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ORIGINAL ARTICLE

REFERENCE INTERVALS FOR SERUM TOTAL CHOLESTEROL, HDL-CHOLESTEROL, LDL-CHOLESTEROL, TRIGLYCERIDES, Lp (a), APOLIPOPROTEIN A-I, A-II, B, C-II, C-III, AND E IN HEALTHY SOUTH INDIANS FROM ANDHRA PRADESH

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ABSTRACT

The incidence of cardiovascular and cerebrovascular disease is steadily increasing in South East Asian countries including Indian sub continent. Many lipids, apolipoproteins and Lp (a) except HDL-C and apo A-I, A-II are implicated as risk factors for coronary artery disease and cerebrovascular disease. There is great need to have national guidelines for each country like the ATP III guidelines recommended for U.S. population. For recommending appropriate medical decision limits, it is mandatory that each country establishes reference intervals pertaining to their population due to dietary, genetic and environmental diversity. In the present study, reference intervals for serum lipids, apolipoproteins and Lp (a) were established in a total of 1923 healthy Indian reference individuals comprising 1161 healthy men and 762 healthy women from Andhra Pradesh. For each analyte viz., serum total cholesterol, HDL-C, LDL-C, triglycerides, Lp (a), Apo A-I, Apo A-II, B, C-II, C-III and E, mean, two SD, median, confidence limits of mean, different percentile values are presented. The study also includes decade wise changes in each analyte and comparison of lipids, lipoproteins and Lp (a) among few populations covering U.S., India, Japan, Sweden, Finland and China. Reference Intervals for all lipid and lipoprotein parameters will immensely help in assessing associated risk for cardiovascular and cerebrovascular diseases in India. Additionally, the results will be beneficial in formulating our own guidelines pertaining to Indian population.

KEY WORDS

Blood Lipids, Cholesterol, Triglycerides, Apolipoproteins, Reference Intervals, South Indian Population.

INTRODUCTION

Ischemic heart disease and cerebrovascular disease are the leading causes of mortality and morbidity throughout the world (1-6). Incidence of coronary artery disease increases with advancing age in men beyond 40 years and in postmenopausal women. Recently, the prevalence of these disorders is also reported in younger individuals (7-10). Available global data have clearly established relationship of lipids and other risk factors with cardiovascular and cerebrovascular events (11-19). Though not fully understood, the role of apoliproteins for predicting coronary artery as well as cerebrovascular diseases is highlighted often (20-27). Widely accepted various risk factors for atherosclerotic diseases include elevated total cholesterol, LDL-cholesterol (28-32), triglyceride (33-36), apolipoprotein B (26, 37), lipoprotein (a) (39-41), Lp(a) and reduced HDL-cholesterol (13, 42) and apolipoprotein A (23, 27). Higher levels of Lp (a) are associated with cardiovascular, premature coronary artery disease, peripheral vascular diseases and cerebro vascular disease. Hence, the study of modifiable risk factors in asymptomatic healthy men and women is of immense value in preventing future events due to coronary and carotid artery atherosclerosis.

During past two decades, expert panels from western and

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eastern countries (43-46) including National Cholesterol Education Programme (NCEP) of U.S (47 -54) have released clear cut guidelines for preventing mortality from coronary artery disease. NCEP expert committee has clearly defined the appropriate medical decision cut off points for serum total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides for their population. Since, serum lipids and apoliproteins levels are very much dependent upon genetic background, ethnicity and dietary pattern of a particular population; it became mandatory to establish reference intervals for serum lipids and apoliproteins for healthy Indian men and women. (5, 18, 25, 43)

Apo A-I, known for its protective role against atherosclerosis, is the main protein component of HDL. Apo B is the main protein component of LDL, known to render potential risk for atherosclerosis and is important for the transport of cholesterol and triglycerides and their subsequent uptake by the cells. Apo C-II and Apo C-III exist widely in VLDL and HDL. Apo C-II activates lipoprotein lipase (LPL), whereas Apo C-III inhibits LPL on vascular endothelial cell surface. Apo E is a major protein constituent of the chylomicrons, VLDL and HDL. Apo E binds to LDL receptors on liver parenchymous cells and Apo E receptors. Apo E is known to cause an early coronary artery disease. Lipoprotein (a) is LDL-like lipoprotein containing a unique apoprotein called Apolipoprotein (a).

The objective of the present study was to quantitate serum total cholesterol, HDL cholesterol, LDL cholesterol, VLDL cholesterol, triglycerides, Lp (a), apolipoprotein A-I A-II, B, C-II, C-III and E in healthy Indian men and healthy Indian women in order to establish reference intervals for different serum lipids, Lp (a) and Apolipoproteins.

MATERIALS AND METHODS

A total of 1923 apparently healthy subjects including 1161 healthy men and 762 healthy women from Andhra Pradesh were enrolled in the study. The age of reference individuals ranged from 20 to 70 years and beyond. Reference individuals comprised selected employees of all cadres at our hospital, their friends and general public. Smokers, alcoholics, patients with history of diabetes, any chronic disease, recent surgery, diseases causing alterations in lipids, hypothyroid, hyperthyroid, past cardiac problem, coronary bypass graft, drugs affecting lipid concentrations, hormone therapy and women on oral contraceptives were excluded from the study.

