Prevalence of New Coronary Risk Factors in Thai Population

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Abstract

Many new cardiovascular biomarkers of atherosclerosis have recently been emerging. However, there is a paucity of these data in the Thai population. This study aims to determine the prevalence of these biomarkers of atherosclerosis and the relationship between these new risk factors and other conventional risk factors for atherosclerosis in the healthy Thai population. As a yearly check-up program, we surveyed 3,615 normal healthy populations for their conventional risk factors and some new cardiovascular biomarkers for atherosclerosis. The authors found hyperhomocysteinemia and high level of Lp(a) in 27 per cent and 32 per cent of the cases respectively. Prevalence of recent and past chlamydial infection was found in 30 per cent and 51 per cent respectively.

Key word : Biomarker, Atherosclerosis, Hyperhomocysteinemia, Chlamydial Infection, Lipoprotein (a)

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Although many risk factors for atherosclerosis are known (e.g., hyperlipidemia, hypertension, smoking, and diabetes), much of attributable risk remains unexplained. Recently, many possible new risk factors for atherosclerosis have emerged. Researchers have paid considerable attention to the possible role of these new risk factors such as chlamydial infection[1-4], hyperhomocysteinemia [5-12] and high Lp(a) in heart disease causation. However, the prevalence of these risk factors in the Thai population is not known and possible relationship with other conventional risk factors for athero-

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sclerosis have not yet been defined. The objective of this study is to determine the prevalence of chlamydial infection, hyperhomocysteinemia, and high Lp(a) in the healthy Thai population. Also, the association between these new risk factors and other conventional risk factors for atherosclerosis has been evaluated.

MATERIAL AND METHOD

Study population:

During January 1999 to February 1999, in a study approved by the ethical committee of Siriraj Hospital, we studied 3,615 employees from Shinawatra Corporation, a telecommunication business company, as a yearly check-up program. All the participants were informed about the study and given a confidential questionnaire a week before being examined by the cardiologists. They were asked to complete the questionnaire themselves at home. All the information; including demographic data, medical history, physical activity, etc., was obtained from the completed questionnaires and interviews conducted by cardiologists. The weight and height were recorded by the same balanced scale. Blood pressures were measured twice with a mercury sphygmomanometer after resting for at least 5 minutes and to the nearest of 2 mmHg. The average of the two measurements was used for statistical analysis.

Laboratory Procedures:

On the same morning of physical examination of the employees, and after fasting at least 12 hours, blood samples were taken using a standardized method. All samples were immediately placed on ice, protected from light, centrifuged at 4°C within 1 hour and stored at –70°C. Measurement was performed by using an automated method (Hitachi 717 and Hitachi 917 automation system). The quality assessment program and quality control service from Roche Diagnostics; Switzerland, were used for external and internal control of our laboratories. The coefficient of variation in all assays was lower than 5 per cent.

Hyperhomocysteinemia was defined as fasting plasma homocysteine level more than 11 μmol/L in this study. A level of Lp(a) above 30 mg/dl is generally considered elevated[13]. Prevalence of chlamydial infection was presented as IgA and IgG, which represented recent and late infection respectively.

Statistical analysis:

Data are expressed as count and percentage or mean ± SD as appropriate. Associations among categorical factors were assessed by using chi-square test. The difference between groups of quantitative variables was determined by using the unpaired *t*-test. Binary logistic regression was applied for the multivariate analysis. A p-value less than 0.05 was considered as statistically significant.

RESULTS

Table 1 shows the demographic data of the study group that included 731 Shinawatra emplo-

Table 1. Baseline demographic and biochemical data (N=731).

	Mean ± SD	Range
Age (yrs)	30.7 ± 5.5	21-61
Sex (Male)	44.6%	
BMI (kg/m^2)	21.7 ± 3.1	15.5 - 36.1
Creatinine (mg/dL)	1.1 ± 0.2	0.7 - 1.8
Hematocrit (%)	43.5 ± 5.6	16.5 - 60.9
FBS (mg/dL)	89.3 ± 9.8	54 - 168
Total Cholesterol (mg/dL)	207 ± 37	98 - 335
Triglyceride (mg/dL)	92 ± 59	29 - 412
HDL-C (mg/dL)	64 ± 16	13 - 127
LDL-C (mg/dL)	125 ± 34	33 - 247
Hypertension (%)	58 (7.9%)	
Smoking (%)	130 (18.4%)	
* Lipoprotein (a) (mg/dL)	29.6 ± 26.2	1 - 174.8
** Homocysteine (mmol/l)	9.8 ± 4.2	1.1 - 50.0
*** Chlamydial infection - IgG	50.6%	
- IgA	29.4%	

* N = 534, ** N = 501, *** N = 718

Table 2. Level of Lipoprotein (a) and homocysteine at various percentile ranks.

