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Screening for Hypercholesterolaemia in Patients with Other Risk Factors for Coronary Heart Disease

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ABSTRACT

Objective: To determine the prevalence of hypercholesterolaemia in individuals with other major risk factors of coronary heart disease and markers of hypercholesterolaemia.

Methods: A community-based cross-sectional study on a random sample of 261 persons aged between 35 and 69 years residing in the flatted housing estate of West Coast, Singapore, was conducted in 1997. A questionnaire, together with a medical examination and investigation involving the use of Reflotron machine, were used to collect the information required.

Results: 43.2% of the population had at least 1 major risk factor, with 18.1% being smokers, 18.1% with hypertension, 6.5% with diabetes mellitus, 5.1% being obese, and 5.0% with a family history of coronary heart disease. Higher percentages of individuals with hypercholesterolaemia were found when each risk factor was present. 9.5% had 2 or more risk factors, of which, 21.1% had high cholesterol levels. A high prevalence of hypercholesterolaemia that was statistically significant was found amongst subjects with corneal arcus below the age of 60.

Conclusions: The risk factors of coronary heart disease remain prevalent in our population. We recommend screening for serum cholesterol only in those with at least 2 major risk factors of coronary heart disease in the general population between 35 and 69 years of age.

Keywords: smoking, hypertension, diabetes mellitus, obesity, corneal arcus

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INTRODUCTION

The Singapore National Health Survey of 1992 found that 53% of the study population had a serum total cholesterol level of ≥ 5.2 mmol/L and 19% had a level of ≥ 6.2 mmol/L[1]. The mean total serum cholesterol level was 5.3 mmol/L. Richter in the Bavarian Screening Project showed that in the Bavarian study population, 37.3% of women and 38.1% of men had total cholesterol levels between 201 – 250 mg/dL(5.2 – 6.4 mmol/L)[2]. In addition, 42.2% of women and 33.7% of men had values > 250 mg/dL. The mean value for men was 231 ± 53 mg/dL and for women, 243 ± 52 mg/dL .

Hypercholesterolemia is defined as a high level of total cholesterol in the blood. Serum total cholesterol consists of 60% – 70% low density lipoprotein (LDL), 20% – 30% high density lipoprotein (HDL) and 10% – 15% very-low density lipoprotein (VLDL). Epidemiological studies show that there is a direct relationship between the level of serum total cholesterol and low density lipoprotein with the rate of coronary heart disease[3]. The relationship is continuous and the risk of coronary heart disease increases steadily when total cholesterol is above 6.2 mmol/L[3,4].

The known risk factors for coronary heart disease are[3,5]:

1. Age and gender: men ≥ 45 years old and women ≥ 55 years old or premature menopause without oestrogen replacement therapy.
2. Family history of premature coronary heart disease: definite myocardial infarction or sudden death before 55 years old in father or other primary male relative, or before 65 years old in mother or other primary female relative.
3. Hypertension: blood pressure ≥ 140/90 mmHg or taking anti-hypertensive medication.
4. Diabetes mellitus.
5. Current cigarette smoking: especially more than 10 sticks per day.
6. High low density lipoprotein levels (> 4.1 mmol/L or 160 mg/dL).
7. Low high density lipoprotein levels (< 0.9 mmol/L or 35 mg/dL).
8. Obesity (body mass index ≥ 30).

Each risk factor doubles the risk for coronary heart disease. Therefore a person with 4 risk factors is at 16-fold[2,4] increased risk of developing coronary heart disease compared to a person who has the same total cholesterol level without any risk factors.

There are 2 known markers of hypercholesterolemia. Hughes et al found that corneal arcus was associated with high serum levels of low density lipoprotein levels in people aged 30 – 49 years old but not in those aged 50 – 69[6]. Ribera et al showed that subjects with xanthelasma palpebrarum had higher cholesterol and low density lipoprotein levels than controls[7]. They also had a higher prevalence of personal and familial history of cardiovascular disease and were more overweight than controls.

