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PLASMA LIPOPROTEIN COMPOSITION IN DIFFERENT TYPES OF HYPERLIPOPROTEINEMIAS IN NORTHERN INDIA

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SUMMARY

In fasting plasma of 35 healthy normal subjects and 52 subjects with hyperlipidemia, lipoprotein electrophoresis was carried out and complete analysis of lipids was done for total cholesterol, cholesterol in three major fractions of lipoproteins i.e. VLDL, LDL and HDL, total triglycerides and uric acid. A comparison between control values for Indian and Western population showed high total cholesterol, LDL cholesterol and HDL cholesterol values in Western population and high total triglyceride values in Indian population. VLDL difference is non-significant.

A comparison between control and hyperlipoproteinemic Indian population, show that all cholesterol fractions change significantly except HDL and LDL cholesterol in type IV patients. Triglyceride changes are significant. Uric acid changes are non-significant except in type II-B patients. Range of values is provided. A comparison between hyperlipoproteinemic values for Indian and Western population showed high values of VLDL cholesterol in Indian population and high values of LDL and HDL cholesterol in Western population except for non-significant changes in type II-B patients for HDL contents.

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INTRODUCTION

Hyperlipidemias are known to be associated with various disease processes like coronary artery disease (CAD), diabetes mellitus (DM), obesity (O), etc. The concentration of total cholesterol and triglycerides in plasma are commonly measured to evaluate the presence of hyperlipidemias which gives indication to the lipoprotein abnormalities. Since plasma lipids do not circulate free in the body and are bound to proteins as lipoproteins, the diagnosis and the management of hyperlipidemias in terms of lipoproteins has been associated with lipoprotein electrophoresis in combination with lipoprotein quantitation for its major fractions viz. VLDL, LDL and HDL.

In India, though considerable data is available on serum cholesterol and triglycerides in health and disease[1-4] no data is available on plasma lipoprotein composition in different types of hyperlipoproteinemias on the basis of lipoprotein phenotyping.

The present study was undertaken to quantitatively study the lipoprotein pattern in normal northern Indian population and a heterogenous group of patients with hyperlipoproteinemias classified on the basis of lioprotein phenotyping with a view to establish any correlation that may exist in various groups and to compare these values with Western literature.

MATERIAL AND METHODS

Thirty-five normal healthy subjects with no manifestation of any disease and 52 subjects with different disease status i.e. obesity, diabetes mellitus and coronary artery disease either alone or in combination with one another (Table 1)

TABLE 1

Group	IIA	IIB	IV	Total
Obesity	1	3	2	6
DM	3	1	1	5
CAD	7	4	4	15
O+CAD	1	4	3	8
DM+CAD	1	1	1	3
O+DM	1	3	6	10
O+DM+CAD	—	1	4	5
Total	14	17	21	52

Distribution of 52 patients according to disease status.

from middle class families were investigated for complete lipid analysis. Whereas obesity is defined as an increase in weight in excess of 10 per cent optimum weight of an individual and for this study standard height and weight chart of Life Insurance Corporation of India is referred for optimum weight of an individual. Subjects with more than 120 mg per cent fasting glucose in plasma are taken to be suffering from diabetes mellitus and subjects with known ischemic heart diseases are referred to be the one with coronary heart diseases. The venous blood sample was obtained in the morning after 12 to 14 hours of complete fasting in tubes containing 1 mg/ml disodium EDTA. Plasma was separated by centrifugation for 20 min. at 2,500 x g. Right from the time of collection of blood to the time of analysis (normally within 24 to 48 hours) the samples were kept at 4°C.