Blood samples were obtained after 10-12 hour overnight fast. Reagent kits for all the lipid and apoliproteins except cholesterol and triglycerides were procured from Sekisui Medical Co., Ltd. (formerly Daiichi Pure Chemicals Co., Ltd) Japan and the estimations were carried out on Roche Hitachi-912 autoanalyser. The reagents for total cholesterol and triglycerides were procured from Accurex Biomedical Pvt. Ltd, India and both these analytes were measured by enzymatic methods. HDL cholesterol was measured by direct HDL assay in which HDL was solubilized by detergent, LDL, VLDL and chylomicrons are not disrupted. After HDL is selectively disrupted, HDL cholesterol was measured enzymatically. Direct LDL cholesterol was measured by homogeneous method using detergent technology. Lp (a) was measured using latex agglutination immunoturbidimetric method and apolipoproteins A-I, A-II, B, C-II, C-III and E were measured by immunoturbidimetry. Quality Control serum from Daiichi Chemical Company was run with each batch of analysis. The results of all parameters were accepted only within one SD limit. Statistical analysis was performed using SAS version 8.0 soft ware. For each analyte (serum total cholesterol, HDL-C, LDL-C, triglycerides, Lp (a), Apo A-I, Apo A-II, B, C-II, C-III and E) mean, 2 SD, Median, Confidence limits of mean and different percentile values are presented. Study also includes decade-wise changes in each analyte. P value of less than 0.05 was considered statistically significant. The study protocol was approved by the ethical review committee of Nizam's Institute of Medical Sciences, a medical university hospital. Informed consent was obtained from each reference individual after detailed explanation about purpose and nature of study.

RESULTS

The demographic details of reference individuals (Table 1) showed mean ages of 42 years in men and 40 years in women,

Table 1: Demographics for Indian men and women

		n	Mean	SD	Median	Min, Max
Age (Yrs)	Men	1161	42	13	42	20, 96
	Women	762	40	14	40	20, 90
Height (cm)	Men	1161	167	7	166	125, 198
	Women	762	155	7	155	122, 178
Weight (kg)	Men	1161	66	11	66	35, 106
	Women	762	60	12	60	28, 100
Waist circumfe-rence (cm)	Men	1161	86	12	87	28, 117
	Women	762	75	19	80	22, 115
BMI	Men	1161	24	4	24	15, 43
	Women	762	25	5	25	12, 47
Hip circu-mference (cm)	Men	1161	94	11	95	33, 127
	Women	762	89	22	95	28, 130

Table 2: Lipids (mg/dl) in healthy Indian men and women

		n	Mean	SD	Median	Min-Max	CL for Mean	p value
Total Cholesterol	Men	1161	175.1	34.8	173	92, 375	173.11-177.11	
	Women	762	175.4	34.3	175	95, 291	173.01-177.88	
	Total	1923	175.3	34.6	174	92, 375	173.69-176.79	0.8366
Direct HDL-C	Men	1161	41.9	9.8	40	18, 90	41.39-42.51	
	Women	762	47.2	10.4	46	12, 82	46.5-47.97	
	Total	1923	44	10.3	42	12, 90	43.58-44.51	<.0001
Direct LDL-C	Men	1161	102.4	29.5	99	14, 242	100.66-104.06	
	Women	762	99.2	30.6	95	11, 232	97.05-101.39	
	Total	1923	101.1	30	97	11, 242	99.78-102.46	0.0245
Triglycerides	Men	1161	139.9	63.5	127	25, 503	136.21-143.52	
	Women	762	120	54.8	107	35, 352	116.12-123.91	
	Total	1923	132	60.9	121	25, 503	129.27-134.73	<.0001
Total Cholesterol	Men	1161	4.35	1.15	4	2, 9	4.28 – 4.41	
/HDL ratio	Women	762	3.85	1.02	4	1-8	3.78 – 3.92	
	Total	1923	4.15	1.13	4	(1,9)	(4.1,4.2)	<.0001

