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Original research article

Study of biochemical abnormalities in chronic kidney disease

[1]Dr. Prakash D, [2]Dr. Devaraja GN, [3]Dr. Shameen Samad

[1]Senior Consultant and Head, Department of General Medicine, DNB Institute of Chitradurga, Hospital, Chitradurga, Karnataka, India

[2]Senior Consultant, Department of General Medicine, DNB Institute of Chitradurga, Hospital, Chitradurga, Karnataka, India

[3]Post-Graduate (DNB), Department of General Medicine, DNB Institute of Chitradurga, Hospital, Chitradurga, Karnataka, India

Corresponding Author: Dr. Prakash D

Abstract

Normally the adult patient is unaware of advancing kidney disease until the GFR has declined to 20ml/min. At this stage, adherence to strict therapeutic principles is of utmost importance to prevent the complications of CKD. It is an observational cross-sectional study of alterations in lipid profiles in patients with kidney disease of duration more than 6 months. An estimation of total cholesterol, triglycerides, serum HDL, cholesterol and VLDL cholesterol was done by enzymatic method by using an autoanalyser in District Hospital Hi-Tech Laboratory. In Renal Function Test, there was a significant difference in all the parameters in the two groups. The Blood urea and Serum creatinine levels were significantly higher in the cases as compared to controls [124.64 (SD=45.46) v/s 15.80 (SD=3.873) and 6.55 (SD=3.727) v/s 0.796 (SD=0.187) respectively]. The difference in Serum Protein was small, but statistically significant [6.248 (SD=0.654) v/s 6.612 (SD=0.364), $p<0.001$]. Similar was the case for Serum Albumin where there was a small but statistically significant difference [3.392 (SD=0.539) v/s 3.960 (SD=0.355); $p<0.001$].

Keywords: Biochemical abnormalities, chronic kidney disease, GFR

Introduction

Many forms of renal disease tend to produce similar anatomic changes. The anatomic interdependence of component parts of the kidney implies that damage to one will secondarily affect the others. Blood vessels affect the glomeruli and glomeruli affect the tubules. Thus there is a tendency for all forms of renal disease to ultimately destroy all the four components of the kidney, culminating in what is called as "end stage kidney". By this time, it is difficult to differentiate one disease entity from another, both clinically and morphologically [1].

In the very early stages, changes of the corresponding disease will be seen. Morphologically, the kidney in chronic kidney disease is a "contracted kidney". It is small and appears granular.

Histologically there is gross destruction of the renal architecture, necrosis, fibrosis, atrophy and other distortions. Changes consequent to vascular alterations are added upon these. Some glomeruli are atrophied and sclerosed. Some are hypertrophied. Tubules were characteristically shown up if they are dilated. In chronic pyelonephritis, there are also inflammatory changes in the medulla, arteriolar changes being prominent [2].

The clinical constellation of signs and symptoms of end stage kidney disease is known as the "Uremic syndrome".

Normally the adult patient is unaware of advancing kidney disease until the GFR has declined to 20ml/min. At this stage, adherence to strict therapeutic principles is of utmost importance to prevent the complications of CKD [3].

The uremic syndrome results from derangements of function of nearly all the organ systems of the body.

Basically, there are two principle theories of pathogenesis, and they are not necessarily mutually exclusive.

The first is that toxic compounds ordinarily excreted by the kidneys are retained in the blood as renal disease progresses.

The second has been termed the "Trade-off hypothesis".

A third theory, the middle molecules theory, is also supported by some workers. This theory could fit into the framework of either of the two major theories of pathogenesis [4].

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Methodology

Method

- Detailed history was taken from patients and meticulous examination was done according to prepared proforma.
- Thorough physical examination of all the systems were done.
- Previous hospital records and investigations were recorded.
- Patients were subjected for investigations wherever required.

Inclusion criteria

- All stages of stable CKD patients.

Exclusion criteria

- Critically ill patients.
- Recent worsening of CKD.
- Acute on chronic renal failure.
- Patients on lipid lowering drugs.
- Associated co-morbid conditions such as febrile illness.

Sample size: 100.

Study design

It is an observational cross-sectional study of alterations in lipid profiles in patients with kidney disease of duration more than 6 months. An estimation of total cholesterol, triglycerides, serum HDL, cholesterol and VLDL cholesterol was done by enzymatic method by using an autoanalyser in District Hospital Hi-Tech Laboratory.

