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Reference range values for blood lipids and CHD guidelines for risk classification in middle-aged subjects

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We determined the serum cholesterol and triglyceride values of 554 normal, non-smoking adults in Bangkok. The subjects were 331 (59.7%) males and 223 (40.3%) females, with ages ranging from 35 to 59 years, attending the annual check up program. Because reference ranges vary widely between laboratories and between geographical regions, it is of great concern to determine each laboratory reference range of blood cholesterol and triglycerides. Our results for total cholesterol result ($\bar{X} \pm 2$ SD) were 260 ± 144 mg/dl (6.72 ± 3.72 mmol/L) in males and 275 ± 144 mg/dl (7.11 ± 3.72 mmol/L) in females, for total triglyceride results ($\bar{X} \pm 2$ SD) were 176 ± 122 mg/dl (1.99 ± 1.38 mmol/L) in males and 137 ± 96 mg/dl (1.55 ± 1.08 mmol/L) in females. Blood cholesterol and triglyceride values among 554 healthy subjects are sex and age dependent. Our lipid means and ranges are much higher than the data of the National Cholesterol Education Program (NCEP) among the North American population. We also established our own CHD risk guidelines by using blood cholesterol levels above the 75th percentile but below the 90th percentile for borderline risk and above the 90th percentile for high risk. Our results were that the desiralbe level was < 288 mg/dl (<7.45 mmol/L), the borderline level was 288 - 314 mg/dl (7.45 - 8.12 mmol/L), and the high risk level was > 314 mg/dl (>8.12 mmol/L). This study has shown that regional and continent-wide inter-laboratory comparability is necessary for successful clinical monitoring of blood lipids and it is recommended that each laboratory should set own reference range values for blood lipids.

Key words: *Blood lipids, Reference values, CHD guidelines*

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นวพรรณ จารุรักษ์, ปราณี ไกรลาศศิริ, สาคร ปิงสุทธิวงศ์. ค่าอ้างอิงของระดับไขมันในเลือดและค่าที่ระดับความเสี่ยงต่าง ๆ ต่อโรคหลอดเลือดเลี้ยงหัวใจอุดตัน เนื่องจากระดับไขมันในเลือดสูงในกลุ่มวัยกลางคน. จุฬาลงกรณ์เวชสาร 2537 สิงหาคม 38(8): 461-470

ระดับไขมันในเลือดมีความสำคัญในการวินิจฉัย รักษา และติดตามผลการรักษาโดยเฉพาะผู้ป่วยด้วยโรคหลอดเลือดเลี้ยงหัวใจอุดตันเนื่องจากระดับไขมันในเลือดสูง และเนื่องจากค่าอ้างอิงเป็นค่าเฉพาะสำหรับการวิเคราะห์แต่ละวิธีแต่ละห้องปฏิบัติการ นอกจากนี้ค่าไขมันในเลือดมีความแตกต่างเนื่องจากปัจจัยต่าง ๆ มากมาย เช่น เชื้อชาติ อายุ เพศ อาหาร การสูบบุหรี่ การออกกำลังกาย โรคต่าง ๆ ตลอดจนยา ฯลฯ การศึกษานี้จึงมีวัตถุประสงค์เพื่อหาค่าอ้างอิงของระดับไขมันในเลือด และ ค่าที่ระดับความเสี่ยงต่าง ๆ ในกลุ่มวัยกลางคนชาวกรุงเทพฯ โดยศึกษาในคนทำงานในกรุงเทพฯ จำนวน 554 คน ที่มีสุขภาพแข็งแรงเป็นชาย 331 คน คิดเป็นร้อยละ 59.7 และเป็นหญิง 223 คน คิดเป็นร้อยละ 40.3 ผลการศึกษาได้ค่ามัชฌิมเลขคณิต ($\bar{X}$) และค่ามัชฌิมเลขคณิต $\pm$ 2 เท่าค่าเบี่ยงเบนมาตรฐาน ($\bar{X} \pm SD$) ดังนี้ cholesterol เท่ากับ 260 $\pm$ 144 mg/dl (6.72 $\pm$ 3.72 mmol/L) ในเพศชาย และเท่ากับ 275 $\pm$ 144 mg/dl (7.11 $\pm$ 3.72 mmol/L) ในเพศหญิง ส่น triglycerides เท่ากับ 176 $\pm$ 122 mg/dl (1.99 $\pm$ 1.38 mmol/L) ในเพศชาย และเท่ากับ 137 $\pm$ 96 mg/dl (1.55 $\pm$ 1.08 mmol/L) ในเพศหญิง และเมื่อใช้ค่า cholesterol ที่สูงกว่าค่าที่ percentile ที่ 75 สำหรับเป็นค่าที่ความเสี่ยงระดับกลางและ ค่าที่สูงกว่าค่าที่ percentile ที่ 90 สำหรับค่าที่ความเสี่ยงระดับสูงได้ค่าความเสี่ยงระดับกลางเท่ากับ 288-314 mg./dl (7.45-8.12 m mol/L) และค่าความเสี่ยงระดับสูงที่ระดับ > 314 mg/dl (> 8.12 m mol/L)

