glucose	-0.02 NS	0.19***	-0.03 NS	-0.06+	0.02 NS	-0.02 NS
Uric acid	0.03 NS	0.09**	-0.08**	0.01 NS	0.09**	0.07*

N = 1116
NS: Not significant at P ≤ 0.05
*+, *, **, ***: Significant at P ≤ 0.10, 0.05, 0.01 and 0.001 respectively.*

correlated with HDL-C but positively correlated with all the other serum lipid components. A somewhat similar situation was observed in the correlations between blood pressure and serum lipid components. While their relationships were mostly positive, it is noteworthy that like BMI, diastolic blood pressure was negatively correlated to HDL-C.

Fasting blood glucose showed significant correlation with TG and to a limited degree with LDL-C (P < 0.10). There was also a positive but low correlation between uric acid and TG. However, uric acid was negatively correlated with HDL-C.

A high level of HDL-C is generally regarded as protective with regard to coronary heart disease. The negative correlations between HDL-C and the following parameters, namely BMI, diastolic blood pressure and uric acid as mentioned earlier, serve to further strengthen the value of HDL-C in the prediction of coronary heart disease risk.

Table IX
Effects of cigarette smoking and alcohol drinking on serum lipid abnormality of healthy subjects in a city clinic

Serum lipid	Habit	Non		Occ/Freq		Chi-square value (df = 1)
		N	A%	N	A%	
TG	Smoking	805	11.6	236	25.0	24.47***
	Drinking	596	12.3	445	17.5	5.73*
HDL-C	Smoking	803	18.8	234	27.8	8.85***
TC:HDL-C	Smoking	803	24.5	234	35.5	11.00***
LDL:HDL-C	Smoking	798	29.2	231	36.8	5.73*

**, *** P ≤0.05 and 0.001 respectively*
N: Sample size
A%: Per cent abnormality
Non: No smoking or drinking habit
Occ/Freq: Occasional/frequent smoking or drinking habit

Effect of Lifestyle on Serum Lipid Levels

Smoking, alcohol consumption and exercise are some known factors which could influence serum lipid levels. Their effects have been tested (indirectly) using contingency Chi-square method. The levels of certain lipid components eg. TG, HDL-C, TC:HDL-C and LDL:HDL-C were shown to be dependent on smoking habits. The effects of exercise and alcohol consumption on lipid levels were not detected in most cases. However, the TG level was shown to be influenced by alcohol consumption.

The effects of smoking and alcohol consumption in relation to lipid abnormality were indicated in Table IX. Smokers were found to have higher lipid abnormalities than non-smokers with respect to TG, HDL-C, TC:HDL-C and LDL:HDL-C. Alcohol drinkers were found to have higher abnormal TG level than non-drinkers.

Discussion

The Sample

This is the first lipid study originating from a private medical clinic and therefore unusual compared to previous published studies. The fact that the subjects were patients who visited the clinic has automatically put a bias on them. In other words, the subjects do not represent the general population but were healthy and health-conscious people who came for health screening or advice.

As the subjects were sampled in Kuala Lumpur and whose occupations ranged from professionals and executives to the small business men, this study may well be a partial reflection of an urban middle to upper middle income group in Peninsular Malaysia.

Serum Lipid Profile

The mean total cholesterol of the healthy subjects studied was estimated to be 5.4 mmol/l. This value is higher than these described by Chong *et al*[10], Lim *et al*[12], Chong and Khoo[4] who found the mean total cholesterol to be around 5.0 mmol/l (viz 5.00, 5.05 and 5.18 mmol/l) in the 1970s. Moreover, the value of mean total cholesterol was below 5.0 mmol/l in the 1960s[6,7,9]. There is thus a rising trend of the mean total cholesterol from the 1960s through 1970s to 1980s from below 5.0 mmol/l, about 5.0 mmol/l to currently 5.4 mmol/l. This is in keeping with the increase of coronary artery disease from the 1960s through the 1980s as reported by Khoo *et al*[2]. The possibilities for the rise of cholesterol could be due to a more urbanised way of life including increased income, lack of exercise and the Westernization of diet.

This high mean total cholesterol is a cause of concern as the mean total cholesterol in the United States is only 4.9 mmol/l[28]. However, compared to Singapore[29] where the mean total cholesterol in males is 6.07 mmol/l and in females, 6.33 mmol/l, the mean TC found in Malaysia is lower.

In all the local studies the Chinese had the lowest mean total cholesterol followed by the Malays and the Indians.

