

Hyperlipidemia In Patients With Chronic Renal Failure

By

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SUMMARY

Fasting levels of plasma cholesterol, triglycerides, lipoproteins, sugar and post-heparin lipolytic activity (PHLA) were measured in 40 chronic renal failure (C.R.F.) patients. Out of these 40 patients, 20 were being managed conservatively (Group II) and 20 were on regular hemodialysis (Group III). Twenty healthy persons were included in the study as controls (Group I). Fasting hypertriglyceridemia was seen in 50% of Group II and 35% of the Group III patients. Majority of these patients having hypertriglyceridemia belonged to Type IV pattern of hyperlipoproteinemia as per Fredrickson's classification. The most striking finding was the low values of PHLA, a measure of lipoprotein lipase in both the groups of patients (90% in Group II and 45% in Group III).

INTRODUCTION

With the improvement in conservative management and dialysis, the life span of patients with chronic renal failure (CRF) has increased. As the patient's survival has approached the 10 year mark, there is an increasing indication that accelerated atherosclerosis may remain a major unresolved problem threatening the longevity of CRF patients.⁸ With the implication of plasma lipids in the pathogenesis of atherosclerosis and ischaemic heart disease,¹¹ it becomes worthwhile to study the behaviour of various lipid fractions in C.R.F. patients. Hyperlipidemia in C.R.F. patients, whether on regular dialysis or being managed conservatively, is well known in the western popula-

tion.^{2,3,5,10,15} However, the two studies conducted so far in India have failed to show any lipid abnormality in C.R.F. patients.^{11,14} In view of these conflicting findings the present study was undertaken and the findings reported.

MATERIAL AND METHODS

Forty patients of chronic renal failure who were either admitted or being followed up in the nephrology department of the K.E.M. Hospital, Bombay were studied. Twenty normal persons were included as healthy controls (Group I). Out of the 40 patients, 20 were undialysed patients, being managed conservatively (Group II) and the other 20 were on regular hemodialysis (Group III). The

3 groups of patients studied were comparable as regards to the age and sex distribution. The male to female ratio in the 3 groups was 2.3:1. Their ages varied between 16 and 55 years.

Patients having a proteinuria of 3 gm or more per day or serum albumin of less than 3 gm% were excluded from the study since nephrotic syndrome itself is known to produce lipid abnormalities. Similarly, diabetic patients and persons who were obese (body weight > ideal body weight by 10%), were not included in the study. Patients who were on drugs like steroids which are known to alter serum lipids were excluded from the study. All patients of C.R.F. were stable (their body weight was more or less the same over a period of 7 days). They were not having any infection and were on good oral intake without vomiting. In majority of patients, the C.R.F. was due to tubulointerstitial disease or chronic glomerulonephritis.

In the dialysed group, patients had received, on an average, twenty hemodialyses at the time of the study. All these patients were dialysed with Meltec (1 sq.m.) or TMI (0.6 sq.m.) parallel flow dialysers for 6 hours per dialysis, using glucose and acetate-free dialysate. 5000-8000 units of heparin were injected during each dialysis.

A detailed dietetic history was recorded in all the patients. Blood was collected after an overnight fast of 12 hours, for estimations of cholesterol, triglycerides, free fatty acids, lipoproteins and blood sugar. Ten units of heparin per kg. of body weight were injected intravenously and blood was collected 10 minutes later for estimation of post-heparin lipolytic activity (PHLA). All blood samples were collected with proper anticoagulants and

transported immediately to the laboratory. The plasma lipids were estimated by the following methods.