การศึกษานี้พบว่าค่าไขมันในเลือดในกลุ่มวัยกลางคนของคนที่ทำงานในกรุงเทพฯ มีค่าสูงกว่าค่าที่ The National Cholesterol Education Program (NCEP) ได้ทำการศึกษาในคนอเมริกัน ฉะนั้นห้องปฏิบัติการแต่ละแห่งจึงควรหาค่าอ้างอิง และค่าระดับความเสี่ยงของไขมันในเลือดขึ้นเอง

While our mortality rate is decreasing, coronary heart disease (CHD) is still our major cause of death, and since total cholesterol and triglyceride values are the chemical indicators of potential risk for CHD[1-3] the ability to evaluate them is extremely important. As a basis to define normal and abnormal blood lipid levels in our patients for possible initiation of treatment and further follow up,[1] we report here a study on the assessment of the appropriate blood lipid value ranges of 544 healthy Bangkok workers. Since the oriental life-style is different from the western way, and blood lipid levels vary widely between laboratories, geographical regions[4,5] and are influenced by many factors such as genetics, age, sex,[1,2] smoking,[6,7] nutrition,[8,9] exercise,[10] alcohol intake,[11] etc., we determined to compare our reference ranges ($\bar{X} \pm 2$ SD) of cholesterol and triglycerides with data from the National Cholesterol Education Program (NCEP).[12] For identifying CHD risk in our population we also developed our standards to use blood cholesterol levels above the 75th perecentile for borderline risk and above the 90th percentile for high risk, according to the recommendations of the NCEP.[13]

Our data provides reference (normative) ranges for cholesterol and triglycerides in a middle-aged population and our data recommendations are much higher than the recommendatory data of the NCEP.

Materials and methods

Blood samples were drawn by using evacuated tubes (Venoject ^{R}) 5 ml as clot blood after a 12 hours fast,[14] on healthy subjects attending the annual check up program at the Department of Laboratory Medicine, Faculty of Medicine, Chulalongkorn Hospital. The serum was separated by centrifuge at 2500 rpm. and analysed by the enzymatic colorimetric method using Technicon ^{R} RA-1000 and a commercial reagent of Bayer Thai Co., Ltd. The accuracy and precision of determination was established by daily calibration standards, as well as control reagents.

The age, gender, history of illness, and current medications of each subject was noted at the time of sample collection. Physical examinations were performed by the physicians. The 554 (331 males, 223 females) subjects out of 696 persons age 35 to 59 years were chosen for the study. The other 144 subjects were excluded due to having received drug therapy or having a history of myocardial infarction (MI),[15] hypertension (HT),[16] nephrotic syndrome (NS),[17] diabetese mellitus (DM),[4,5,18,19] organ transplantation ,[20] smoking, or obesity (weight>standard weight 20%).[21] Pregnant women[22] and those having abnormal results of physical examinations were also excluded.