This study sought to determine the prevalence of hypercholesterolemia in individuals with other risk factors of coronary heart disease and with markers of hypercholesterolemia.

MATERIALS AND METHODS

Study and site of population

The study area was West Coast, Singapore. Fifteen blocks of Housing Development Board flats in the area were chosen to be our study population as it was typical of the Singaporean population and was reflective of most Singaporean living conditions. One stage cluster, disproportionate, stratified sampling was used to randomly draw 230 households, targeting 300 individuals.

The eligible subjects in these households were individuals aged 35 – 69, residing in West Coast during the study period of 11 to 13 January 1997. Various studies have shown that testing total serum cholesterol in people less than 35 years old and more than 70 years old was not useful[3,5,8,9].The household response rate was 72.1% while the individual complete response rate was 73.7% (196 subjects) and individual partial response rate was 24.4% (65 subjects). Complete responders were individuals who completed the whole study (both questionnaire and medical examination), while partial responders completed only the questionnaire. Five subjects (1.9%) either did not respond or could not be contacted.

Questionnaire

All respondents were interviewed by teams of trained medical students who used a structured questionnaire (with English, Chinese and Malay translations) that had been field tested in a pilot study. The interview was conducted at the respondent's house with informed consent.

The questionnaire was divided into 3 parts: (1) part A covered the respondent's age, sex and housing type; (2) part B covered known cases of hypercholesterolemia, purpose for previous cholesterol testing and treatment prescribed, and (3) part C examined the presence of 4 major risk factors for coronary heart disease, namely smoking, diabetes mellitus, hypertension and family history of coronary heart disease. Respondents were asked if they smoked, the number of cigarettes they smoked each day and the number of years they had been smoking. Respondents were judged to be diabetic or hypertensive if they were taking the respective medications, as they were more likely to be at an increased risk for coronary heart disease.

Medical examination

All respondents were examined by teams of trained medical students using a structured examination format. Respondents were examined for corneal arcus and xanthelesma and their weight and height measured. Their body mass index (BMI) was calculated using the formula, BMI = Weight (kg) ÷ [Height (m)]$^{(2)}$ and used as an indication of their weight status. Respondents with a BMI $\geq$ 30 were classified as obese and BMI $\geq$ 25 but $<$ 30 were over-weight. Those with BMI $\geq$ 20 but $<$ 25 were of healthy weight and BMI $<$ 20 were classified as underweight.

Respondents also had a random test of their serum total cholesterol using the Reflotron machine. Thirty-two microlitres of the respondent's blood was drawn from a finger-pulp pin-prick and applied onto a special test strip. The colour change on the test strip was read using reflectance photometry in the Reflotron machine and the readout recorded. This dry chemistry method has been found to have good correlation with standard accepted wet chemistry methods in other clinical studies[10,11].

Respondents were divided into 3 groups based on their total serum cholesterol measurements. The definition used followed that in the Singapore National Health Survey of 1992, which in turn used that of the American National Heart, Lung and Blood Institute[1].

Normal (desirable) cholesterol level	$<$ 5.2 mmol/L (200 mg/dL)
Borderline-high cholesterol level	$\geq$ 5.2 mmol/L, but $<$ 6.2 mmol/L (240 mg/dL)
High cholesterol level	$\geq$ 6.2 mmol/L

These will hereafter be known as normal, borderline and high cholesterol levels respectively.

Data analysis

Statistical analysis was performed using Statistical Package for Social Sciences for Windows and Epistat computer programs and it involved descriptive summary measures of central tendency, frequency and associations, with tests of statistical significance where appropriate. Confounding of the association between variables was assessed by stratified analysis.

RESULTS

The distribution by sex, age, ethnic groups and housing types in the study population was similar to the latest demographic data of the general population of Singapore in 1995 (Table I).