Lipoprotein quantitation was done using dual precipitation technique of Wilson and Spinger, 1973[5] to separate the major lipoprotein classes for cholesterol content. Total cholesterol in plasma as well as in three major classes of lipoproteins i.e. VLDL, LDL and HDL was determined by the method of Chiamori and Henry, 1959.[6] Triglycerides in plasma were determined by the micro-method of Van-Handel and Zilversmit, 1955.[7] Uric acid was determined by the method of Henry, 1964.[8] Lipoprotein electrophoresis on plasma samples were carried out on precasted buffered agarose gel slides by the Biogram. A Liopoprotein-A profile system obtained from Bio-rad laboratories, California and samples were classified according to Fredrickson and Lees, 1965.[9] Type II hyperlipoproteinemias are further classified as type IIA (Increase of beta lipoprotein (LDL) and type IIB (Increase of Beta (LDL) as well pre beta lipoprotein (VLDL) as per recommendations of Beaumont *et al*, 1970.[15]

RESULTS

Table 2 shows the mean concentration of total cholesterol, cholesterol in three plasma lipoprotein fractions viz. VLDL, LDL and HDL, triglycerides and uric acid in plasma of normal subjects and the patients with hyperlipoproteinemia.

Total cholesterol in normal subjects varied from 110 mg to 210 mg/100 ml with a mean of 167.37 mg/100 ml. The mean cholesterol concentration in VLDL fraction was 23.14 mg/100 ml with range of 8 to 45 mg/100 ml, in LDL fraction it was 119.02 mg/100 ml. with a range of 70 to 158 mg/100 ml and HDL fraction it was 25.20 mg/100 ml with a range of 8 to 41 mg/100 ml. The triglyceride values in normal subjects range from 60 to 180 mg/100 ml with a mean of 118.94 mg/100

TABLE 2

Group	n	Tc mg%	VLDLc mg%	LDLc mg%	HDLc mg%	TG mg%	UA mg%	CH/TG
Control	35	167.37 ± 30.5 (110 to 210)	23.14 ± 9.1 (8 to 46)	119.02 ± 24.4 (70 to 158)	25.20 ± 12.3 (8 to 41)	118.94 ± 27.85 (60 to 180)	4.14 ± 1.23 (2.4 to 7.8)	1.40
Type IIA	14	239.78 ± 35.9 (208 to 354)	33.71 ± 11.8 (20 to 60)	167.42 ± 38.2 (126 to 281)	38.64 ± 9.7 (21 to 60)	151.42 ± 60.4 (70 to 250)	4.68 ± 1.39 (2.4 to 7.8)	1.58
Type IIB	17	262.70 ± 49.5 (194 to 349)	61.94 ± 17.2 (23 to 89)	165.23 ± 40.3 (109 to 240)	34.88 ± 11.0 (16 to 54)	239.29 ± 67.1 (81 to 388)	4.93 ± 1.50 (2.4 to 7.8)	1.10
Type IV	21	237.28 ± 47.9 (151 to 347)	73.57 ± 36.0 (27 to 177)	134.47 ± 33.7 (39 to 188)	29.42 ± 8.4 (16 to 44)	250.28 ± 59.6 (123 to 368)	4.70 ± 1.22 (2.4 to 6.5)	0.95

Concentration of cholesterol (mg/100 ml) plasma and three plasma lipoprotein classes, VLDL, LDL and HDL.
Triglycerides (mg/100 ml) and Uric acid (mg/100 ml), in different groups of hyperlipoproteinemias and controls.

ml. Uric acid levels ranged from 2.4 to 7.8 mg/100 ml with a mean of 4.19 mg/100 ml. The ratio between total cholesterol and total triglycerides was 1.40 among the normals.

On the basis of lipoprotein electrophoresis, out of 52 patients studied with hyperlipoproteinemia, 27 per cent had type IIA hyperlipoproteinemia, 33 per cent had type IIB hyperlipoproteinemia and 40 per cent had type IV hyperlipoproteinemia. None had type III or type V hyperlipoproteinemia.

The mean total cholesterol concentration in type IIA hyperlipoproteinemias (14 subjects) was 239.78 mg/100 ml with a range of 208 to 354 mg/100 ml. The mean cholesterol concentration in VLDL fraction was 33.71 mg/100 ml with a range of 20 to 60 mg/100 ml, in LDL fraction it was 167.42 mg/100 ml with a range of 126 to 281 mg/100 ml and in HDL fraction it was 38.64 mg/100 ml with a range of 21 to 60 mg/100 ml. Mean triglyceride levels in type IIA hyperlipoproteinemias were 151.42 mg/100 ml with range from 70 to 250 mg/ml. and mean uric acid level were 4.68 mg/100 ml with a range of 2.4 to 7.8 mg/100 ml. The ratio between total cholesterol and total triglycerides was 1.58 among the type IIA hyperlipoproteinemias.