Table 3: Decade-wise Lipids (mg/dl) in healthy Indian men and women

Age group, yrs		20-29	30-39	40-49	50-59	60-69	≥ 70	Over All
n	Men	243	265	306	265	46	35	1160
	Women	188	180	206	126	37	25	762
	Total	431	445	512	391	83	60	1922
Mean Total-	Men	159.9±34.5	176.5±34.1	179.5±35.3	180.7±31.6	181.5±32.3	181.2±34.2	175.1±34.8
Cholesterol ± SD	Women	156.1±30.7	169.7±26.4	183.1±32.9	187.5±34.2	200±34.3	202±38.8	175.4±34.3
	Total	158.2±32.9	173.7±31.4	181±34.4	182.9±32.6	189.8±34.3	189.9±37.3	175.3±34.6
Mean HDL-C± SD	Men	40.9±9.2	40.7±8.9	43±10.5	42.6±10.3	42.9±8.3	43.3±8.9	41.9±9.8
	Women	46.4±9.9	46±10.3	47±10	50±10.6	48.8±11.8	48.4±12.2	47.2±10.4
	Total	43.3±9.9	42.8±9.8	44.6±10.5	45±10.9	45.5±10.4	45.5±10.6	44±10.3
Mean LDL-C ± SD	Men	96.2±27.9	101.6±30.1	103.8±29.4	105.9±29.1	104.7±29.4	109.7±35.2	102.4±29.5
	Women	87.9±26.1	96.9±25.9	101.8±30.4	109.9±34.7	106.5±35.3	115.3±35.5	99.2±30.6
	Total	92.6±27.4	99.7±28.5	103±29.8	107.2±31	105.5±32	112±35.1	101.1±30
Mean TG ± SD	Men	120.7±60.7	153.2±73.8	143±56.8	140.9±59.9	137.7±56.1	140.8±62	139.9±63.5
	Women	100.1±50.1	116.6±51.2	125±53.2	128.1±50.3	151.1±59.3	166.5±76.3	120±54.8
	Total	111.7±57.2	138.4±68	135.8±56	136.8±57.2	143.7±57.6	151.5±68.9	132±60.9
Total Cholesterol /	Men	4.1±1.2	4.5±1.2	4.4±1.2	4.4±1.1	4.4±1	4.2±1	4.35±1.15
HDL ratio ± SD	Women	3.8±1	3.5±0.9	3.9±1	4.0±1	3.9±1	4.3±1.2	3.85±1.02
	Total	3.8±1.1	4.3±1.2	4.2±1.1	4.3±1.1	4.4±1.1	4.3±1.2	4.15±1.13
Mean LDL-C /	Men	2.5±0.9	2.6±1.1	2.6±0.9	2.6±0.9	2.5±0.9	2.6±1.1	2.6±0.9
HDL-C ratio ±SD	Women	2.0±0.8	2.2±0.8	2.3±1.2	2.3±0.9	2.3±0.9	2.5±1.0	2.2±1
	Total	2.3±0.9	2.5±1	2.5±1	2.5±0.9	2.4±0.9	2.6±1	2.4±1

Table 4: Percentile values of Lipids (mg/dl) in healthy Indian men and women

		n	5th percentile	25th percentile	50th percentile	75th percentile	95th percentile
Total Cholesterol	Men	1161	121	151	173	196	235
	Women	762	119	150	175	196	235
	Total	1923	120	151	174	196	235
Direct HDL-C	Men	1161	28	36	40	47	60
	Women	762	32	40	46	53	67
	Total	1923	29	38	42	50	64
Direct LDL-C	Men	1161	61	82	99	119	157
	Women	762	57	77	95	118	157
	Total	1923	60	80	97	119	157
Triglycerides	Men	1161	58	96	127	175	262
	Women	762	54	80	107	152	218
	Total	1923	56	88	121	166	248
Total Cholesterol /HDL-C ratio	Men	1161	3	3.54	4.27	4.97	6
	Women	762	2	3.15	3.73	4.45	6
	Total	1923	3	3.35	4.04	4.74	6
LDL-C / HDL-C ratio	Men	1161	3	3.54	4.27	4.97	6
	Women	762	2	3.15	3.73	4.45	6
	Total	1923	3	1.75	2.29	2.92	6

an average height of 167 cm in men and 155 cm in women, an average weight of 66 kg in men and 60 kg in women, waist circumference of 86 cm in men and 75 cm in women, mean BMI of 24 in men and 25 in women, hip circumference of 94 cm in men and 89 cm in women. Except for slightly higher BMI in women, all other parameters were higher in men compared to women. The mean, median, range (minimum - maximum value), 5th to 95th percentile, confidence limits for mean, T-CHO/HDL-C ratio, LDL-C/ HDL-C ratio and decade-wise changes in all analytes of lipids and Apolipoproteins are presented in Tables 2-7.

The overall mean cholesterol for all ages was same 175 mg/dl in healthy men as well as in healthy women (men 175.1 ± 34.8, women 175.4± 34.3 mg/dl). The median values of 173 mg/dl in men and 175 mg/dl in women were quite similar to mean values in men and women. The confidence limits for mean ranged from 173.11 to 177.11 mg/dl in men and from 173.01 to 177.88 mg/dl in women (Table 2). Decade-wise analysis of serum cholesterol showed steady increase of mean and median cholesterol levels from 20-29 years to advancing decades until 6th decade in both healthy men and healthy women groups (Table 3).

The overall mean HDL cholesterol for all ages in women was significantly higher (47.2±10.4 mg/dl) compared to men (41.9 ±9.8 mg/dl).The median values in women were also higher (46 mg/dl) as compared to men (40 mg/dl). The confidence limits in men and women were 41.39-42.51 mg/dl and 46.5-47.97 mg/dl respectively (Table 2). A steady increase in HDL cholesterol concentration was not seen with advancing decades in both healthy men and women except for slight progressive increase from 3rd decade to 5th decade in women and men (Table 3).