The arithmatic mean ($\bar{X}$), mode, standard deviation (SD), and 5th, 50th, 75th, 90th 95th percentiles of each parameter were calculated. The reference values were estimated by $X \pm 2$ SD. The upaired t-test was used to test the significance between male and female for cholesterol and triglycerides. The anova test was used to test the significance of different ages. The factors with p-value < 0.05 were considered statistically significant.

Results.

A total of 554 subjects were analysed, 331 (59.7%) males and 223 (40.3%) females. The mean and range ($\bar{X} \pm 2$ SD) of each parameter was male cholesterol 260 ± 144 mg/dl (6.72 ± 3.72 mmol/L), female cholesterol 275 ± 144 mg/dl (7.11 ± 3.72 mmol/L), male triglycerides 176 ± 122 mg/dl (1.99 ± 1.38 mmol/L), and female triglycerides 137 ± 96 mg/dl (1.55 ± 1.08 mmol /L). Tables 1 and 2 demonstrate our cholesterol and triglyceride means, mode, and 5th, 50th, 95th percentiles in each 5 year interval. The 5th, 50th, and 95th percentiles of cholesterol and triglycerides of the NCEP study are shown in Tables 3 and 4. Figures 1 and 2 present 5 year intervals of cholesterol and triglyceride data for both sexes. The histogram of cholesterol and triglycerides of both sexes also are shown in figures 3,4,5, and 6, respectively. For identifying CHD risk in our population we found that our desirable level was < 288 mg/dl (<7.45 mmol/L), the borderline level was 288-314 mg/dl (7.45-8.12 mmol/L), and the high risk level was>314 mg/dl (>8.12 mmol/L).

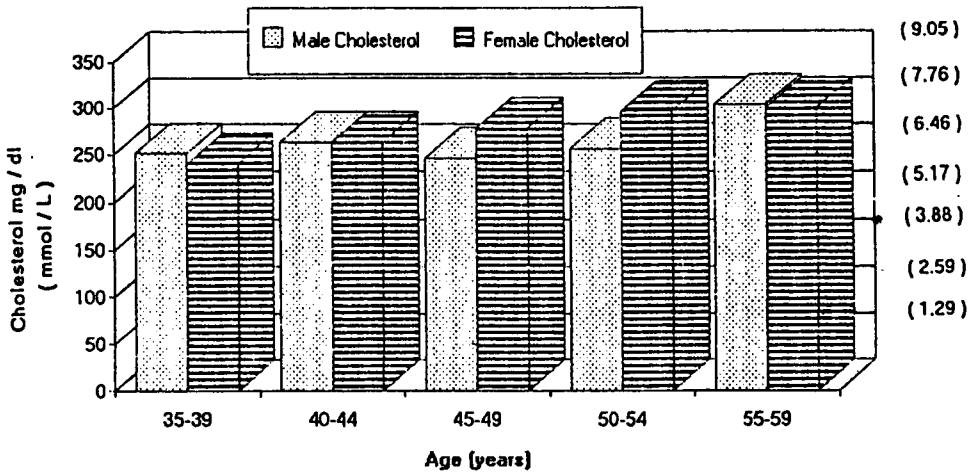

Figure 1. Five year interval histogram of male and female cholesterol.