Except the study of Zaraihan *et al*[16], all the local studies found the total cholesterol to be higher in the males as compared to females.

The mean fasting triglycerides obtained in this study was 1.58 mmol/l in males and 1.09 mmol/l in females with a mean of 1.45 mmol/l and with no significant ethnic differences though higher value was found in the Indians (Chinese, 1.45 mmol/l; Malays, 1.42 mmol/l and Indians, 1.68 mmol/l). This is very close and in agreement with other local studies of Chong *et al*[10], Khoo[5], Teo *et al*[15] and Zaraihan *et al*[16]. The values were also similar to the Singapore reference[29].

The mean HDL-C level in this study was 1.15 mmol/l with the males having lower values than the females at 1.09 mmol/l and 1.34 mmol/l. These values are consistent with the studies of Chong *et al*[13], Teo *et al*[15] and Zaraihan *et al*[16].

Hughes *et al*[29] found the mean HDL-C level in Indians was lower compared with the Chinese and Malays. In our study, we found the same situation where the HDL-C of the Indians was also lower than the other ethnic groups, although statistical significance was not detected. Serum HDL cholesterol show marked variation among certain communities. The inverse relationship of HDL-C with ischaemic heart disease is evident within virtually all population studied.

In the population studied, the mean LDL-C was 3.61 mmol/l. The other local studies by Teo *et al*[15]; Zaraihan *et al*[16] gave a range of 3.69 to 4.17 mmol/l for LDL-C. Males generally showed higher LDL-C than females. However, Zaraihan *et al*[16] reported LDL-C was slightly higher in female contrary to the current teaching. This descrepancy may be due to the small sample size and/or age group studied by Zaraihan *et al*[16]. In the U.S.A, Rifkind and Segal[28] reported that the LDL-C of white males was 3.2 mmol/l while in females 3.1 mmol/l.

The TC:HDL-C and LDL:HDL-C, ratios measure the cardiovascular risk of a subject or a population. Both these ratios (TC:HDL-C = 4.74; LDL:HDL-C = 3.43) were found slightly higher than that of Zaraihan *et al*[16] but lower than that reported by Teo *et al*[15]. Males had higher ratio than the females in our study. The Indians had the highest TC:HDL-C ratio of 6.28 and LDL:HDL-C of 3.43 and these high ratios could explain their increased incidence of CHD compared to other ethnic groups. This observation was similar to that of Teo *et al*[16] and Zaraihan *et al*[16].

The phenomenon of higher lipid levels in males than females (except HDL-C which was the reverse) and a higher levels of serum lipids after menopause (around the 50 age group) in females than males had been noted in line with many other studies. The decline of female hormones after menopause was believed to be the main explanation for this reversal in trend in lipid levels between the two sexes.

Prevalence of Lipid Abnormality

According to the EAS classification[25], 700 cases (62.7%) had abnormally raised lipids (cholesterol and/or triglycerides). The majority (47.9%) had hypercholesterolaemia. Of these cases 0.8% had severe hypercholesterolaemia where the total cholesterol is higher than 7.8 mmol/l. This type of hypercholesterolaemia was usually of genetic origin and was associated with tendon xanthoma, arcus senilis and family history of coronary heart disease. This was well known in Malaysia and had been previously described by Khoo[5].

In an earlier study, Khoo[5] reported that 10% (118 cases) of the subjects studied had raised cholesterol and triglycerides (mixed hyperlipidaemia). Among them one had moderately raised lipids. The patient did not have palmar xanthoma or pancreatitis. There was however one case of mixed hyperlipidaemia where the patient had palmar xanthoma and pancreatitis described in

Malaysia[5]. In the present study the rare condition of remnant hyperlipidaemia was however not seen.

Elevated triglycerides were not common in this study. 4.2% (47 cases) had raised triglycerides. Of these, only 3 cases had moderately raised triglycerides of above 4.6 mmol/l. None of these was due to secondary causes such as alcohol, uncontrolled diabetes or diuretics. Primary severe hypertriglyceridaemia was a relatively uncommon condition. A rare case had been described in Malaysia by Chong and Alhardy[30] with severe hypertriglyceridaemia and pancreatitis.

The incidence of lipid abnormalities based on EAS and NCEP classifications for the present sample studied was fairly high. In a study of 1025 healthy subjects from urban population in the 1970s only 9% was reported to have hypercholesterolaemia, 13% hypertriglyceridaemia and 1% mixed hyperlipidaemia[4,31].