Normal healthy individuals without any significant systemic medical illness, individuals with normal biochemical profile and normal USG abdomen were taken for study, however individuals with hypertension, diabetes and significant systemic medical illness were excluded from this.

For all patients urine: Albumin, Sugar, Microscopy, Specific gravity, 24 hours urinary protein was done.

Biochemical: Blood Hb%, Blood urea, serum creatinine, serum total proteins, serum albumin, serum calcium, serum phosphorus, serum electrolytes, total cholesterol, triglycerides, HDL, LDL, VLDL. Chest X-ray, ECG, Ultrasound abdomen and ECHO was done.

Results

Table 1: Age Distribution of cases and controls

Age (years)	Group		Total
	Case	Control	
<=30	14	8	22
31-40	14	32	46
41-50	42	20	62
51-60	16	28	44
61-70	10	8	18
>70	4	4	8
Total	**100**	**100**	**200**

Table 2: Sex Distribution of cases and controls

Sex	Group		Total
	Case	Control	
Female	33 (33.0%)	20(20.0%)	53 (26.5%)
Male	67 (67.0%)	80 (80.0%)	147 (73.5%)
Total	**100**	**100**	**200**

The age of the participants ranged from 19 to 80 years. Mean age was 46.24 (SD=13.747) years in the case group and 46.40 (SD=13.036) years in control group. There was no significant difference in the age of the two groups. (p=0.933). Majority of the patients were males in both groups (67% in cases and 80% in controls).

Table 3: Bio-chemical data in cases and controls

	Group	N	Mean	Std.	Mean	P-value

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				Deviation	Difference	(t- test)
Blood Urea	Case	100	124.64	45.460	108.84	<0.001
	Control	100	15.80	3.873		
Serum Creatinine	Case	100	6.550	3.727	5.740	<0.001
	Control	100	0.796	0.187		
Serum Protein	Case	100	6.248	0.654	-0.3640	<0.001
	Control	100	6.612	0.364		
Serum Albumin	Case	100	3.392	0.539	-0.5680	<0.001
	Control	100	3.960	0.355		

In Renal Function Test, there was a significant difference in all the parameters in the two groups. The Blood urea and Serum creatinine levels were significantly higher in the cases as compared to controls [124.64 (SD=45.46) v/s 15.80 (SD=3.873) and 6.55 (SD=3.727) v/s 0.796 (SD=0.187) respectively]. The difference in Serum Protein was small, but statistically significant [6.248 (SD=0.654) v/s 6.612 (SD=0.364), p<0.001]. Similar was the case for Serum Albumin where there was a small but statistically significant difference [3.392 (SD=0.539) v/s 3.960 (SD=0.355); p<0.001].

Table 4: Bio-chemical (Lipid Profile) data in cases and controls

	Group	N	Mean	Std. Deviation	Mean Difference	P-value (t- test)
TCH (mg%)	Case	100	202.86	44.977	17.380	<0.001
	Control	100	185.48	16.451		
Triglycerides (mg%)	Case	100	166.589	71.267	69.449	<0.001
	Control	100	97.140	14.143		
HDL (mg%)	Case	100	37.748	5.636	-12.732	<0.001
	Control	100	50.480	7.141		
LDL (mg%)	Case	100	134.693	46.016	16.841	<0.001
	Control	100	117.852	10.456		
VLDL (mg%)	Case	100	32.858	12.134	12.510	<0.001
	Control	100	20.348	4.035		
HDL/TCH	Case	100	0.197	0.0585	-0.0820	<0.001
	Control	100	0.279	0.0537		

In case of Lipid Profile, there was a significant difference in all the parameters in the two groups. The Total Cholesterol and Triglyceride levels were significantly higher in the cases as compared to the controls. [202.86 (SD=44.977) mg% v/s 185.48 (SD=16.451) mg% and 166.589 (SD=71.267) mg% v/s 97.140 (SD=14.143) mg%, respectively]. HDL level was significantly lower in the cases [37.748 (SD=5.6360 mg% v/s 50.480 (SD=7.141) mg%], while LDL and VLDL level were significantly higher as compared to controls [134.693 (SD=46.016) mg% v/s 117.852 (SD=10.456) mg% and 32.858 (SD=12.134) mg% v/s 20.348 (SD=4.035) mg%, respectively]. The HDL to Total Cholesterol ratio was also significantly lower in the cases as compared to controls [0.197 (SD=0.0585) v/s 0.279 (SD=0.0537)]. Lipid profile was abnormal in 54% of the cases.