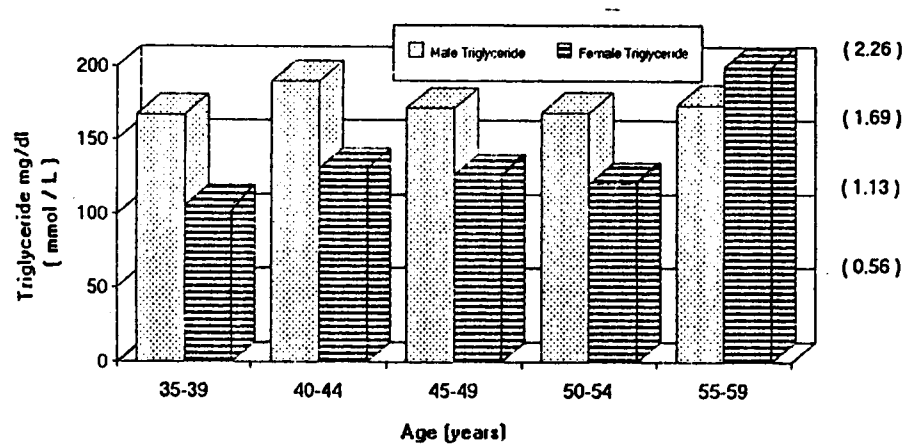

Figure 2. Five year interval histogram of male and female triglyceride.

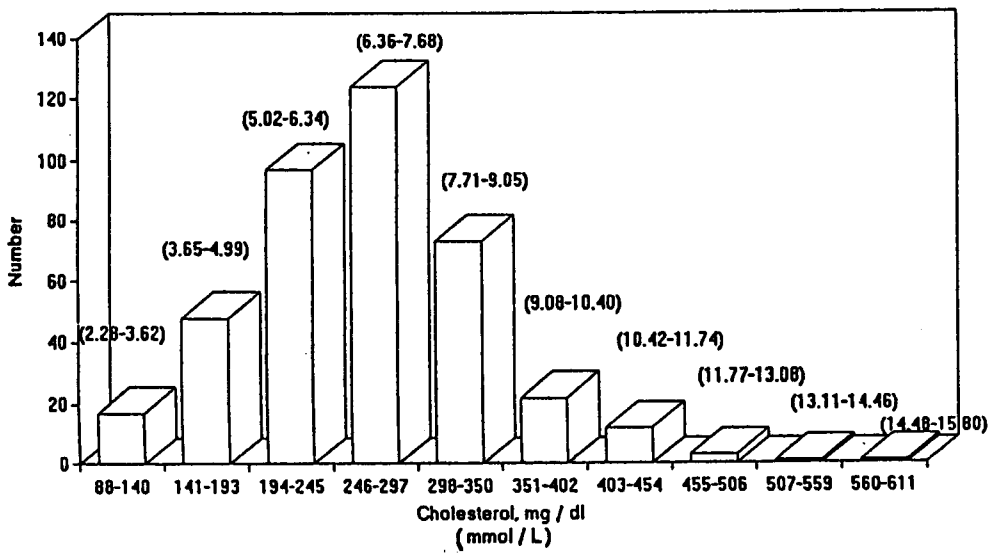

Figure 3. Histogram of male cholesterol distribution.

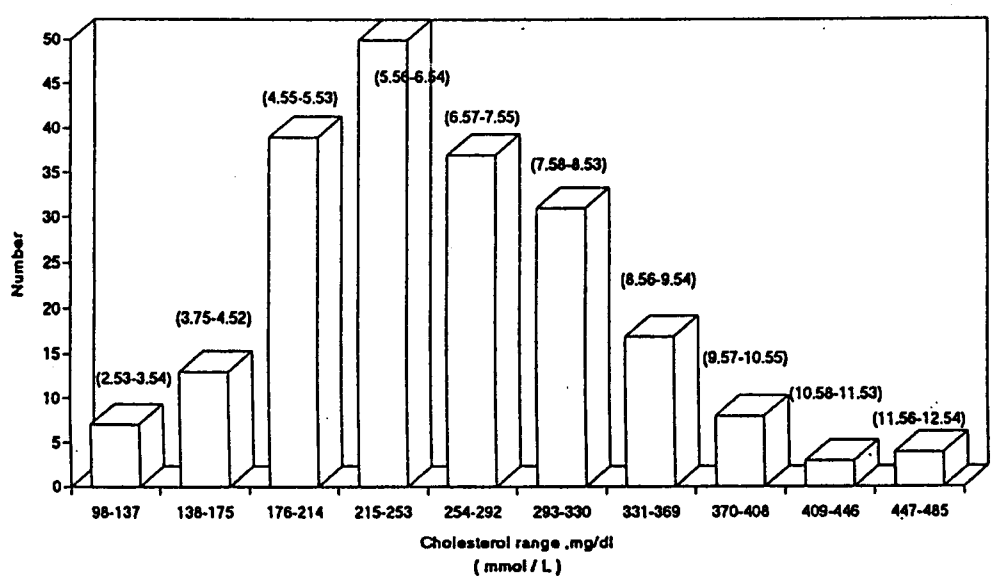

Figure 4. Histogram of female cholesterol distribution.