Percentile	Lipoprotein (a) (N = 534)	Homocysteine (N = 501)
50	20.8	9.2
60	25.9	9.8
70	31.2	10.7
75	39.0	11.1
80	46.0	11.8
85	53.8	12.5
90	65.4	13.5
95	84.2	15.1

yees. The mean age was 31 years and 44 per cent were male. Mean body mass index (BMI) was 22 kg/m^2. Surprisingly, current smokers and hypertension were found in only 18 per cent and 8 per cent respectively. Table 2 shows the level of homocysteine and Lp(a) at various percentile ranks.

Homocysteine Indices:

Table 2 shows the homocysteine level at varied percentile ranks. The mean fasting homocysteine level was 9.8 mmol/L. Twenty-seven per cent of the group had a homocysteine level greater than 11 mmol/L and 5 per cent of the subjects had a homocysteine level greater than 15 mmol/L. Association between homocysteine and other variables are shown in Table 4.

Lp(a) Indices:

The mean Lp(a) was 29.6 mg/dl and the median Lp(a) level was 20.8 mg/dL. As shown in

Table 3. Relationship between chlamydial infection and other factors.

Factors	IgG			IgA		
	+ve (n=363)	-ve (n = 355)	p-value	+ve (n = 211)	-ve (n = 507)	p-value
Age (yr)	30.7 ± 5.3	30.7 ± 5.6	0.87	29.9 ± 5.0	31.0 ± 5.6	0.009
Sex - male	57.3%		0.001	32.7%		0.08
- female	45.1%			26.7%		
Weight (kg)	58.5 ± 11.1	56.4 ± 11.2	0.017	58.8 ± 11.4	56.9 ± 11.1	0.038
Height (cm)	163.0 ± 8.0	161.5 ± 8.2	0.01	163.5 ± 7.8	161.8 ± 8.3	0.010
Waist (cm)	71.5 ± 10.6	69.9 ± 10.6	0.038	71.2 ± 10.2	70.5 ± 10.9	0.485
BMI (kg/m^2)	21.88 ± 3.17	21.51 ± 3.13	0.31	21.88 ± 3.27	21.62 ± 3.10	0.31
Total cholesterol (mg/dL)	209.1 ± 39.4	205.8 ± 33.6	0.226	209.2 ± 35.7	206.8 ± 37.1	0.433
HDL-C (mg/dL)	62.6 ± 14.8	65.0 ± 16.4	0.041	63.1 ± 15.4	64.1 ± 15.8	0.430
LDL-C (mg/dL)	127.3 ± 35.3	123.2 ± 31.3	0.102	127.1 ± 31.7	124.5 ± 34.1	0.336
Triglyceride (mg/dL)	95.1 ± 59.8	88.3 ± 58.4	0.125	92.4 ± 54.8	91.4 ± 61.0	0.832
FBS (mg/dL)	88.7 ± 9.2	89.8 ± 10.4	0.133	87.8 ± 8.9	89.9 ± 10.1	0.008
Creatinine (mg/dL)	1.15 ± 0.21	1.11 ± 0.22	0.026	1.15 ± 0.21	1.12 ± 0.22	0.077
Hypertension (%)	33 (9.1%)	24 (6.8%)	0.253	20 (9.5%)	37 (7.3%)	0.33
Smoking (%)	80 (22.7%)	49 (14.3%)	0.004	40 (19.9%)	89 (18.0%)	0.562

Table 4. Associations between fasting plasma homocysteine level and other risk factors