This dramatic increase of the serum lipid abnormalities had certainly called for immediate attention to educate the public and execute measures to lower the serum lipid levels of the present population to avoid premature death due to coronary heart disease.

Relationships between Serum Lipids and other CHD Risk Factors

In the interrelationship studies among serum lipid parameters, a strong positive association between TC and LDL-C, and a moderate negative association between TG and HDL-C were established. TC and LDL-C are surrogates which explain a high positive association and this had also been reported elsewhere[10]. An inverse relationship of moderate degree between HDL-C and fasting TG had been observed in Singapore[32] and in many other studies: Framingham[33], the Lipid Research Clinics Programme[34] and the British Regional Heart Study[35].

Other serum lipid components which showed relationships included TC and TG (positive) and LDL-C and HDL-C (negative) with moderate degree (r=-0.2) while TC and HDL-C had very low negative association (r=-0.06). No association between TG and LDL-C was found in this study in contrast to a local study of Chong *et al*[10].

It has been generally known that aside from age, sex and ethnic groups there were other factors such as obesity, hypertension, blood glucose, uric acid, alcohol consumption, physical exercise and smoking that also affect serum lipid concentrations. Results of the present study have provided additional information on this subject in local conditions.

Our study showed a positive correlation of BMI with TC, TG and LDL-C while a negative correlation was obtained for BMI and HDL-C. Our current knowledge suggests that obesity commonly precedes the development of hypertension, dyslipidaemia and glucose intolerance. Several studies had shown strong positive correlations between the degree of adiposity and fasting TG, even after correcting for age and other variables. In the Lipid Research Clinics Prevalence Study[36], there was a strong independent correlation of TG levels and BMI in both men and women. On a lesser degree, TC was also positively correlated with BMI while HDL-C was inversely correlated with BMI. Strong positive correlations were observed between blood pressure and lipid components of TC for TG; and in a lower degree with LDL-C. It was well known that abnormal lipid levels occurred commonly among hypertensive patients. Family studies showed that approximately 12% of patients with essential hypertension had abnormal lipid levels[37]. Dawber *et al*[38] from Framingham had described the association between hypertension and hypercholesterolaemia. Stamler *et al*[39], on the other hand, reported TC was not significantly related to blood pressure with the exception of a significant correlation with diastolic pressure for 30-40 age group in white and black females in Chicago community, U.S.A. The Tromso study[40] reported a positive relationship between LDL-C and blood pressure but not in Tecumseh study[41], or the Singapore study[32].

There was a positive correlation between glucose and TG levels and a negative correlation between glucose and HDL-C level. The spectrum of lipid abnormalities seen in NIDDM and their mechanism had been reviewed by Reaven[42]. The most frequent abnormalities were hypertriglyceridaemia and reduced HDL-C, as occurred in obesity. An increase of plasma immuno-reactive insulin was common in both situations reflecting insulin resistance and was probably responsible for the cause of hypertriglyceridaemia[43].

However, the link between high glucose and low HDL-C was less clear because, unlike the link between hyperglycaemia and hypertriglyceridaemia, it sometimes fails to correct under insulin therapy.

Hypertriglyceridaemia, glucose intolerance, hyperinsulinaemia and vascular diseases all commonly accompany obesity. This had been described under various names – Reavan's syndrome, syndrome X, the deadly quartet, the deadly quintet.

A weak correlation between certain lipid components and uric acid, a reflection of gout condition, has been detected. It was well known that hypertriglyceridaemia was a common accompaniment of gout. Bluestone *et al*[44] described eight out of 33 gout patients with normal renal function had a fasting triglyceride of above 2 mmol/l, two of whom had values of above 1.4 mmol/l. One of these had a type V phenotype of hyperlipidaemia. The rest were of type IV hyperlipidaemia. There appeared to be no direct link between hyperuricaemia and hypertriglyceridaemia, in that the treatment with allopurinol had no effect on triglyceride levels, and the relationship might simply reflect the fact that obesity, alcohol and thiazides were common causes of both abnormalities. However, patients with primary type IV hyperlipoproteinaemia often had raised uric acid levels and it had been reported that fenofibrate[45] reduced both TG and uric acid levels in such individuals. In contrast, nicotinic acid compounds reduced TG but aggravated hyperuricaemia[46].