The overall mean and median LDL-cholesterol for all ages was significantly higher in men (mean 102.4±29.5 mg/dl and median 99 mg/dl) compared to values in women (mean 99.2±30.6 mg/dl) and median 95 mg/dl).The confidence limits of mean were also higher in men (100.66-104.06 mg/dl) compared to women (97.05-101.39 mg/dl) (Table 2). The mean LDL cholesterol increased steadily from 2nd decade to 5th decade in women as well as in men. However, no change was observed in 6th & 7th decades compared to 5th decade (Table 3). The overall mean and median values of triglycerides for all ages were also significantly higher in men (mean 139.9±63.5 and median 127 mg/dl) compared to women (120±54.8 and 107 mg/dl) (Table 2). The increasing concentration of triglyceride was observed in women group with advancing decades from 2nd to 7th decade. However,

Table 5: Apolipoproteins (mg/dl) in healthy Indian men and women

		n	Mean	SD	Median	Min, Max	Confidence Limits for Mean	p value
Lp (a)	Men	1161	31.1	20.3	27	2,221	29.9, 32.24	0.0499
	Women	762	33.2	24.7	27	2,234	31.42, 34.93	
	Total	1923	31.9	22.14	27	2,234	30.91,32.89	
Apo A- I	Men	1161	120.2	19.4	122	27,216	119.11, 121.35	0.8427
	Women	762	120.1	18.5	121	56,211	118.74, 121.37	
	Total	1923	120.16	19.08	122	27,216	119.31, 121.02	
Apo A-II	Men	1161	27.5	5.2	27	14,71	27.2, 27.8	0.2605
	Women	762	27.2	5	27	14,49	26.88, 27.58	
	Total	1923	27.39	5.09	27	14,71	27.16, 27.62	
Apo B	Men	1161	90.1	20.1	89	4,165	88.9, 91.21	<.0001
	Women	762	86.2	18.4	86	16,175	84.85, 87.46	
	Total	1923	88.51	19.51	89	4,175	87.64, 89.38	
Apo C-II	Men	1161	3.8	2.7	3	0,27	3.63, 3.94	<.0001
	Women	762	3.3	2.5	3	0,20	3.08, 3.44	
	Total	1923	3.58	2.63	3	0,27	3.46, 3.7	
Apo C-III	Men	1161	7.7	3.2	7	0,37	7.55, 7.92	0.0001
	Women	762	7.2	3	7	0,26	6.96, 7.38	
	Total	1923	7.51	3.14	7	0,37	7.37, 7.65	
Apo E	Men	1161	4	1.5	4	0,11	3.87, 4.04	0.7807
	Women	762	3.9	1.5	4	0,17	3.83, 4.04	
	Total	1923	3.95	1.49	4	0,17	3.88, 4.02	

such increase was not evident beyond 4th decade in group of men (Table 3).

The overall mean total cholesterol to HDL-C ratio (Table 2) was higher in men (4.35) compared to women (3.85). Similarly the ratio of LDL-C / HDL-C (Table 3) was higher in men (2.6) compared to women (2.2) (Table 3). The overall mean serum Lp (a) for all ages in men (31.1±20.3 mg/dl) were significantly lower compared to mean values of Lp (a) in women (33.2± 24.7 mg/dl). The median values were 27 mg/dl in both women and men. The large variance of Lp (a) in men and women groups ranged from 2-221 mg/dl and 2-234 mg/dl. However, the confidence limits for mean were 29.9-32.2 mg/dl in men and 31.42-34.93 mg/dl in women (Table 5). Decade-wise analysis did not show significant change from 20 years to 59 years. The men during the 7th decade and women during 6th and 7th decade showed remarkably high concentrations of mean Lp (a) (Table 6).

There was no significant change in overall mean serum concentrations of Apo-A1 for all ages in healthy men (120.2± 19.4 mg/dl) compare to healthy women (120.1± 18.5 mg/dl). The median concentration in men and women group was 122 and 121 mg/dl. The confidence limits for mean in men were 119.11-121.35 mg/dl and in women were 118.74-121.37 mg/dl (Table 5). Decade-wise analysis showed slight increase in mean Apo A-I concentration in men from 2nd to 4th decade. In women, the values did not increase with advancing age from 20 years to 49 years. However, the slight increase in mean values was observed from 5th and 6th decade. Further decline in Apo A-I was noticed beyond 70 years (Table 6).