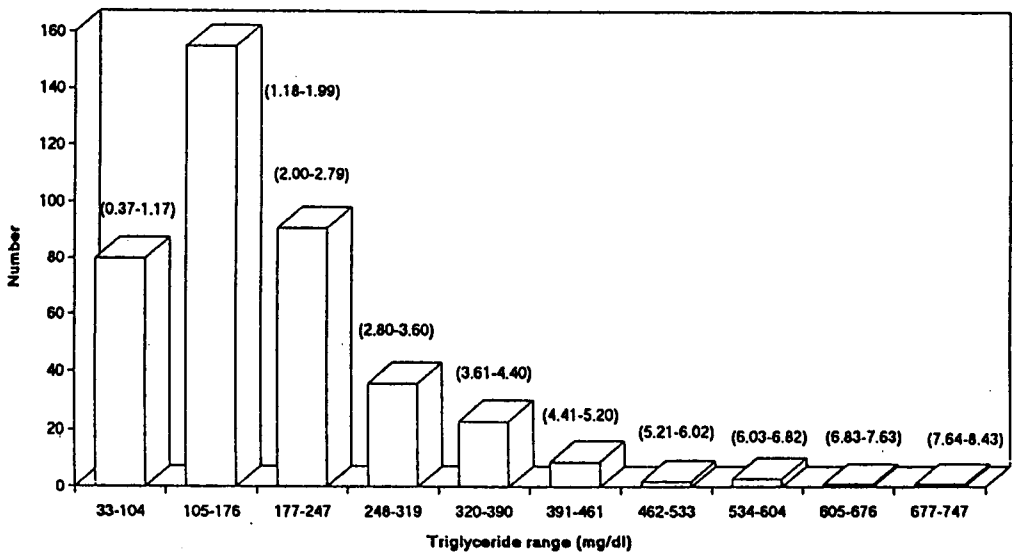

Figure 5. Histogram of male triglyceride distribution.

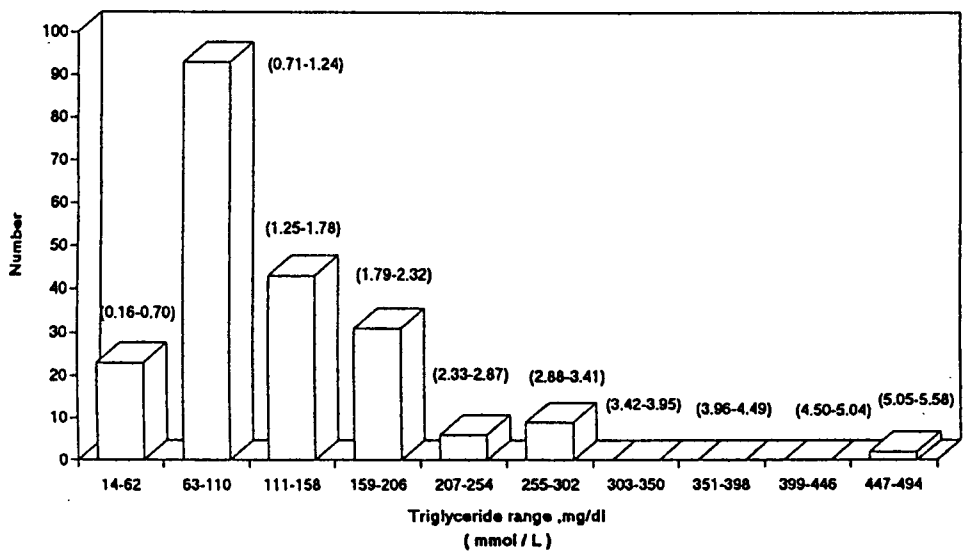

Figure 6. Histogram of female triglyceride distribution.