Risk factors of coronary heart disease

The individuals in the study population was divided according to the number of major risk factors of coronary heart disease (ie. obesity, diabetes mellitus, hypertension, smoking, family history of coronary heart disease) they had based on the questionnaire result (Table II).

43.2% of the population (86 individuals) had at least 1 major risk factor of coronary heart disease (other than hypercholesterolaemia).

9.5% of the population (19 individuals) had 2 or more risk factors of coronary heart disease. Amongst them, 4 (21.1%) individuals had high cholesterol levels.

There was an increasing trend in the mean cholesterol level in each group, as the number of risk factor increased up to 3. (Note: there was only 1 subject with 4 risk factors). However on further analysis using Duncan test, this was found to be not statistically significant (p = 0.345).

The prevalence of individual risk factors of coronary heart disease in the study population were as followed: 36 (18.1%) smokers, 36 (18.1%) with

Table I – Demography of study subjects comparing with that of the Singapore population[12]

Variable	Study (%) (n = 261)	Singapore population (%)
Sex		
Male	46.8	50.3
Female	53.2	49.7
Ethnic group		
Chinese	77.0	77.4
Malay	18.4	14.2
Indian	3.4	7.2
Others	1.1	1.2
Age group (years)		
35 – 39	19.5	26.0
40 – 44	16.5	22.2
45 – 49	22.2	17.5
50 – 54	16.1	10.7
55 – 59	11.9	9.6
60 – 64	6.5	7.8
65 – 69	7.3	6.1
Housing type		
1 and 2-room	15.0	11.6
3-room	40.4	41.6
4-room	32.5	32.1
5-room	12.1	14.6

Table II – Number of risk factors in the sample population (n = 199)

No. of risk factors	No. of individuals	Percentage	Mean cholesterol level (mmol/L)
0	113	56.8	5.26
1	67	33.7	5.42
2	16	8.0	5.52
3	2	1.0	5.98
4	1	0.5	4.42
5	0	0	-

Note: Individuals who were taking lipid-lowering drugs were automatically placed in the category of high cholesterol (≥ 6.2 mmol/L) regardless of their blood results.

Table III – Prevalence of risk factors of coronary heart disease

	No. of individuals with risk factor		Percentage with risk factor present
	Present	Absent	
Smoking	36	163	18.1
Hypertension	36	163	18.1
Diabetes mellitus	13	186	6.5
Obesity	10	185	5.1
Family history	10	189	5.0

Note: Obesity was obtained from calculation of BMI, and only 195 subjects participated in the measurement of height and weight from which BMI is calculated.

hypertension, 13 (6.5%) with diabetes mellitus, 10 (5.1%) obese persons, and 10 (5.0%) with a family history of coronary heart disease (Table III).

Comparing the percentage of individuals with hypercholesterolaemia (borderline and high) between those with and without each risk factor, consistently higher percentages of individuals with hypercholesterolaemia were found in the group with risk factor present. The difference was most obvious in the obese group, with a difference of 27% more individuals with hypercholesterolaemia compared to non-obese group. However analysis using Fisher's exact probability test showed no statistically significant difference between each of the groups (Table IV).

Markers of hypercholesterolaemia

Forty-four (22.4%) subjects were found to have arcus senilis. Recognising age as a potential confounder for the causation of arcus senilis, the sample population was stratified to the age groups above and below 60 years old in the analysis of the association between arcus senilis and hypercholesterolaemia (Table V).

For the group below 60 years of age, there was a statistically significant difference (p = 0.0133) in the prevalence of hypercholesterolaemia between subjects with and without arcus senilis using Fisher's exact probability test.

For the group above 60 years of age, no statistical significant difference (p = 0.66) was found in the prevalence of hypercholesterolaemia between subjects with and without arcus senilis.

Only 9 persons with xanthelasma were identified in our sample population. This was felt to be too small a number to commence analysis.