Discussion

There is marginal rise of serum total cholesterol in chronic kidney disease patients compared to controls, but this rise was statistically significant (P<0.001).

Shah BV, *et al*., in their study showed no significant change in levels of total cholesterol [5].

Gerald Appel, found low values of cholesterol in CKD patients [6].

Anderson Sharon, *et al*., found hyper cholesterolemia in 20% of patients [7]. Hypercholesterolemia has long been recognized as a significant risk factor for coronary heart disease.

Attman *et al*., in this study showed no significant change in levels of total cholesterol [8].

There was decrease in HDL cholesterol seen in patients compared to controls, which was statistically significant (P<0.001)

Goldberg AP, *et al*., found decrease in HDL concentration in patients compared to controls [9].

Rapport J, Aviram M., study showed there is no decrease in HDL concentration in chronic kidney disease patients [10].

Fuh MMT *et al*., [11], found decrease in plasma HDL cholesterol concentration seen in patients with chronic kidney disease is associated with decrease in both the fractional catabolic rate and the total synthetic rate of apoAI/HDL. The worse the renal function is the slower the fractional catabolic rate and the lower the apoAI/HDL. The changes in lipoprotein lipase activity the enzyme that are responsible for VLDL-triglyceride hydrolysis may play a major role in this regard. For example lipoprotein lipase activity is decreased in patients with chronic renal failure. The lower the lipoprotein lipase activity is the lower the plasma HDL concentration. There is also evidence that patients with chronic kidney disease have a factor in the plasma which inhibits lipoprotein lipase. Thus there are several possible mechanisms

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involving an abnormality in VLDL-triglyceride hydrolysis which could result in abnormal HDL metabolism and HDL concentration in patients with chronic renal failure. Alternatively the slow fractional catabolic rate of apoAI in patients with chronic kidney disease could be a primary event resulting from a decrease in the synthesis or secretion of apoAI. ApoAI is synthesized and secreted by intestine, liver and it is certainly possible that these functions could be suppressed in patients with chronic renal failure.

There is significant raise in VLDL levels in chronic kidney disease patients compared to controls (P<0.001). Cheung AK, showed increase in very low-density lipoproteins [12].

Gerald Appel, *et al*., [6], showed normal or decrease in VLDL.

The LDL levels were marginally raised in patients as compared to controls and this was statistically significant (P<0.001).

Anderson *et al*., showed increase in LDL levels [7]. Gerald Appel, *et al*., [6], normal or decrease in LDL levels.

The concentration of the most atherogenic lipoprotein LDL is usually normal or only marginally increased. In Uremia LDL lipoproteins qualitatively altered. *In-vitro* studies have shown that LDL isolated from uremic patients is a poor ligand for the LDL apo B/E receptors.

LDL clearance is often abnormally low in patients with chronic renal failure. The delayed clearance of LDL, increases in the time of residence of LDL in the circulation. This leads to number of disturbances in the LDL metabolism modification of LDL such as carbamylation, oxidation. Internalization with glycosaminoglycans suggested to cause accelerated atherosclerosis.

Anderson *et al*., and Marion Morena *et al*., showed LDL value directly propotional to coronary heart disease [7]. In addition to abnormalities in serum total lipoprotein concentration uremic patients exhibit potentially atherogenic abnormalities in lipoprotein composition. Most notable is an elevated concentration of APO CIII. Besides, decreased concentration of APOA-I and APO-II. APO-CIII and APO-E are also abnormally distributed. These apolipoproteins are usually found in HDL, but in chronic renal failure, 60 to 80% APO CIII and APO E are found in VLDL and LDL. The shift of APO CIII from predominantly HDL particles to predominantly triglyceride rich particles represents a catabolic defect in triglyceride metabolism that results in the accumulation of a variety of remnant particles including IDL. The defect is seen even in patients of chronic kidney disease with seemingly normal lipid profiles.

There is significant reduction in HDL/TC ratio in patients compared to controls, this was statistically significant (p<0.001).

Conclusion

There is significant increase in triglyceride and VLDL concentration in CKD patients.

The HDL-cholesterol level was found to be significantly lower in CKD patients compared to control group.

Total cholesterol and LDL marginally raised in patients of CKD compared to controls.

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