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ORIGINAL ARTICLE

STUDY OF LIPID PROFILE AND HOMOCYSTEINE LEVELS IN CASES OF CHRONIC KIDNEY DISEASE

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ABSTRACT: Chronic Kidney Disease (CKD) is a spectrum of different pathophysiologic processes associated with abnormal kidney function and a progressive decline in GFR. Chronic renal failure results in profound lipid disorder which stem largely from deregulation of high density lipoprotein (HDL) and triglyceride rich lipoprotein metabolism. Hypertriglyceridemia is the most common plasma lipid abnormality in patients with renal failure, coexisting with normal cholesterol level. Plasma homocysteine is strongly correlated to Glomerular Filtration rate. High homocysteine level leads to endothelial dysfunction. It is proposed to study lipid profile and homocysteine levels as attributable risk factors for chronic kidney disease. The objective of the study is to analyze the lipid profile and homocysteine levels in cases of chronic kidney disease. This study was carried out in patients admitted to Rama Medical College & Hospital Research Centre Mandhana, Kanpur. Study sample consisted of 40 patients of chronic renal disease with renal failure and 30 age and sex matched healthy controls. Patients were arbitrarily divided into 2 groups of patients >45 years age and patients<45 years age. Prevalence of lipid abnormalities and homocysteine levels, were studied in cases and controls. In study group A, dyslipidemia is found in 18 out of 20 cases (90%). Lipid levels significantly deranged in cases than controls. Dyslipidemia was present in 90% patients in study group A and 60% subjects in study group B. Our study highlights the fact that dyslipidemia and hyperhomocysteinemia are important risk factors in patients with chronic renal disease and these abnormalities are more prevalent in patients with end-stage renal disease and more in patients with other risk factors.

KEYWORDS: Homocysteine, chronic kidney disease, dyslipidemia.

INTRODUCTION: Chronic Kidney Disease (CKD) is a spectrum of different pathophysiologic processes associated with abnormal kidney function and a progressive decline in GFR.

Classification of CRD

Stage	GFR, ml/min per 1.73m^2
0	>90a
1	>90b
2	60-89
3	30-59
4	15-29
5	<15

a = with risk factor for CKD.

b = with demonstrated kidney damage.

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Chronic renal failure is decrease in GFR to <60 ml/min/1.73 m^2 for >3 consecutive months with multiple etiologies. Chronic renal failure results in profound lipid disorder which stems largely from dysregulation of high density lipoproteins (HDL) & triglyceride-rich lipoprotein metabolism. Hypertriglyceridemia is the most common plasma lipid abnormality in patients with renal failure, coexisting with cholesterol level within normal range. The Hypertriglyceridemia associated with the nephritic syndrome results from impaired catabolism of triglyceride-rich lipoproteins while hypercholesterolemia is due to increased hepatic synthesis of apo-B containing lipoproteins. In diabetic patients, dyslipidemia was found to be a predictor of albuminuria.

Homocysteine is a sulfur containing amino acid that occurs naturally in all humans. It is broken down in body through two metabolic pathways. Plasma homocysteine is strongly correlated to Glomerular Filtration rate. Homocysteine is cleared from body by urinary excretion after glomerular filtration just like creatinine. High homocysteine levels lead to endothelial dysfunction. Identification of chronic kidney disease is a major risk factor for cardiovascular morbidity and mortality. It is proposed to study lipid profile and homocysteine levels as attributable risk factors for chronic kidney disease.

AIMS AND OBJECTIVES:

Primary Objective: Study of lipid profile and homocysteine levels in cases of chronic kidney disease.

Specific Objectives:

- To find changes in lipid profile occurring in patients suffering from chronic kidney disease.
- Correlation of deranged lipid profile with severity of chronic kidney disease.
- To find changes in plasma homocysteine levels inchronic kidney disease patients.

MATERIAL AND METHODS: This study was carried out in patients admitted to Rama Medical College & Hospital Research Centre Mandhana, Kanpur.

Inclusion criteria:

1. All new or old chronic kidney disease patients with GFR <60 ml/min reporting to OPD or admitted to Rama Medical College & Hospital Research Centre Mandhana, Kanpur.
2. All new or old chronic kidney disease patients on conservative treatment and/or on maintenance hemodialysis.

Exclusion criteria:

- Patients not willing to give consent.
- Patients who are on drugs like steroids, lipid lowering drugs.
- Chronic liver disease.

METHODS:

1. History
    - Duration of renal disease
    - Symptoms to renal failure
    - H/o associated or causative diseases, e.g., Diabetes mellitus, hypertension.
    - Systemic enquiry with special reference to cardiovascular and cerebrovascular events in form of congestive heart failure, coronary artery disease, arrhythmia, TIA, stroke.