DISCUSSION

Coronary heart disease is the second leading cause of mortality in Singapore[12] and thus the study of hypercholesterolaemia and other risk factors for coronary heart disease is important and timely. The levels used to define hypercholesterolaemia in our study were based on those in the National Health Survey of 1992, thus allowing us to compare our findings[1].

In our own study, the complete individual response rate of 73.7% was good. The similar demographic characteristics of our study sample to the general population reflect this.

Our study was based on a standardised questionnaire and physical examination for height, weight, corneal arcus, xanthelasma, as well as measurement of total serum cholesterol by the Reflotron machine. Although elevated LDL is the risk factor of coronary heart disease, we have measured serum total cholesterol, as it is a good estimate of serum LDL[3,4].

We have determined people on medication for hypertension and diabetes mellitus to have disease of sufficient severity to pose a significant risk factor for coronary heart disease. Thus only hypertensives and diabetics on medication were considered in these categories when analysing data.

We found that 43.2% of our study sample had at least 1 major risk factor of coronary heart disease (not considering hypercholesterolaemia). More importantly, 60.9% of subjects who had at least 1 other risk factor of coronary heart disease also had hypercholesterolaemia. Richter et al in the Bavarian Screening Project, which carried out screening on 150,089 subjects, found that 70% of subjects with cholesterol levels between 5.2 mmol/L and 6.5 mmol/L had at least 1 additional risk factor of coronary heart disease[2].

Only 9.5% of our study sample had at least 2 risk factors, a markedly lower percentage compared to the 43.2% having at least 1 risk factor. Only 21.1% of subjects with 2 or more risk factors had serum total cholesterol levels ≥ 6.2 mmol/L .

Table IV – Hypercholesterolaemia amongst subjects with and without risk factors of coronary heart disease

	Risk factor present		Risk factor absent	
	Number of individuals with Chol ≥5.2 mmol/L	Percentage	Number of individuals with Chol ≥5.2 mmol/L	Percentage
Smoking	23	63.9	87	53.4
Hypertension	21	58.3	89	54.6
Diabetes mellitus	9	69.2	100	53.8
Obesity	8	80.0	98	53.0
Family history	6	60.0	103	54.5

Footnote: Chol - serum cholesterol level

Table V – Arcus senilis in different age group and hypercholesterolaemia

	Number of individuals with age < 60 years		Number of individuals with age ≥ 60 years	
	Chol ≥ 5.2	Chol < 5.2	Chol ≥ 5.2	Chol < 5.2
Arcus senilis	18	7	15	4
No arcus senilis	67	79	5	1

Footnote: Chol - serum cholesterol level

We feel that there are implications here in deciding who should be screened for hypercholesterolaemia if we were to extrapolate the results to the general population. If cholesterol screening was to be done for people with at least two risk factors of coronary heart disease, then only 9.5% of the population would be involved. Of these, usually only those with cholesterol levels ≥ 6.2 mmol/L (21.1% of those screened) would be started on lipid-lowering drugs[5], ie. about 2% of the general population between 35 and 69 years of age.

This is a far more economical approach to screening than simply advocating it for everybody regardless of their individual risk of coronary heart disease. It will be a lighter financial burden to be borne by the community as only a small proportion of the population is screened and treated with medication.

This is in line with the Ministry of Health's efforts to control rising healthcare costs. The Ministry of Health has issued a circular warning against the indiscriminate use of screening tests without proven benefit, mentioning in particular, cholesterol screening[13]. It is also reasonable to consider screening only when more than one risk factor is present as a person with two known risk factors of coronary heart disease is at twice the risk of related mortality or morbidity compared to a person with only one risk factor[3,5].