Smoking was positively correlated to TG and HDL-C in the study. In the Framingham Offspring Study[47] smokers had HDL-C levels which were significantly lower than non-smokers or ex-smokers of more than one year duration. Studies of the mechanism involved suggested that smoking impairs lipolysis and prevents the increase in HDL_2 normally seen in non-smokers after a fatty meal. The explanation was supported by the independent correlation observed between smoking and plasma TG.

Much had been written about the effect of exercise on serum lipids and lipoproteins. Aerobic exercise, such as jogging, cross country or skiing, when performed with sufficient intensity and frequency, resulted in appreciable reduction in fasting TG, TC and LDL-C and marked increase in HDL-C. Such differences were even more evident in marathon runners than joggers. The extent of these changes correlated with the degree of fitness observed as gauged by maximal oxygen consumption, and was independent of other influences such as body weight and cigarette consumption. However, dietary factors including alcohol consumption may play a role in determining the extent of rise in HDL-C in runners. The amount of exercise required to influence lipoprotein levels is considerable, equivalent to running 10 miles/week for 6-12 months[48].

In this study, correlation between exercise and serum lipids was not detected. The exercise taken by the subjects studied included – playing golf several times a week or badminton 3 times a week, daily walk for half an hour, 'qi-gong' exercise, etc. Perhaps, the extent of the exercise which was considered frequent was not able to achieve the desirable effect as described.

Our study showed a positive correlation between alcohol consumption and TG. There was no correlation with HDL-C. Other studies showed regular consumption of alcohol leads to appreciable increase in HDL-C, an effect independent of all other variables. In the Cooperative Lipoprotein Phenotyping Study, people drinking two units per day had HDL-C levels which were 0.33 mmol/l higher than non-drinkers. There was also an association between alcohol consumption and serum TG levels, although the correlation was much weaker than for HDL-C.

The effect of alcohol consumption on HDL-C level was not demonstrated in this study and this may be due to an insufficient amount and frequency of appropriate type of alcohol consumption for the locals. It may also be related to the genetic make-up of the local population which may not have this favourable response on alcohol intake in relation to HDL-C as found in the Caucasians.

Conclusion

Among the 1116 healthy subjects in a city clinic studied, the total serum cholesterol was estimated to be 5.4 mmol/l. This has risen gradually from below

5.0 mmol/l in the 1960s to 5.0 mmol/l in the 1970s and 5.4 mmol/l in the 1980s. Although no significant difference was shown between the major ethnic groups, the Indians appeared to have a higher TC value than the Malays followed by the Chinese. The Indians also had a higher TG mean value than the Chinese and the Malays. Similarly, the Indians had shown to have a significantly higher mean LDL-C than the other two groups. On the contrary, the Indians had the lowest mean for HDL-C followed by the Malays and the Chinese.

Based on the classification of the National Cholesterol Programme, 58.6% of the subjects studied had TC values equal or higher than 5.2 mmol/l and they would require treatment by way of dietary advice plus lipid lowering medication if the levels were very high. 19.0% of the subjects studied had a mean TC greater than 6.2 mmol/l. 27.3% of the subjects had high LDL-C of more than 4.1 mmol/l; 26.6% had high TC:HDL-C ratio of more than 6.0 and 30.6% had high LDL:HDL-C of more than 4.0. On the other hand, 20.8% of the subjects studied had low HDL-C values of less than 0.9 mmol/l. In addition, there were 14.8% of the subjects with TG level above 2.3 mmol/l.

Male subjects generally showed higher mean lipid values (except HDL-C which showed a reverse trend) than female subjects. A somewhat reverse in trend between the sex groups with reference to mean lipid values was noted in age group 50 - 59 and older. This condition was mainly attributed to the lowering of the lipid protective factors (female hormones) during menopause in females.

According to the European Atherosclerosis Society standard, 47.9% (n=535) of the "healthy" urban Malaysians would have been classified as having hypercholesterolaemia; 4.2% (n=47) had hypertriglyceridaemia and 10.6% (n=118) with mixed hyperlipidaemia.

Correlations among certain lipid parameters and their relationship with certain coronary risk factors such as BMI, blood pressure, fasting blood glucose, smoking and alcohol consumption were demonstrated. The findings are in general agreement with other studies.

The relatively high percentage of lipid abnormality found in the present study should prompt the attention of the Malaysian public and the government regarding its seriousness. Urgent and intensive preventive measures should therefore be taken to educate the public to have healthy diets, good habits and lifestyles so that premature coronary death could be reduced or avoided.

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