Similarly overall mean values of Apoprotein A-II for all ages did not differ significantly in men (27.5 ± 5.2 mg/dl) compared to mean values in women (27.2 ± 5.0). The median values of A-II in men and women groups were same (27 mg/dl). The confidence limits of mean were quite same in men (27.2-27.8 mg/dl) and in women (26.88-27.58 mg/dl) (Table 5). There was no change in Apo A-II concentrations with advancing decade in men, but women did show slight progress increase from 3rd decade to 6th decade (Table 6). The overall mean serum Apo B concentration for all ages was significantly raised

Table 6: Decade-wise Apoliproteins (mg/dl) in healthy Indian men and women

Age group, yrs		20-29	30-39	40-49	50-59	60-69	≥ 70	Over All
n	Men	243	265	306	265	46	35	1160
	Women	188	180	206	126	37	25	762
	Total	431	445	512	391	83	60	1922
Mean Lp (a) ± SD	Men	33±25.6	29.6±16.6	30.9±20.7	29.8±16.2	32.2±18.5	37.4±28	31.1±20.3
	Women	29.4±18.2	31.3±25.4	35.1±23.3	32.7±20	44.4±52.3	45.5±22.5	33.2±24.7
	Total	31.5±22.7	30.3±20.6	32.6±21.9	30.7±17.5	37.7±37.8	40.8±26	31.9±22.1
Mean Apo A-I ± SD	Men	114.6±20.5	120.2±18.5	123.8±19.1	120.5±19.5	123±14.9	123.7±18.7	120.2±19.4
	Women	119.2±18.6	118.5±17.2	119.6±19.6	124.7±17.4	124.7±16	111.6±22.4	120.1±18.5
	Total	116.6±19.8	119.5±18	122.1±19.4	121.8±19	123.8±15.4	118.6±21	120.2±19.1
Mean Apo A-II ± SD	Men	27.3±5.6	27.8±5.1	27.8±5.2	27±5	27±4.5	28±5.2	27.5±5.2
	Women	26.3±4.8	26.8±4.8	27.5±5.2	28.3±5	29.5±4.2	26.4±4.6	27.2±5
	Total	26.9±5.3	27.4±5	27.7±5.2	27.4±5	28.3±4.5	27.1±5	27.4±5.1
Mean Apo B ± SD	Men	83.6±19.2	92.3±20.7	93.7±19.9	89.8±19.6	89.4±18.6	88.3±18.8	90.1±20.1
	Women	79.7±18.4	85.8±18	89.1±17.9	89±17.4	94±19	87.4±16.3	86.2±18.4
	Total	81.9±18.9	89.6±19.9	91.9±19.3	89.5±18.9	91.5±18.8	87.9±17.7	88.5±19.5
Mean Apo C-II ± SD	Men	3.3±2.8	3.9±2.8	4.1±2.5	3.9±2.7	3±1.8	3.8±2.4	3.8±2.7
	Women	2.6±2.3	3.6±2.8	3.4±2.5	3.6±2.5	3.5±2.2	2.8±1.9	3.3±2.5
	Total	3±2.6	3.8±2.8	3.8±2.5	3.8±2.7	3.3±2	3.4±2.3	3.6±2.6
Mean Apo C-III ± SD	Men	6.9±3.4	7.9±3.6	8.1±2.9	7.9±3	7.8±2.4	8.1±2.7	7.7±3.2
	Women	6.1±2.9	7.6±3.2	7.2±2.9	7.8±2.9	8±2.5	7.1±2.5	7.2±3
	Total	6.6±3.2	7.8±3.5	7.7±2.9	7.9±2.9	7.9±2.4	7.7±2.6	7.5±3.1
Mean Apo E ± SD	Men	3.8±1.5	4.1±1.5	3.9±1.5	4±1.6	3.8±1.1	3.6±1.2	3.9±1.5
	Women	4±1.6	3.7±1.2	4±1.4	4.1±1.8	4.4±1.1	3.6±1	3.9±1.5
	Total	3.9±1.6	4±1.4	3.9±1.4	4.1±1.7	4±1.1	3.6±1.1	4±1.5

in men (90.1 ± 20.1 mg/dl) compared to women (86.2 ± 18.2 mg/dl). The median values in men and women were 89 and 86 mg/dl respectively. The confidence limit for mean was 88.9-91.21 mg/dl in men and 84.85-87.46 mg/dl in women (Table 5). Mean values of Apo B in women increased steadily from 2nd decade to 6th decade and subsequently declined beyond 7th decade. However such change was not observed in men except for slight reduction beyond 5th decade (Table 6).

Highly significant elevation was also observed in overall mean concentrations of Apo C-II for all ages in men (3.8±2.7 mg/dl) compared to mean values in women (3.3±2.5 mg/dl). However, the median value for both the groups was 3 mg/dl. The confidence limits in men and women were 3.63-3.94 mg/dl and 3.08-3.4 4mg/dl respectively (Table 5). Apo C-II increased slightly from 2nd to 4th decade in women and 2nd to 3rd decade in men (Table 6). The highly significant increase of overall mean concentrations of Apo C-III for all ages was observed in men (7.7±3.2 mg/dl) compared to mean values in women (7.2±3 mg/dl). Both the groups had median value of 7 mg/dl. The confidence limits for Apo C-III in men and women group were 7.55 – 7.92 mg/dl and 6.96 -7.38 mg/dl respectively (Table 5). Apo C-III did show slight increase with advancing decades in both groups of men and women (Table 6). No significant difference was observed in mean values of serum Apo E in men (4±1.5 mg/dl) compared to women (3.95±1.49 mg/dl). The confidence limits were 3.87-4.04 mg/dl in men and 3.83-4.04 mg/dl in women. Apo E values did not increase with advancing decades except for slight decline during 7th decade (Table 6). The frequency distribution of each lipid and apolipoprotein analyte (Fig 1, 2) showed normal Gaussian distribution of all analytes except for slight skewing of triglycerides, Lp (a) and Apo-CII.