1. Plasma cholesterol was estimated by the method of Abell *et al.*¹
2. Plasma triglycerides were estimated by the method of Van Handel.¹⁶
3. Free fatty acids were estimated in Doles' extract by using cobalt soap formation method.¹³
4. Lipoprotein electrophoresis was performed on agarose gel using barbitone buffer (pH = 8.6, ionic strength $\mu = 0.05$). Slides were stained by Sudan Black and scanned on Joyce-Lobel Chromoscan.¹²
5. Post-heparin lipolytic activity (PHLA) was measured using corn oil and tween 60 as substrate. The activity was expressed in terms of free fatty acids released per minute after the incubation of plasma with the substrate at 37°C (pH: 8.5) for 1 hour.⁷

RESULTS

Lipid abnormalities in C.R.F.

As seen in Table 1, the levels of fasting free fatty acids were significantly lower in the dialysed group of patients ($p < 0.05$). The fasting serum triglycerides were significantly elevated in both the groups of renal failure patients ($p < 0.02$). The percentage of alpha lipoproteins and PHLA were significantly lower in the undialysed group of patients ($p < 0.02$ and < 0.001 respectively).

Considering the individual values, 50% of the patients in the undialysed group and 35% in the dialysed group had elevated serum triglycerides (Tables 2 and 3).

TABLE 1
Values of serum lipids and blood sugar (Mean \pm Standard Deviation)

Parameter	Control	Undialysed patients	Dialysed patients	Sharma et al ¹⁴	Mani et al ¹⁹	
					Undialysed	Dialysed
1. Free fatty acids (mEq/L)	1.260* ± 0.982	1.061 ± 0.389	0.775* ± 0.440	—	—	—
2. Serum cholesterol (mg%)	184.000 ± 26.190	192.150 ± 47.320	185.550 ± 63.600	185.50 ± 63.60	172.25 ± 29.15	185.04 ± 29.06
3. Serum triglycerides (mg%)	107.350 ± 39.060	150.000** ± 66.170	144.650** ± 51.450	96.40 ± 16.80	90.31 ± 46.60	97.10 ± 48.45
4. Lipoproteins %						
Alpha	30.390 ± 6.710	18.936** ± 6.990	21.600 ± 6.521	32.10 ± 7.96	23.69 ± 3.22	23.82 ± 2.27
Beta	52.078 ± 6.125	62.270 ± 0.078	58.390 ± 7.430	67.90 ± 7.96	55.66 ± 4.13	55.79 ± 4.29
Prebeta	17.240 ± 3.730	19.198 ± 5.590	19.000 ± 7.000	—	—	—
5. PHLA (mEq/ml./min.)	0.179 ± 0.0105	0.119*** ± 0.037	0.162 ± 0.042	—	—	—
6. Blood sugar (mg%)	84.620 ± 24.010	88.950 ± 21.050	86.000 ± 26.150	—	—	—
7. Caloric intake (K. Cal./day)	—	1840 ± 460	2200 ± 345	1000-1500	—	2360 —
8. Ratio of poly-unsaturated to saturated fatty acids	—	1 : 1.12	1 : 1.36	—	—	1.26 : 1

* $p < 0.05$.** $p < 0.02$.*** $p < 0.001$.

TABLE 2

Values for serum triglycerides and PHLA in individual patients studied in Group II

Patient Number	Serum triglycerides (mg%)	PHLA (meq./ml./min.)
1	90	0.150
2	100	0.190
3	105	0.190
4	100	0.110
5	180	0.110
6	182	0.150
7	104	0.150
8	196	0.100
9	200	0.110
10	200	0.090
11	250	0.090
12	180	0.110
13	200	0.150
14	48	0.070
15	85	0.112
16	269	0.110
17	78	0.110
18	169	0.050
19	130	0.120
20	85	0.090

TABLE 3

Values for serum triglycerides and PHLA in individual patients studied in Group III

Patient Number	Serum triglycerides (mg%)	PHLA (meq./ml./min.)
1	130	0.115
2	150	0.210
3	40	0.184
4	90	0.220
5	130	0.080
6	145	0.190
7	120	0.160
8	300	0.180
9	136	0.110
10	150	0.154
11	140	0.160
12	120	0.150
13	165	0.120
14	100	0.200
15	145	0.210
16	220	0.170
17	130	0.220
18	140	0.140
19	152	0.080
20	190	0.180