	Homocysteine level (μmol/L)		p-value
	≤ 11.0	> 11.0	
N	365	136	
Age (yr)	31.5 ± 5.6	30.5 ± 5.1	0.053
Sex - male	34.2%	75.7%	<0.001
- female	65.8%	24.3%	
Weight (kg)	57.1 ± 11.5	60.8 ± 10.4	0.001
Height (cm)	161.2 ± 8.1	165.7 ± 7.4	<0.001
Waist (cm)	70.7 ± 10.7	75.0 ± 9.9	<0.001
BMI (kg/m^2)	21.85 ± 3.24	22.06 ± 2.86	0.502
Total cholesterol (mg/dL)	207.0 ± 35.1	215.3 ± 42.8	0.045
HDL-C (mg/dL)	64.6 ± 15.5	60.1 ± 14.6	0.003
LDL-C (mg/dL)	123.3 ± 32.5	133.8 ± 36.5	0.002
Triglycerides (mg/dL)	95.9 ± 63.6	103.9 ± 62.7	0.209
FBS (mg/dL)	89.4 ± 9.7	90.9 ± 9.6	0.116
Creatinine (mg/dL)	1.02 ± 0.15	1.16 ± 0.14	<0.001
Hct (%)	42.9 ± 6.5	45.3 ± 7.4	<0.001
Hypertension	5.5%	12.6%	0.007
Smoking	17.4%	25.4%	0.048

Table 5. Associations between Lp(a) and other risk factors.

	Lp(a) (mg/dL)		OR	p-value
	≤ 30	> 30		
N	362	172		
Age (yr)	31.5 ± 5.4	30.8 ± 5.5		0.20
Sex - male	47.5%	37.2%	0.66	0.03
- female	52.5%	62.8%		
Income (Baht) > 20,000	63.2%	59.8%	0.9	0.45
Smoking	18.1%	19.6%	1.1	0.68
Stress	30.9%	33.9%	1.1	0.49
Regular exercise	28.4%	33.3%	1.3	0.52
Education (Graduate)	73.1%	74.7%	1.1	0.70
Hypertension	8.6%	4.1%	0.45	0.09
BMI (kg/m^2)	22.0 ± 3.1	21.6 ± 3.0		0.15
Chol (mg/dL)	205.0 ± 36.9	218.8 ± 36.8		<0.001
HDL (mg/dL)	63.0 ± 15.8	65.3 ± 15.1		0.13
TG (mg/dL)	98.6 ± 62.5	94.4 ± 63.3		0.47
FBS (mg/dL)	89.7 ± 9.5	89.0 ± 9.8		0.43
Creatinine (mg/dL)	1.1 ± 0.2	1.0 ± 0.2		0.37
Hct (%)	43.0 ± 6.0	44.5 ± 9.1		0.02

Table 2, Lp(a) levels greater than 30 mg/dl were found in 32 per cent of our cases with the highest level being 175 mg/dL. Table 5 shows the univariate analysis of plasma Lp(a) and other variables. The factors that were associated with high plasma Lp(a) were the female sex, total cholesterol level, and hematocrit level.

Chlamydial Infection Indices:

As shown in Table 1, about 30 per cent and 50 per cent of the group had positive IgA and positive IgG respectively. A higher prevalence of Chlamydial infection was demonstrated in the male sex as shown in Table 3 with a significant difference in the IgG group. Also, smoking was more prevalent in the positive IgG group. The body size (weight and height) was unexplainably larger in the Chlamydial-infected group. Using the multivariate analysis, factors that related with a positive IgG were the male sex and smoking. Factors that associated with a positive IgA were age and weight.

DISCUSSION

Increasing evidence suggests that homocysteine may act as an independent risk factor for CAD[5-12]. Homocysteine promoted the progression of atherosclerosis by causing endothelial dysfunction[14], increasing oxidant stress, and promoting vascular smooth muscle cell growth. These adverse effects are pronounced with plasma homocysteine levels greater than 10 μmol/L. Plasma homocysteine increases with age, postmenopausal state, renal disease, and with administration of diphenylhydantoin and carbamazepine[15]. Fasting plasma levels of plasma homocysteine in a normal population generally range from 5-15 μmol/L[16]. Even mild elevations are associated with increased risk of atherosclerotic vascular disease, and a homocysteine level in excess of 16 μmol/L is associated with a 3-fold increase in risk of coronary heart disease[17]. However, in this study we defined hyperhomocysteinemia as a plasma homocysteine level of more than 11 μmol/L.