DISCUSSION

The incidence of cardiovascular and cerebrovascular disease is steadily increasing in South East Asian countries and also

Table 7: Percentile values of Apolipoproteins in healthy Indian men and women

		N	5th percentile	25th percentile	50th percentile	75th percentile	95th percentile
Lp (a)	Men	1161	10	18	27	38	70
	Women	762	10	18	27	39	77
	Total	1923	10	18	27	38	74
Apo A-I	Men	1161	88	108	122	130	151
	Women	762	90	107	121	131	150
	Total	1923	88	108	122	130	151
Apo A-II	Men	1161	20	24	27	30	36
	Women	762	20	24	27	30	36
	Total	1923	20	24	27	30	36
Apo B	Men	1161	57	78	89	100	125
	Women	762	58	74	86	96	117
	Total	1923	57	77	89	98	123
Apo C-II	Men	1161	0	2	3	5	9
	Women	762	0	2	3	4	8
	Total	1923	0	2	3	4.6	9
Apo C-III	Men	1161	3	6	7	9	13
	Women	762	3	5	7	9	12
	Total	1923	3	5	7	9	13
Apo E	Men	1161	2	3	4	5	7
	Women	762	2	3	4	5	6
	Total	1923	2	3	4	5	6

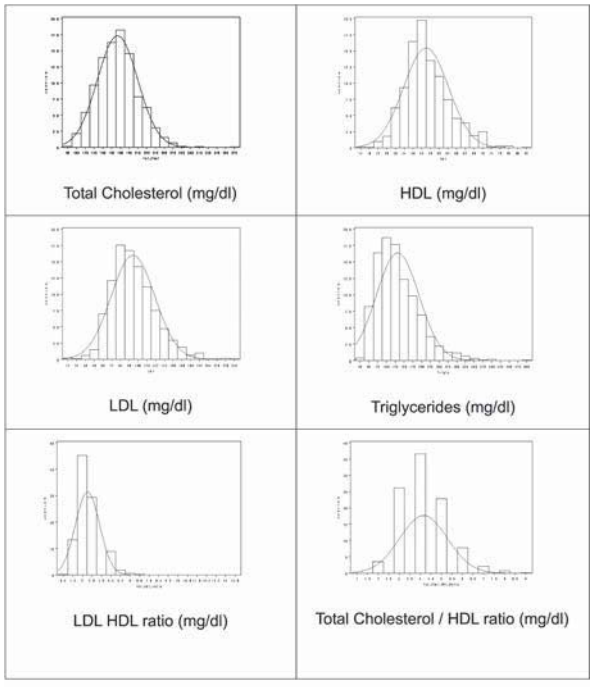

Fig 1: Frequency distribution (Histogram) of Lipids in healthy Indian men and women

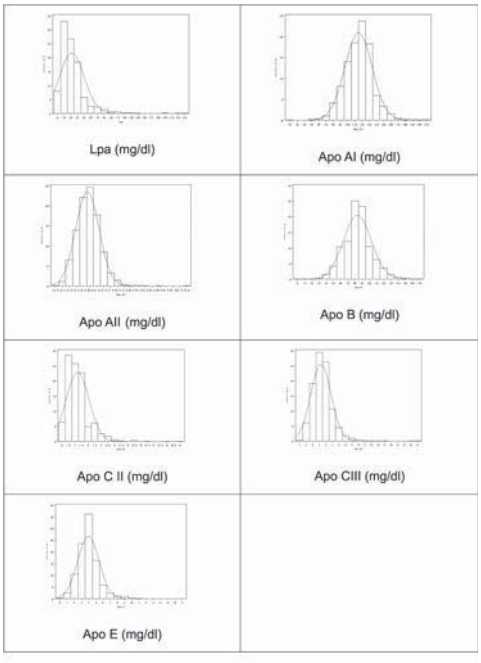

Fig 2: Frequency distribution (Histogram) of Apolipoproteins in healthy Indian men and women