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2. Examination
   A. General Examination
      - Pallor
      - Pulse
      - Blood Pressure
      - Weight

   B. Systemic Examination
      - Cardiovascular Signs of
        (I)Heart failure
        (II)Pericardial disease- pericarditis/effusion
      - Respiratory System
        (I)Pulmonary oedema
        (II)Infection
      - Per-abdomen
        Signs of
        (I) ascites
        (II)Infection
      - Central Nervous System
        (I)Level of consciousness
        (II)Focal neurological deficit
        (III)Evidence of peripheral neuropathy

1. INVESTIGATIONS:

General:

- Complete hemogram
- Blood sugar – fasting and postprandial, Serum urea/Creatinine/Na/K
- Serum Prot/Alb
- Serum Calcium/PO_4
- Urine – routine and microscopic
- 24 hrs. Proteinuria
- EKG
- 2D Echo (Wherever needed)
- USG-(KUB region)
- Cardiac enzymes (Whenever needed)
- X-ray chest PA view.

Specific investigation

- Fasting lipid profile
  - Total cholesterol
  - Triglycerides
  - VLDL- Cholesterol
  - LDL- Cholesterol
  - HDL- Cholesterol

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- Fasting Plasma homocysteine
    - Fasting Plasma homocysteine and lipid profiles were done at emergency pathology in Rama Medical College & Hospital Research Centre,Mandhana, Kanpur and private pathology labs in Kanpur, whereas rest of investigations were done at Rama Medical College & Hospital Research Centre Mandhana,Kanpur.
    - Total cholesterol, triglycerides and HDL cholesterol were determined by enzymatic in vitro test for the quantitative determination in human plasma on automated clinical chemistry analysis described by Roeschlau and Allain, LDL and VLDL cholesterol was calculated using the Friedewald equation.

OBSERVATIONS:

- Our study sample consisted of 40 patients of chronic renal disease with renal failure and 30 age and sex matched healthy control subjects having no renal disease, diabetes mellitus or cardiovascular disease.
- Patients were arbitrarily divided into 2 groups of patients >45 years age and patient <45 years age.

	Cases	**Controls**
Number	40	30
Mean	42.55	41.95
S.D.	13.86	11.59

TABLE 1: Age Distribution of the Study Group

Sex	**Group**		**Controls**	
	No.	%	No.	%
Male	22	55	18	60.0
Female	18	45	12	40
Total	**40**	**100**	**30**	**100**

TABLE 2: Sex Distribution of the Study Group

Signs/Symptoms	**No. (total =40)**	**Percentage(%)**
Anemia	34	85
Hypertension	20	50
Diabetes Mellitus	8	20
Edema	25	62.5
Uremic Encephalopathy	8	20
Signs of heart failure	15	37.5

TABLE 3: Clinical Profile of Patients

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Sex	Cases(40)						Control		
	Study Group A(>45yrs)			Study Group B(>45yrs)					
	No.	Dyslip	%	No.	Dyslip	%	No.	Dyslip	%
M	129	11	91.68	12	7	58.3	20	8	40
F	8	7	87.5	8	5	62.5	10	5	50
Total	**20**	**18**	**90**	**20**	**12**	**60**	**30**	**13**	**43.33**

TABLE 4: Prevalence of Dyslipidemia in cases and controls

Sex	Cases(40)						Control		
	Study Group A(>45yrs)			Study Group B(>45yrs)					
	No.	↑Homocystiene	%	No.	↑Homocystiene	%	No.	↑Homocystiene	%
M	12	11	90.66	12	11	91.66	20	0	0
F	8	7	87.5	8	7	87.5	10	0	0
Total	**20**	**18**	**90**	**20**	**18**	**90**			

TABLE 6: Prevalence of High Homocysteine (>10 µ mol/1)
in malesand females in cases and controls

	Cases		Controls
	Study Groups A (>45yrs)	Study Groups B (>45yrs)	
No. of Patients	20	20	30
Mean level of homocysteine(µ mol/L)	29.07	24.58	6.51
S.D.	9.48	7.73	1.80

TABLE 7: Mean Levels of Homocysteine in cases and controls

	Haemodialysis	Conservative t/t
No. Of Subjects	9	9
Mean level of homocystiene(µ mol/L)	27.84	24.45
S.D.	11.33	7.00

TABLE 8: Comparison of Homocysteine in patients
on Haemodialysisvs conservative treatment

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	↑Lipids	Normal
No. of Subjects	30	10
Mean level of homocystiene(μ mol/L)	26.58	24.80
S.D.	8.08	8.30

TABLE 9 : Study of homocysteine in cases with dyslipidemia vs in Patients with normal lipids