Discussion

Our sample population of 554 subjects consisted of 59.7% men and 40.3% women. A large proportion (60%) of our sample population was under 45 years. Our data (means; 5th, 50th, 95th percentiles) of each interval in both sexes (Table 1 and 2) are higher than the reference values recommended by the NCEP[12] (Table 3 and 4). Our cutpoints for identifying our sample risk at each level also are higher than the NCEP recommendations. Of course lipid levels are altered by many factors other than age, sex, and genotype, including race, liver dysfunction, die, weight, physical exertion, stress, alcohol intake, cigarette smoking, hypertension, renal disease, thyroid function, and birth control pills and other drugs.[1,2,4,] The oriental life-style is different from the western way, but because of the adoption of some western life-styles such as food, drink cigarette smoking change of city life-style that increases life-tension, and inadequate quantity and quality of sport clubs resulting for inadequate exercise, our Bangkok life style should be a serious consideration, and further population screening for blood lipid levels should be carried out Tables 1,2 and Figures 3,4,5,6 show that the mean value of each age interval group is greater than the 50th percentile for that group. This indicates that the serum cholesterol and triglyceride values did not form a normal distribution. The mode values is always less than the means and is also below the 50th percentiles for almost all groups, especially triglycerides. These findings indicate that the values tend to cluster at the low end of the distribution. Our ranges show the great disparity between upper and lower values. It indicates that our data disperses widely, especially at the high interval age groups, since we have a small amount of data when compared to the younger interval age groups. It was found that the serum cholesterol and triglyceride values among the 554 healthy subjects are sex dependent ($p<0.01$) and age dependent ($p<0.05$) (Figures 1 and 2). Since our study showed highly variable reference ranges and indicated that our population has unacceptably high blood cholesterol levels, reconciliation of the resultant high reference ranges and acceptable or "healthy" levels of blood cholesterol is of great concern and should be further studied. Our results are also higher than those of a previous study in Thai subjects (Viranuvati V, 1972[23] and Isarasena T, et al., 1974[24]). Many factors should be considered; firstly, the technique of blood lipid determination has been developed, nowadays we use the more sensitve and specific method secondly, the changing life-style, especially in big cities, and thirdly, the different criterias of each study could affect the results.

Table 1. Cholesterol levels of 554 healthy subjects.

Age (years)	Sex	Number No.(%)	Cholesterol, mgdl(mmol/L)				
			Mean	Mode	Percentiles 5th	50th	95th
35-39	Male	96(17)	251(6.49)	302(7.81)	110(2.84)	248(6.41)	371(9.59)
	Female	78(14)	240(6.21)	193(4.99)	136(3.52)	230(5.95)	369(9.54)
40-44	Male	97(18)	230(5.95)	301(7.78)	153(3.96)	263(6.80)	399(10.32)
	Female	63(11)	263(6.80)	234(6.05)	165(4.27)	259(6.70)	344(8.89)
45-49	Male	62(11)	248(6.42)	297(7.68)	147(3.80)	248(6.41)	388(10.03)
	Female	50(9)	277(7.16)	231(5.97)	149(3.85)	265(6.85)	434(11.22)
50-54	Male	49(9)	258(6.67)	282(7.29)	132(3.41)	252(6.52)	338(8.74)
	Female	23(4)	296(7.65)	262(6.78)	188(4.86)	287(7.42)	408(10.55)
55-59	Male	27(5)	308(7.96)	239(6.18)	201(5.20)	285(7.37)	575(14.87)
	Female	9(2)	275(7.11)	305(7.89)	250(6.47)	300(7.76)	317(8.20)

Table 2. Triglycerides levels of 554 healthy subjects.