Table 8A: Mean Lipids Concentrations In Different Populations

	Ref no.	n	T-CHO	HDL-C	LDL-C	TG
Men						
Noma et al, 1991 Japan 2	62	677	184±24	52.6±12.6		95±27
Ashavaid et al, India 2005	57	375	199±37.54	44±8.95	122±30.57	128±53.89
Present study, 2008, India		1161	175.1±34.8	41.9±9.8	102.4±29.5	139.9±63.5
Indian Industrial population						
Reddy et al 2006 (20-69 yrs)	58		177.1±40	41.5±10.1		137.4±78.6
Rahmani et al 2002, Iran	27	73	174±34	52±13	100±32	112±42
All races (white & Black) 20-74 yrs, Fulwood et al, U.S, 1986	28	5604	211±1.2	45.2±0.4 (N=4562)	3.31±0.06 (N=1037)	145±2. 9 (N=1269)
White U.S	28	4883	211±1.2	44.4±0.4 (N=4019)	3.39±0.07 (N=906)	149±3.3 (N=1111)
Black, U.S	28	607	208±2.5	51.8±0.7 (N=462)		166±8.8 (N=133)
Kottke et al, 1986, US (23-75 yrs)	22	135	204±40	42±12**		126±63
Li et al 2005, China	61	8572	180.1	49.03**	100.56	148.2
Li et al 1988, China	60	8027	117.84	51.80**	105.93	106.75
Women						
Noma et al, 1991 Japan	62	467	183±24	59±11.5		83±26
Ashavaid et al, India, 2005	57	277	196±36.13	52±11.77	118±28.01	99±46.07
Present study, India , 2008		762	175.4±34.3	47.2±10.4	99.2±30.6	120±54.8
Indian Industrial population						
Reddy et al 2006 (20-69 yrs)	58		175.7±40	44.6±10.9		114.1±61.6
All races (white & Black) 20-74 yrs, Fulwood et al, U.S, 1986	28	6260	215±1.2	53.7±6.4 (N=5235)	2.79±0.05 (N=1246)	124±2.3 (N=1111)
White U.S	28	5418	216±1.3	53.4±0.4 (N=4563)	2.82±0.05 (N=1084)	126±2. 4 (N=1290)
Black, U.S	28	729	212±3.1	56.2±0.9 (N=581)		104±4.2 (N=166)
Li et al 2005, China	61	6391	183.25	57.99**	104.77	118.125
Li et al 1988, China	60	5256	178.99	59.92**	102.06	91.875

* Median Value, ** Precipitation method, *** RIA

in India (55). Numerous reports are available in literature relating to serum/plasma lipids, lipoprotein (a), Apolipoproteins and their sub-fractions as important risk assessment parameters for atherosclerosis causing cardiovascular and cerebrovascular disorders (56). Being a very appropriate drug targets, the total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides are monitored routinely in almost all diagnostic laboratories for both the risk assessment and as follow-up investigations subsequent to administration of various statins. The concentrations of these analytes are very much dependent upon ethnicity, specific dietary habits, and genetic make up, advancing age, gender, life style, and environmental factors. Defining reference intervals for important lipids, lipoprotein (a) and Apolipoproteins has become a necessity for formulating both (1) suitable medical decision limits and (2) the guidelines in predicting future risk for CHD and CVD in different populations due to their vast ethnic diversity. The summary of noticeable variations in mean values of lipids, lipoprotein (a) and Apolipoproteins observed in different populations are listed in Tables 8A and 8B. Salient important features to highlight are relatively lower concentration of total cholesterol, LDL-C and HDL- C Apo A-1, Apo B, Apo C-II, Apo C-III and higher concentration of triglycerides, Lp(a) in both the groups of men and women residing in Andhra Pradesh state compared to their counterparts residing in Maharashtra state of India. Apo A remained the same in both genders (57).

TABLE 8B: Mean Apoliporoteins, Lp(a) Concentrations in Different Populations

	Ref No.	n	Lp(a)	Apo A-1	Apo A-II	B	C-II	C-III	E
Men									
Sakurabayashi et al 2001 Japan 1	63	1018	14.1±16.0 / 16.7* (N=957)	137±18	31±5	91±18	3.2±1.4	7.9±2.1	3.5±0.8
Noma at al, 1991 Japan 2	62	677		128±24	30.5±5.5	84±15	3.2±1.1	8.1±2.6	3.9±0.8
Ashavaid et al, India 2005	57	375	11.7*	123±17.86	28±4.26	98±21.29	5.1±3.14	8.5±2.71	4.3±1.62
Present study, 2008, India		1161	31.1±20.3 / 27*	120.2±19.4	27.5±5.2	90.1±20.1	3.8±2.7	7.7±3.2	4±1.5
Rahmani et al 2002, Iran	27	73		164±18		79±15			
Kottke et al, 1986, US (23-75 yrs)	22	135		160±25***	53±14***	89±23***			
Cointois et al 1996 white Men, US	69, 70	1879 1880		134±23		103±24			
Jungner et al, 1998 <20-> 80yrs, Sweden	72	83112		136±22		131±35			
Leino et al, 1995, Finland	71		19 / 8.6* ***	138		121			
Women									
Sakurabayashi et al 2001 Japan 1	63	1167	13.5±15.2 (N=911)	146±20	29±4	84±18	2.7±1.2	7.2±1.8	3.7±0.9
Noma at al, 1991 Japan 2	62	467		141±23	30.1±5.1	82±15	2.8±1.0	7.7±2.1	4.2±0.9
Ashavaid et al, India, 2005	57	277	15.9*	132±18.44	28±4.24	91±20.71	3.8±2.67	7.5±2.42	4.4±1.55
Present study, India , 2008		762	33.2±24.7	120.1±18.5	27.2±5.0	86.2±18.4	3.3±2.5	7.2±3.0	3.9±1.5
Cointois et al 1996 white Women, US	69, 70	1939 1944		154±28		96±26			
Jungner et al, 1998 <20->80yrs Sweden	72	64464		151±24		122±36			
Leino et al, 1995, Finland	71		16.9 / 8.5* ***	158		109			