More than one-fourth of our subjects had plasma homocysteine levels of greater than 11 μmol/L. Higher homocysteine levels were detected in males with the odds ratio of 4.3-8.8 at any homocysteine levels greater than 10 μmol/L. Table 4 shows the univariate analysis of plasma homocysteine levels and other variables. In the higher homocysteine levels' group, the subjects were more obese and had higher levels of total cholesterol, triglycerides and LDL. Using the multivariate analysis however, factors that were associated with high fasting homocysteine levels were the male sex, high creatinine levels, and older age.

Lp(a) level has been shown in a number of clinical studies to be an independent risk factor for CAD[18]. The mechanism by which Lp(a) may increase risk for CAD is complex. This particle may

interfere with the generation of plasmin because of structural similarities between Apo(a) and plasminogen[19]. *In vitro* studies have demonstrated that Lp(a) enhances LDL entry into the arterial wall, facilitates the oxidation of the LDL, enhances LDL uptake by macrophages to produce foam cells, and helps stimulate smooth muscle cell proliferation.

As shown in Table 5, total cholesterol level was significantly higher in the high Lp(a) group but there was no difference in the level of triglyceride and HDL. However, female sex and increased hematocrit level were the only factors that associated with high Lp(a) level from the multivariate analysis.

There is widespread consensus that atherosclerosis is an inflammatory disease and recent reports have suggested that *Chlamydia pneumoniae* may play a role in the pathogenesis of atherosclerosis. The evidence for *C. pneumoniae* as a potential causative agent is based on findings of numerous sero-epidemiological studies[20,21], examination of atheromatous plaque specimens[22,23], *in vitro* animal models and recently, pilot anti-chlamydial antibiotic intervention trials[24]. Antibody prevalence studies suggest that more than 50 per cent of adults have been exposed to *C. pneumoniae*[25]. Although a high prevalence of antichlamydial antibodies has consistently been found in CAD patients, its predictive value has varied given the high level of exposure in the general adult population.

Prevalence of recent chlamydial infection in our study group was 30 per cent and past Chlamydial infection was 51 per cent. There was more prevalence of both recent and past chlamydial infections in the male sex but there was statistical significance only in the IgG group. Younger age was more prevalent in the positive IgA but not in the positive IgG group.

SUMMARY

Prevalence of New Risk Factors of CAD: From this normal healthy population the authors found that 27 per cent had homocysteine levels greater than 11 mmol/L and 32 per cent had high Lp(a) level. The prevalence of recent chlamydial infection was 30 per cent and past chlamydial infection was 51 per cent.

Factors Associated with New Risk and Conventional Risk Factors: A higher homocysteine level was more prevalent in the male sex, increased creatinine level and older age. The female sex and increased hematocrit levels were found in the high Lp(a) group. The factors that were associated with recent chlamydial infection were younger age and increased weight. The male sex and smoking were related with past Chlamydial infection.

Limitation of the Study

This study was done in a selected group of healthy Thai people that were rather young, active and from a medium to high socioeconomic status. It might not be a representation of the whole Thai population and data from other groups of the population would be useful.

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ความชุกของปัจจัยเสี่ยงใหม่ของโรคหลอดเลือดหัวใจตีบในคนไทย

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โรคหลอดเลือดหัวใจตีบเป็นปัญหาด้านสาธารณสุขที่สำคัญของประเทศไทย และมีปัจจัยเสี่ยงต่างๆ หลายประการที่มีผลต่อการเกิดโรค คณะผู้วิจัยได้ทำการศึกษาในพนักงานบริษัทชินวัตร จำนวน 3,615 คน โดยมีวัตถุประสงค์เพื่อให้ทราบถึงความชุกของปัจจัยเสี่ยงใหม่ๆ บางอย่างต่อการเกิดโรคนี้ ได้แก่ระดับ homocysteine, Lp(a) และการติดเชื้อ *Chlamydia pneumoniae* และเพื่อให้ทราบถึง association ระหว่างปัจจัยเสี่ยงใหม่ๆ เหล่านี้กับปัจจัยเสี่ยงเดิมที่ทราบอยู่แล้ว ผลการศึกษาพบว่ามี hyperhomocysteine สูงถึง 27%, ระดับ Lp(a) สูง 32% และพบอัตราของการติดเชื้อ *Chlamydia pneumoniae* ประมาณ 30% และ 51% ตามลำดับใน recent และ past infection

คำสำคัญ : ความชุก, ปัจจัยเสี่ยง, โรคหลอดเลือดหัวใจตีบ

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