The prevalence of the various risk factors of coronary heart disease in our study was similar to that of the National Health Survey, Singapore 1992, except for diabetes mellitus[1]. The prevalence of obesity in our study was 5.13% compared to 5% in the National Health Survey, Singapore 1992. The prevalence of smoking was 18.1% compared to 18%, and the prevalence of hypertension was 18.1% as compared to 13.6% in 1992. The prevalence of diabetes mellitus was 6.53% (age 35 – 69 years) compared to 11.9% (age 30 – 69 years). The difference in prevalence can be explained by the different criteria defining a person as having diabetes mellitus in the 2 studies. In our study, the current use of anti-diabetic agents was the defining criteria whereas an oral glucose tolerance test was used to detect diabetes mellitus in the National Health Survey in 1992.

Although there were no statistically significant associations (at $p < 0.05$) there were varying strengths of association between hypercholesterolaemia and the studied risk factors of coronary heart disease. Obesity was the most strongly associated risk factor. This would be reasonable as a diet high in fat would lead to obesity as well as hypercholesterolaemia (especially if the diet is high in saturated fat). Smoking had the next strongest association. The other risk factors with less association were hypertension, diabetes mellitus and a family history of coronary heart disease, in that order.

Corneal arcus was found to be significantly associated ($p < 0.05$) with hypercholesterolaemia in subjects below 60 years of age but not in subjects above 60 years. Thus, corneal arcus may be used as a marker to help determine whether patients less than 60 years old should be sent for cholesterol screening. This association was significant in both genders in our study sample.

There were too few subjects with xanthelasma to comment on its relationship with hypercholesterolaemia.

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REFERENCES

1. Research & Evaluation Department, Ministry of Health, Singapore. National Health Survey 1992, Highlights of main survey findings.
2. Richter WO, Sonnichsen AC, Schwandt P. Results and efficacy of public screening for hypercholesterolemia: the Bavarian cholesterol screening project. J Clin Epidemiol 1995; 48:1307-17.
3. Browner WS. Lipid abnormalities. In: Tierney LM, McPhee SJ, Papadakis MA, eds. Current Medical Diagnosis and Treatment 1997. Appleton and Lange, 1997:1110-21.
4. Garber AM, Browner WS, Hulley SB. Cholesterol screening in asymptomatic adults, revisited. Ann Internal Med 1996; 124:518-30.
5. NCEP Adult Treatment Panel II. Summary of the second report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation and treatment of high blood cholesterol in adults (adult treatment panel II). JAMA 1993; 269:3015-23.
6. Hughes K, Lun KC, Sothy SP, Thai AC, Leong WP, Yeo PB. Corneal arcus and cardiovascular risk factors in Asians in Singapore. Int J Epidemiol 1992; 21:473-7.
7. Ribera M, Pinto X Argimon JM, Fiol C, Pujjol R, Ferrandiz C. Lipid metabolism and apolipoprotein E phenotypes in patients with xanthelasma. Am J Med 1995; 99:485-90.
8. Hulley SB, Newman TB, Grady D, Garber AM, Baron RB, Browner WS. Should we be measuring blood cholesterol in young adults? JAMA 1993; 269:1416-9.
9. Krumholtz HM, Seeman TE, Merrill SS, Mendes de Leon CF, Vaccarino V, Silveramn DI, et al. Lack of association between cholesterol and coronary heart disease mortality and morbidity and all-cause mortality in persons older than 70 years. JAMA 1994; 272:1335-40.
10. Lapienleimu H, Viikari J, Jokinen E, Routi T, Salo P, Hollo O, et al. Cholesterol measurement by reflotron dry chemistry in infants, children and adults. Scand J Clin Inv 1994; 54:61-5.
11. Majeed FA, Turner HJ, Stuart JM, Cooper RD, Laite PA, et al. Audit of near patient testing in occupational health clinics. Occ Med-Oxf 1993; 43:23-6.
12. Chief Statistician. Yearbook of Statistics Singapore 1995. Singapore Department of Statistics, 1995.
13. Ministry of Health Singapore. Health screening. Professional Circular no. 11/94, 20 Oct 1994.