* Median Value, ** Precipitation method, *** RIA

Another study, conducted on ten big industrial populations across India on a total of 19973 subjects (20≥60 yrs), established a surveillance network for CVD risk factor in an industrial setting, in which the present first author was one of the biochemistry co-investigators, reported mean total cholesterol of 177mg/dl in men and 176mg/dl in women, HDL 41.5 mg/dl in men and 44.6 in women, triglycerides of 137 mg/dl in men and 114 mg/dl in women. Though the study selected mixed population in which 40.2% of men, 34.4% of women had dyslipidemia, 28.6% of men, 18.2% of women had hypertriglyceridemia (58). By and large the lipid levels were lower in their study and also in our present study compared to Americans, Europeans, Japanese and Chinese. American white men had higher total cholesterol, lower HDL and triglycerides compared to American blacks whereas American white women had higher total cholesterol and triglycerides and slightly lower HDL compared to American black women (59). The observations from the present study and other published reports from India (57, 58). China (60, 61), Japan (62) and US (59) revealed highest total cholesterol in American men and women of all races followed by China, Japan and India. Indians seem to have relatively lower cholesterol compared to other populations. The Japanese men had lower values triglycerides, Lp (a), Apo B, Apo E and higher values of total cholesterol, HDL cholesterol, Apo A-1, Apo-II compared to Indian men in the present study. The Japanese women had lower values of triglycerides, Lp (a), Apo B, Apo C-II and higher values of total cholesterol, HDL C, Apo A-1, Apo A-II, Apo C-III and Apo E compared to Indian women group in our study (62).

Two reports from Japan (62, 63) showed slight variations in Apo A-1 and Apo B in both sexes in their population. The average cholesterol levels of healthy Americans were more than 200 mg/dl. Interestingly, the reports from same populations documented striking changes in these parameters over different time periods of study (59, 64-66). Another study on 580 healthy volunteers revealed marked variation of lipids and lipoproteins intervals among populations from six cities (67). The variations in lipids concentrations were also observed with respect to rural and urban population residing in same country (66, 68). Cointois et al (69-70) reported 13% lower reference values of Apolipoprotein-A1 in white American men (mean 134 mg/dl) compared to white women (mean 154 mg/dl), whereas mean Apo-B values were significantly higher in white American men (103 mg/dl) than the mean for white women (96 mg/dl). Report from Finland (71) and Sweden (72) documented higher value of Apo A-I and lower value of Apo B in their women compare to men in their respective population. The comparative data among men from different population indicated highest concentration of Apo A-I in Iran followed by US, Finland, Japan, Sweden and India. The comparative data among women indicated highest Apo A-1 in Finland followed by US, Sweden, Japan and Indian. Men in Sweden had highest value of Apo B followed by men in Finland, China, India and Iran. Among women the highest Apo B was observed in Sweden followed by Finland, China, India and Japan. Comparison of our results on 1923 healthy Indians (1161 men and 762 women) from city of Hyderabad (south India) with earlier reports from city of Bombay (western part of India) on 652, healthy Indians (375 men and 277 women) have revealed striking variations, such as significantly higher concentration of total cholesterol, LDL- C in both genders and significantly higher mean HDL in women study group of Mumbai. Contrary to this, mean values of TG were higher in both men and women in our study compared to Mumbai study group. Reference Intervals for all lipid and lipoprotein parameters will immensely help in assessing associated risk for cardiovascular and cerebrovascular diseases in India. Additionally, our results may be beneficial in future in formulating medical decision limits for serum lipids and Apolipoproteins pertaining to Indian population. The National Cholesterol Education program (NCEP) in US involved about forty partners from private and public sectors and combined both public health, clinical or a high risk approach. The public health approach promoted life style modification habits leading to healthy heart whereas clinical risk approach was reflected in formulating Adult Treatment Panel I, II & III guidelines for cholesterol management. ATP III recommended assessment of the prospective ten year risk for CHD in patients with 2 or more risk factors e.g. cigarette smoking, hypertension, low HDL cholesterol, diabetes, advancing age or family history of premature CHD. The NCEP experts highlighted 1) Appropriate medical decision cut off limits for all lipid analytes in individuals with and without associated risk factors. 2) Future risk assessment and 3) importance of various life style modifications.

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