In Group II out of the 10 patients having hypertriglyceridemia, 6 had elevated pre-beta lipoproteins indicative of Type IV hyperlipoproteinemia of Fredrickson's

classification.⁴ The remaining 4 had Type IIb pattern. In group III, out of the 7 patients having hypertriglyceridemia, 4 had elevated prebeta lipoproteins indica-

TABLE 4

The caloric intake and fat ratio in patients with and without lipid abnormalities (Mean \pm Standard deviation)

Parameter	Undialysed patients		Dialysed patients	
	With hypertriglyceridemia (N = 10)	Without hypertriglyceridemia (N = 10)	With hypertriglyceridemia (N = 7)	Without hypertriglyceridemia (N = 13)
Caloric intake (K. Cal./day)	1930 ± 370	1750 ± 550	2310 ± 320	2090 ± 370
Ratio of polyunsaturated to saturated fats	1 : 1.18	1 : 1.06	1 : 1.49	1 : 1.23

tive of Type IV pattern and the other three had Type IIb pattern of hyperlipoproteinemia. The most striking result was the low values of PHLA in 90% of the patients in Group II and 45% of patients in Group III (Table 2 and 3).

As seen in Table 4, there was no statistically significant relationship between the hypertriglyceridemia and the caloric intake in both the groups of patients. However, the intake of saturated fats was more in patients with hyperlipidemia.

DISCUSSION

Hyperlipidemia, manifested as turbidity of plasma after an overnight fast, has been recognised in patients with uremia over a century. However, only recently it has been possible to identify the exact type of lipid abnormality and the underlying mechanism. Fasting hypertriglyceridemia is a well known abnormality in C.R.F. patients of western population.^{2, 3, 10, 15} The majority of these patients belong to Type IV pattern of hyperlipoproteinemia.^{2, 5, 10} Bagdade *et al*² originally found both increased synthesis and decreased clearance of very low density lipoprotein (VLDL), in uremic patients as a cause of hypertriglyceridemia. Although the relative importance of increased synthesis *versus* decreased clearance of VLDL has not been quantified, recent emphasis has shifted towards the latter. Decreased lipoprotein lipase detected as PHLA, has been confirmed in both dialysed and undialysed patients and appears to be one of the most consistent findings.^{3, 8}

In India, Mani *et al*⁹ did not find any lipid abnormality in patients of chronic renal failure either on regular hemodialysis or being managed conservatively. They attributed this to the low calories derived from carbohydrates and the high

intake of polyunsaturated fatty acids in the diet. (Ratio of polyunsaturated fatty acids to saturated fatty acids was 1.26:1). Similarly, Sharma *et al*¹⁴ also did not find any lipid abnormality in patients of C.R.F. being managed conservatively. The caloric intake of these patients was quite low (1000-1500 K.Cal./day). In both these studies PHLA was not measured.

On a close scrutiny, the results of the present study are not grossly different from the previous two Indian studies (Table 1). Although a significant proportion of the patients (50% in the undialysed group and 35% in the dialysed group) had hypertriglyceridemia, the mean values of triglycerides in the undialysed group was only 150 mg% (S.D. \pm 66.17 mg%) compared to 144.65 mg% (S.D. \pm 51.45 mg%) in the dialysed group. Also the highest values of triglycerides in the undialysed group was 269 mg% and in the dialysed group 300 mg%. Hence it can be seen that the degree of hypertriglyceridemia in our population is less although the type of hyperlipoproteinemia is same as in the western population.^{2, 3, 10, 15} This may be related to the dietary pattern in the form of high intake of polyunsaturated fatty acids. It can be postulated from the Indian studies including the present one that diet apparently plays an important role in the genesis of hyperlipidemia in C.R.F.

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