		Sex	No	Ht(%)	DM(%)	Dyslipidemia	Homocystiene (%)(10μ mol/L)
Cases	Study Group (A)	Male	12	8(66.6)	4(33.33)	91.66	91.66
		Female	8	6(75)	6(75)	87.5	87.5
		Total	**20**	**14(70)**	**10(50)**	**90%**	
	Study Group (B)	Male	12	6(50)	0(0)	5(58.33)	91.66
		Female	8	2(25)	0(0)	4(62.5)	87.5
		Total	**20**	**8(40)**	**0(0)**	**9(60)**	**90%**
	Control	Male	20	0(0)	0(0)	2(40)	0(0)
		Female	10	0(0)	0(0)	2(50)	0(0)
		Total	**30**	**0(0)**	**0(0)**	**7(43.33)**	**0(0)**

TABLE 10: Summary of Results

DISCUSSION:

DESCRIPTION OF THE STUDY GROUP: The study group included 40 patients of chronic renal disease with renal failure, admitted in Rama Medical College & Hospital Research Centre Mandhana Kanpur.

Cases were included in study after applying the inclusion and exclusion criteria. Cases were divided into two study groups, arbitrarily. Study group A included 20 patients of chronic renal disease with renal failure aged >45 years and study group B included 20 patients of chronic renal disease, with renal failure aged <45 years. Thirty age and sex matched healthy control subjects having no renal disease, diabetes mellitus, hypertension or cardiovascular disease was taken.

- Prevalence of lipid abnormalities and homocysteine levels, were studied in cases and control.
- Study group A included 12(60%) males and 8(40%) females. Study group B included 12(60%) males and 8(40%) females.
- In study group A, dyslipidemia was found in 18 out of 20 cases. (90%)
- Lipid was significantly deranged in cases than controls.
- Dyslipidemia was present in 90% patients in study group A and 60% subjects in study group B.
- In study group A, increased total cholesterol and increased TG was found in 60% patients, while in study group B increased TG was the most common dyslipidemia found in 60% patients.
- Lipid profile is significantly deranged in all 3 groups; profile get worsens as the serum creatinine level rises.
- But there is no statistical significant difference between lipid profiles of 3 predefined group of serum creatinine.

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- Lipids were significantly deranged in diabetic patients in comparison to non- diabetics.
- Although lipids were higher in patients on haemodialysis in comparison to patients on conservation treatment.
- Samuelson et al[1] conducted a prospective cohort study of 73 non- diabetic patients with chronic renal disease. Plasma total cholestrol, LDL cholesterol and apolipoprotein –B levels at baseline all correlated with the subsequent rate of decline of renal function.
- Indian studies on lipikd profile in CRF have not been consistent –Sharma BK et al [1980][2] and Kunde AA et al [1977] observed no hyperlipidemia in patients of CRF. On the hand, Gupta DK et al [1991][3], Das BS et al [1984] and et al [1994] observed lipid abnormalities similar to those reported in western studies i.e. hypertriglyceridemia and reduced HDL.
- Sharma et al [1980][4] suggested that low calorie low carbohydrate diet intake in their patient population could be the reason for lack of lipid abnormality in their patients of CRF.

PLASMA HOMOCYSTEINE LEVEL:

- In our study, plasma homocysteine value in cases was significantly higher than controls. In case, study groups A ,18 out of cases were hyperhomocystenemic
- Plasma homocysteine is significantly increased in all 3 groups, homocyseine level get worsensedas the serum creatinine level rises.
- But there is no statistical significant difference between homocysteine of 3 predefined groups of serum creatinine.[P >.05]

A study by Francesca et al. (1994)[5] showed that 10 μ mol/L increases in plasma homocysteine was associated with a 35% increase in the incident risk of fatal atherothrombotic events in patients on chronic hemodialysis. Francesca et al, (2002) [6] Malamaci et al (2002) Bachmann et al (1995) [7] and Moustapha et al (1998) reported positive correlations between increased homocystiene and higher rate mortality in dialysis patients.

Ana de lurdesagostinhoCabrita Vieira et al (2010) [8] observed that increased level of plasma homocysteine level in chronic kidney disease patients is a new and independent risk factor for cardiovascular disease.

It seems that hyperhomocysteinemia triggers cardiovascular events by altering the coagulation properties of blood. Our study shows significantly increased homocysteine level in patients of chronic renal failure.

CONCLUSION: Our study highlights the fact that dyslipidemia and hyperhomocysteinemia are important risk factors in patients with chronic renal disease and these abnormalities are more prevalent in patients with end-stage renal disease and more in patients with other risk factors. Further, studies with large number of patients in mild, moderate and severe renal failure and long term follow- up are needed to confirm these facts and also to establish causal relationship of these abnormalities with cardiovascular and cerebrovascular complications inpatient with chronic renal disease.

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