Age (years)	Sex	Number No.(%)	Triglyceride, mg/dl (mmol/L)				
			Mean	Mode	Percentiles 5th	50th	95th
35-39	Male	96(17)	167(1.88)	142(1.60)	54(0.61)	154(1.74)	345(3.90)
	Female	78(14)	106(1.20)	63(0.71)	26(0.29)	92(1.04)	245(2.77)
40-44	Male	97(18)	166(1.87)	142(1.60)	51(0.58)	156(1.76)	418(4.72)
	Female	63(11)	131(1.48)	70(0.79)	56(0.82)	115(1.30)	290(3.27)
45-49	Male	62(11)	193(2.18)	91(1.03)	73(0.82)	159(1.80)	301(3.40)
	Female	50(9)	131(1.48)	206(2.32)	45(0.51)	107(1.31)	241(2.72)
50-54	Male	49(9)	179(2.02)	108(1.22)	58(0.65)	112(1.26)	331(3.74)
	Female	23(4)	120(1.35)	102(1.15)	70(0.79)	114(1.29)	217(2.45)
55-59	Male	27(5)	181(2.04)	151(1.70)	95(1.07)	168(1.90)	261(2.95)
	Female	9(2)	197(2.22)	152(1.72)	58(0.65)	182(2.05)	297(3.35)

Table 3. Cholesterol levels of the NCEP.[12]

Age (years)	Sex	Cholesterol, mg/dl (mmol/L)		
		Percentiles 5th	50th	95th
35-39	Male	147(3.80)	195(5.04)	267(6.90)
	Female	139(3.59)	186(4.81)	249(6.44)
40-44	Male	150(3.88)	204(5.28)	260(6.72)
	Female	146(3.78)	193(4.99)	259(6.70)
45-49	Male	163(4.22)	210(5.43)	275(7.11)
	Female	148(3.83)	204(5.28)	268(6.93)
50-54	Male	156(4.03)	211(5.46)	274(7.08)
	Female	163(4.22)	214(5.53)	281(2.27)
55-59	Male	161(4.16)	214(5.53)	280(7.24)
	Female	167(4.32)	229(5.92)	294(7.60)

Table 4. Triglyceride levels of the NCEP.(12)

Age (years)	Sex	Triglyceride, mg/dl (mmol/L)		
		Percentiles		
		5th	50th	95th
35-39	Male	52(0.59)	109(1.23)	316(3.57)
	Female	40(0.45)	83(0.94)	205(2.31)
40-44	Male	56(0.63)	123(1.39)	218(2.46)
	Female	45(0.51)	88(0.99)	191(2.16)
45-49	Male	56(0.63)	119(1.34)	279(3.15)
	Female	44(0.50)	94(1.06)	223(2.52)
50-54	Male	63(0.71)	128(1.44)	313(3.53)
	Female	53(0.60)	103(1.16)	223(2.52)
55-59	Male	60(0.68)	117(1.32)	261(2.95)
	Female	59(0.67)	111(1.25)	279(3.15)

The cutpoint recommendations of the NCEP are not reference ranges. Rather, they are delimitaters of risk for CHD, reflecting the approximate dividing lines between desirable levels of a given blood lipid.(5) It is hard to distinguish between reference ranges VS specific risk designation (ie, NCEP cutpoints). Since reference ranges and cutpoints varied widely between laboratories and between geographical regions, and could be established by each laboratory, we designed to set our own reference data and guidelines for risk classification. We hope that our reference values and guidelines for risk classification will be useful for our patients as well as to guide the physician in advising their patients in controllable factors such as nutrition, exercise, cigarette smoking, alcohol intake, drugs, etc. So as to improve their health. The screening for blood lipid levels should be included in annual health check up programs since all adults should know their blood lipid levels, and they should be made aware of the implications of their elevated levels regard to the increased risk of CHD, and they should seek the help of a physician should further evaluation and treatment be necessary. We further hope that our study may animate the improving of life quality of Bangkok residents and reduce our CHD morbidity and mortlity rates.

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