LIPID ABNORMALITIES IN CHRONIC RENAL FAILURE

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ABSTRACT :

Lipid abnormalities remain to be a major cause of early mortality in patients with chronic renal failure (CRF). In present study, 114 (one hundred fourteen) CRF patients without any additional cause of dyslipidemia were divided into groups on the basis of etiologies of CRF. Blood samples from each group were analyzed for total cholesterol, triglyceride and HDL cholesterol along with blood urea nitrogen and serum creatinine. 25 healthy individuals without any obvious disease were taken as control. Patients from all the groups showed a marked hypertriglyceridemia of $232 (SD \pm 77)$ mg/dl ($P < 0.001$) as compared to control. Levels of HDL cholesterol were found to be significantly low $20 (\pm 11)$ mg/dl ($p < 0.001$) in all the groups. LDL cholesterol showed an increase $104 (\pm 30)$ mg/dl as compared to control group which is not statistically significant. Present study reveals that, CRF patients show an uniform dyslipidemia irrespective of etiologies leading to CRF. This dyslipidemia is also independent of serum creatinine levels. Although, these lipid abnormalities may not solely cause mortality in CRF patients, they may act as modulators in accelerating atherogenesis which in turn cause early mortality in CRF patients.

Keywords : Chronic Renal Failure (CRF), High Density Lipids (HDL), Low Density Lipids (LDL), Dyslipidemia, Atherogenesis.

INTRODUCTION

Lipid abnormalities in CRF patients have been reported since long. Hypertriglyceridemia is the most common lipid abnormality in patients with renal failure (1). The major cause of death in about 30-65% of CRF patients is atherosclerotic cardiovascular disease with various predisposing factors like diabetes mellitus, essential hypertension and proteinuria (2). Abnormalities of lipids and lipoproteins occur early in clinical course of patients, but they are not always reflected by hyperlipidemia. Prospective studies suggest that, dietary and/or pharmacological interventions of lipids and lipoproteins provide beneficial effects on cardiovascular events (3). It is not clear that, underlying lipid abnormalities are linked to renal impairments. The mechanisms which contribute to lipid abnormalities in CRF patients are not clearly understood. It is possible that, there is a genetic link between the two abnormalities, or kidney themselves play an important role in lipid

metabolism which is disturbed by onset of proteinuria (4). Increased LDL levels, decreased HDL levels have been reported in patients with diabetes and microalbuminuria. Nondiabetic patients with overt proteinuria also have marked lipid abnormalities (5).

The aim of present study is to further elucidate relationship between dyslipidemia and various etiologies which lead to chronic renal failure.

MATERIALS AND METHODS

Study subjects :

114 patients with end-stage renal disease (ESRD) aged 25-65 years were admitted in the nephrology ward of Cholthram Hospital & Research Centre. These patients (86 men & 28 women) were divided into various groups on the basis of etiologies which resulted in end-stage renal disease. These groups were :

(i) Chronic Glomerulonephritis (CGN) with CRF ($n = 31$), (ii) Chronic Interstitial nephritis (CIN) with CRF ($n = 26$), (iii) Hypertensive Nephrosclerosis (HTN) with CRF ($n = 17$), (iv) Diabetic Nephropathy with CRF ($n = 26$), (v) Others ($n = 14$) which included

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patients with renal calculus disease, Polycystic kidneys and cancer of some organ resulting in CRF and (vi) Acute renal failure (ARF) ($n = 10$). Patients receiving hemodialysis, beta blockers, Angiotensin Converting Enzyme (ACE) inhibitors, androgens or any drugs affecting lipid metabolism were excluded from study.

25 healthy volunteers aged 30-55 years who had no previous history of diabetes, dyslipidemia or any other disease were taken as control. Fasting blood of these subjects was analyzed for cholesterol, triglyceride and HDL cholesterol to establish the normal range.

Estimation of blood constituents

Fasting blood was obtained from all the patients. Blood urea nitrogen and serum creatinine were measured by Urease GLDH Kinetic and Jaffe' Kinetic method respectively on autoanalyzer to assess renal functions.

Total cholesterol was measured by CHOD-PAP method and triglyceride was measured by Trig-GPO-PAP method respectively utilizing reagents manufactured by Boehringer Mannheim Ltd., Mannheim, Germany, on Hitachi-704 autoanalyzer. HDL cholesterol was measured by CHOD-PAP Method using phosphotungstic acid and magnesium chloride as precipitating reagents, on autoanalyzer, LDL cholesterol was calculated by Friedewald formula (6).

Statistical analysis were performed using unpaired student's t-test calculating significance for each group.

RESULTS

Patients divided into various groups on the basis of etiologies which led to CRF showed a significant hypertriglyceridemia HDL Cholesterol levels were also significantly reduced (table 1) in all the groups as compared to control group.

Patients with chronic glomerulonephritis ($n = 31$) showed cholesterol levels in upper normal range. Hypercholesterolemia was observed in few cases irrespective of triglyceride levels. The ratio of total cholesterol to HDL Cholesterol, the risk ratio was 2.6 times higher as compared to control group. The patients with chronic interstitial nephritis ($n = 26$) also showed similar results. The risk ratio was 2.5 times higher as compared to control group. Patients

with hypertensive nephrosclerosis ($n = 17$) showed a marked hypercholesterolemia ($p < 0.01$). LDL cholesterol levels were also increased ($P < 0.01$). Patients with diabetic nephropathy ($n = 26$). Showed highest triglyceride and lowest levels of HDL cholesterol as compared to the rest of the groups. Risk ratio was 3.0 times higher as compared to control group.