Total cholesterol in type II hyperlipoproteinemias (17 subjects) varied from 194 to 394 mg/100 ml with a mean of 262.70 mg/100 ml. The mean cholesterol concentration in VLDL fraction was 61.94 mg/100 ml with a range of 23 to 89 mg/100 ml, in LDL fraction it was 165.23 mg/100 ml with range of 109 to 240 mg/100 ml and in HDL fraction it was 34.88 mg/100 ml, with range of 16 to 54 mg/100 ml. The triglyceride values in type II_B hyperlipoproteinemias ranged from 81 to 388 mg/100 ml, with a mean of 239.29 mg/100

TABLE 3.—*Comparison between Indian and Western population control*

	Tc mg%	VLDLC mg%	LDLC mg%	HDLC mg%	TG mg%
Indian Population n-35	167 ± 31	23 ± 9	119 ± 24	25 ± 12	119 ± 23
Western Population n-50	210 ± 33	21 ± 13	143 ± 27	48 ± 11	78 ± 39
t	6.13	0.84	4.30	9.01	5.63
p	<0.001	N.S.	<0.001	<0.001	<0.001

ml. Uric acid levels ranged from 2.4 to 7.8 mg/100 ml with a mean of 4.93 mg/100 ml. The ratio of total cholesterol to total triglycerides was 1.10 among the type II_B hyperlipoproteinemias.

Total cholesterol in type IV hyperlipoproteinemias (21 subjects) varied from 151 to 347 mg/100 ml with a mean of 237.24 mg/100 ml. The mean cholesterol concentration in VLDL fraction was 73.53 mg/100 ml with range of 27 to 177 mg/100 ml in LDL fraction it was 134.47 mg/100 ml. with a range of 39 to 188 mg/100 ml and in HDL fraction it was 29.42 mg/100 ml with range of 16 to 44 mg/100 ml. The triglyceride values in type IV hyperlipoproteinemias ranged from 123 to 368 mg/100 ml. Uric acid values ranged from 2.4 to 6.5 mg/100 ml with a mean of 4.70 mg/100 ml. The ratio of total cholesterol to total triglycerides was 0.95 among the type IV hyperlipoproteinemias.

DISCUSSION

The values of total cholesterol, triglycerides and uric acid reported here are comparable to earlier values published in India by Bandhopadhyay and Banerjee, 1964[2] and Mathur *et al*, 1960.[3] Comparison of lipid values of healthy Indian population with an average age of 36 years to the Western healthy population of 30 to 39 years[10] show that there are significantly higher mean values of total cholesterol, LDL cholesterol and HDL cholesterol in Western population and significantly higher triglyceride mean values in Indian population (Table 3). There is no significant difference of VLDL cholesterol values among the two populations. The differences noted in two populations may be because of dietary habits, socio-economic condition, seasonal and geographic variations. Padmawati *et al* (1959),[4] demonstrated the influence of various socio-economic groups on the cholesterol levels in Indian population. Bandhopadhyay and Banerjee, 1964[2] gave a normal value of triglycerides to be 125 ± 16 mg per cent in Indian population. It is important to note that the difference in triglycerides values is significant among Indian and Western populations whereas VLDL values are similar. This difference may be due to greater availability of carbohydrates in the diets of the Northern Indian population which allows higher production of glycerophosphate required for the synthesis of triglycerides. The difference in two diet is being looked into for further studies.

Table 4 shows the statistical significance between the control group and hyperlipoproteinemic groups for concentractions of total cholesterol, cholestarol in three major fractions of lipoproteins, total triglycerides and uric acid. Changes in lipid fractions are significant in all the hyperlipoproteinemic group except for LDL and HDL cholestarol in comparison to normal controls. Uric acid changes are

TABLE 4.—*Significant changes between control group and different types of hyperlipoproteinemias*

Groups	Control vs type IIA t= p=	Control vs type IIB t= p=	Control vs type IV t= p=
Tc	7.14	7.29	2.47
	<0.001	<0.001	<0.001
VLDLC	3.37	5.87	15.69
	<0.01	<0.001	<0.001
LDLc	4.39	4.45	1.83
	<0.001	<0.001	N.S.
HDLc	3.65	2.75	1.38
	<0.001	<0.05	N.S.
T.G.	3.90	7.10	9.49
	<0.001	<0.001	<0.001
U.A.	1.34	2.03	1.59
	N.S.	<0.05	N.S.

significant with type IIB group and non significant with type IIA and type IV groups.