In the present study, it is clear that patients with CRF show almost similar dyslipidemia irrespective of etiologies of CRF. Now, a question may arise about relationship between dyslipidemia and degree of renal dysfunction. Serum creatinine remains to be reliable source of assessment of renal function. So, patients of various groups were divided into subgroups on the basis of creatinine levels (table 2).

It is seen from table 2, that the altered values of various lipid parameters like total cholesterol, triglyceride and HDL cholesterol are not reflected by changes in the plasma creatinine levels.

DISCUSSION

Chronic renal failure is frequently associated with abnormalities of lipid metabolism. The mechanisms of these abnormalities in uremic patients are incompletely understood. Experimental studies suggest that nondiabetic subjects with overt proteinuria have marked lipid abnormalities. Increased LDL and decreased HDL have been reported earlier. There is a direct link between proteinuria and abnormalities of lipid profile. Non-diabetic subject with proteinuria have 5 fold increased risk of myocardial infarction (7-8). Autopsy studies have suggested significant relationship between global glomerulosclerosis and atherosclerosis (5). In present study, analysis of data of lipid parameters obtained from 20 CRF patients who died within 3 months of this study suggest that, a sharp decrease in HDL levels can be an important pre-disposing factor of early mortality in CRF patients (Figure).

Prospective studies also suggest correlation between hypertension & hyperlipidemia and they both influence progression of ESRD. There is a relationship between diabetes, hypercholesterolemia and loss of renal function (9-10).

Present study suggests that dyslipidemia is observed in CRF patients irrespective of etiologies and severity of renal dysfunction indicated by serum creatinine levels. All the CRF patients are at risk of accelerated atherosclerotic heart disease.

Table - 1 : Showing cholesterol, triglyceride, HDL & LDL cholesterol levels in various groups of CRF patients and healthy control group.

Group	Cholesterol mg/dl	Triglyceride mg/dl	HDL cholesterol mg/dl	LDL cholesterol mg/dl
1. Chronic glomerulonephritis (n = 31)				
Mean	172	229	21	102
($\pm$ SD)	± 34	± 62	± 11	± 31
P Value	0.10 N.S.	<0.001	<0.001	0.10 N.S.
2. Chronic-interstitial nephritis. (n = 26)				
Mean	173	230	21	96
($\pm$ SD)	± 49	± 82	± 09	± 21
P Value	N.S.	< 0.001	< 0.001	N.S.
3. Hypertensive nephrosclerosis. (n = 17)				
Mean	196	234	26	129
($\pm$ SD)	± 56	± 75	± 10	± 38
P Value	0.01	< 0.001	< 0.001	0.001
4. Diabetic nephropathy (n = 26)				
Mean	151	256	15	93
($\pm$ SD)	± 32	± 90	± 10	± 21
P Value	N.S.	< 0.001	< 0.001	N.S.
5. Others. (n = 14)				
Mean	176	189	26	115
($\pm$ SD)	± 34	± 43	± 8	± 34
P Value	0.05 N.S.	< 0.001	< 0.001	0.05 N.S.
6. Acute renal failure (n = 14)				
Mean	167	226	20	97
($\pm$ SD)	± 24	± 76	± 10	± 22
P Value	N.S.	< 0.001	< 0.001	N.S.
7. All patients (n = 114)				
mean	171	232	21	104
($\pm$ SD)	± 43	± 77	± 11	± 31
8. Healthy Controls (n = 25)				
Mean	157	86	48	89
($\pm$ SD)	± 26	± 28	± 10	± 25

P value calculated with respect to controls. P value < 0.05 is treated as significant. (N.S.—Not significant)

Table-2 : Showing Cholesterol, triglyceride, HDL & LDL cholesterol levels in various groups of CRF patients subgrouped on the basis of serum creatinine levels.

Group	Subgroup Creatinine mg/dl	Total Cholesterol mg/dl	Serum Triglyceride mg/dl	HDL Cholesterol mg/dl	LDL Cholesterol mg/dl
1. Chronic glomerulonephritis (n = 31)	< 5.0 (n = 5)	169 ± 30	234 ± 38	17 ± 8	98 ± 31
	5.0-10.0 (n = 19)	183 ± 34	244 ± 62	22 ± 11	102 ± 34
	> 10.0 (n = 7)	165 ± 21	200 ± 32	25 ± 6	105 ± 17
2. Chronic Interstitialnephritis (n = 26)	< 5.0 (n = 4)	203 ± 34	180 ± 45	21 ± 8	107 ± 21
	5.0-10.0 (n = 15)	172 ± 35	244 ± 72	21 ± 8	96 ± 25
	> 10.0 (n = 7)	167 ± 24	221 ± 70	27 ± 10	93 ± 16
3. Hypertensive Nephrosclerosis (n = 17)	< 5.0 (n = 4)	192 ± 20	206 ± 46	17 ± 9	128 ± 19
	5.0-10.0 (n = 7)	214 ± 39	243 ± 70	24 ± 11	146 ± 30
	> 10.0 (n = 6)	170 ± 39	207 ± 70	29 ± 4	118 ± 31
4. Diabetic nephropathy (n = 26)	< 5.0 (n = 4)	139 ± 28	315 ± 60	05 ± 1	—
	5.0-10.0 (n = 15)	155 ± 28	258 ± 68	18 ± 11	90 ± 20
	> 10.0 (n = 7)	155 ± 32	180 ± 29	22 ± 9	94 ± 23

(Figure) Scattergram showing values of triglyceride, HDL cholesterol and creatinine in 20 patients who died within 3 months of study.

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