Type IIB and type IV have increased cholesterol and triglyceride values whereas type IIA has only increased cholesterol values as compared to control. Cholesterol contents in type IIB are higher than type IV group. Since both cholesterol and triglycerides are independent risk factors for ischemic heart disease, the risk factor involved is more in type IIB group followed by type IV group and type IIA group, more also because of high LDL cholesterol and low HDL cholesterol, Gordon *et al*, 1977[16] demonstrated an inverse relationship of HDL cholesterol with incidence of coronary heart disease ($p < 0.001$). Carlson and Bottiger, 1972[11] also suggested in their data that group IIB carries the highest risk factor followed by group IV and group IIA.

VLDL cholesterol is associated with increase in triglyceride values in direct proportion in all types of hyperlipoproteinemias. Type IIA and type IIB groups have identical LDL cholesterol but triglycerides values are more in type IIB group. LDL cholesterol in type IV group has an inverse relation with triglyceride values. Myyers *et al*, 1976[12] and Carlson 1976[13] has provided data to show inverse relation between LDL cholesterol and triglycerides values in patients with type IIA, type III and types IV hyperlipoproteinemias.

Table 5 shows a comparison between the Indian hyperlipoproteinemias and the Western hyperlipoproteinemias (data

TABLE 5.—*Comparison of values for Indian and Western population hyperlipoproteinemias*

Group	n	VLDL mg%	LDL mg%	HDL mg%
IIA Indian	14	34 ± 12	167 ± 38	39 ± 10
Western	54	24 ± 10	246 ± 6	46 ± 1
		t3.11 xx	t7.76 xxx	t2.62 x
IIB Indian	17	62 ± 17	165 ± 40	35 ± 11
Western	12	52 ± 4	229 ± 3	39 ± 2
		t2.33 xx	t6.57 xxx	t1.47 N.S.
IV Indian	21	74 ± 36	134 ± 34	29 ± 8
Western	65	53 ± 4	149 ± 5	38 ± 1
		t2.67 xx	t2.01 x	t5.17 xxx

x, xx, xxx indicates that the different between two hyperlipoproteinemias was significant at 5, 1 and 0.1% level respectively.

provided by Carlson, 1975[14] on asymptomatic accidently discovered hyperlipoproteinemias and various atherosclerotic manifestated hyperlipoproteinemias) for cholesterol concentrations in three lipoprotein fractions viz. VLDL, LDL and HDL. VLDL cholesterol is significantly more in all the three types of Indian hyperlipoproteinemias i.e. type IIA, type IIB and type IV. Since VLDL contains 50 to 80 per cent of triglycerides, the higher values of triglycerides in Indian population is well justified. High VLDL cholesterol concentration may be also used as an indication of high triglycerides. LDL cholesterol is more in type IIA and type IV patients with non significant difference in type IIB patients from Western population.

From Table I it is clear that fifty per cent of the patients with CAD and 21 per cent with DM fall in type IIA hyperlipoproteinemias; 18 per cent of patients with obesity; 24 per cent with CAD, and 24 per cent with both obesity and CAD besides 18 per cent with obesity and DM fall in type IIB hyperlipoproteinemias and 19 per cent of patients with CAD, 10 per cent with obesity, 14 per cent with CAD and 48 per cent with obesity and DM fall in type IV hyperlipoproteinemias. Type IIB which has highest risk factor has patients with obesity and CAD alone or in combination. Type IV with little less risk has patients with CAD, obesity and DM or in combination and type IIA which involves comparatively less risk factor has patients with CAD and DM alone. It is difficult to set up a pattern of hyperlipoproteinemias on the basis of disease status as such with such a small number of group but the importance of obesity along with coronary artery disease in pathogenesis and management of hyperlipoproteinemias cannot be ignored.

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