Research Article **Biochemistry**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

A CASE-CONTROL STUDY OF PREVALENCE AND TYPE OF DYSLIPIDEMIA IN CHRONIC KIDNEY DISEASE

DR. M.V. BHARGAVI*

Assistant Professor, Department Of General Medicine, Sree Balaji Medical College and Hospital, Bharath University, Chrompet, Chennai, India

ABSTRACT

Chronic kidney disease, a worldwide health problem has extremely high morbidity and mortality from cardiovascular disease. Most patients succumb to cardiovascular disease before ever reaching stage 5 CKD. Our aim is to study the prevalence of dyslipidemia in chronic kidney disease, excluding diabetic and nephrotic aetiology and to compare it with the control population, to examine which type of hyperlipidemia predominates in these patients and to study whether any correlation exist between severity of CKD and lipid alteration. Hospital based 80 CKD patients, irrespective of aetiology except nephrotic proteinuria and diabetes mellitus excluding patients who are obese, on beta - blockers or oral contraceptive pills, pregnancy, smokers and alcoholics were age & sex matched with 80 normal healthy controls. Study group showed an increase in the total cholesterol, triglycerides & LDL and decrease in HDL when compared with the control population and the difference was significant by Odds ratio. Dyslipidemia was present in 45% of the study and 22.5% in the control group which was also significant by Odds Ratio (2.82). There was an increase in the prevalence of dyslipidemia in study group. Hence dyslipidemia should be treated from early stages of CKD to prevent the secondary complications.

KEY WORDS: **Chronic Kidney Disease, Cardiovascular disease, Dyslpidemia.**

*Corresponding author

DR. M.V. BHARGAVI
Assistant Professor, Department Of General Medicine, Sree Balaji Medical College and Hospital, Bharath University, Chrompet, Chennai, *India*

INTRODUCTION

CKD is a worldwide health problem. According to World Health Organization Global Burden of Disease project, CKD is the 12th leading cause of death and 17th cause of disability[1]. The incidence of ESRD is increasing worldwide at an annual growth rate of 8%[2]. ESRD patients have extremely high morbidity and mortality from CVD. Based on data from the U.S. Renal Data System Coordinating Centre - Case Mix Adequacy Study, the prevalence of clinical coronary heart disease in hemodialysis patients is 40%, and CVD mortality is 10 to 30 times higher than in the general population despite stratification by gender, age, race, and the presence of diabetes[3]. The incremental risk of CVD in those with CKD compared to the general population ranges from 10 to 200 fold, depending on the stage of CKD. 30-45% of patients reaching stage 5 CKD already have advanced cardiovascular complications. Thus, the focus of patient care in earlier CKD stages should be directed to the prevention of cardiovascular complications[4]. India is projected to become the major reservoir of chronic diseases like diabetes and hypertension. Since 25–40% of these subjects may develop CKD, the ESRD burden will rise.The increased prevalence of vascular diseases in CKD patients derives from both traditional ("classic") and non-traditional (CKD-related) risk factors. Traditional risk factors include hypertension, hypervolemia, dyslipidemia, sympathetic over activity and hyper-homocysteinemia. Non Traditional Risk Factors are proteinuria,homocysteinemia, lipoprotein(a)[5] and apolipoprotein(a) isoforms abnormality, anemia, abnormal calcium / phosphate metabolism, extracellular fluid overload, oxidative stress, inflammation, malnutrition and thrombogenic factors.The most common dyslipidemia observed in patients with CKD is atherogenicdyslipidemia—a combination of hypertriglyceridemia and low levels of high-density lipoprotein cholesterol[6]. Dyslipidemia is believed to play a role in both the development of cardiovascular disease and the progression of renal disease regardless of the underlying cause (e.g., diabetes, hypertension) [7,8]. Increased levels of lipoprotein(a) are also common in CKD[5]. Consequently, detecting & treating dyslipidemia in this population is as important as in populations without renal disorders, in- order to prevent the development of CVD.The principal reason of this study is to find out the prevalence of dyslipidemia in CKD patients, irrespective of aetiology except Diabetes Mellitus &Nephrotic syndrome (since they are independent risk factors for dyslipidemia) & to find out the type of hyperlipidemia in these patients and to compare it with the age & sex matched controls.

AIMS AND OBJECTIVES

1. To study the prevalence of dyslipidemia in chronic kidney disease, excluding diabetic and nephrotic aetiology and to compare it with the control population.
2. To examine which type of hyperlipidemia predominates in these patients.
3. To study whether any correlation exist between severity of CKD and lipid alteration.
4. To study whether there is any difference in the pattern of dyslipidemia between CKD patients on conservative treatment and those on hemodialysis.

MATERIALS AND METHODS

STUDY POPULATION

Hospital based 80 CKD (out-patient & in-patient).

CONTROL POPULATION

Age & sex matched 80 normal healthy controls are selected from the same hospital, who came with different illness other than the study disease.

SELECTION CRITERIA FOR CASES

1. CKD patients, irrespective of aetiology except nephrotic proteinuria and diabetes mellitus.
2. Patients with serum creatinine ≥ 2 mg/dl AND bilateral contracted kidneys.

- Patients are selected if they have bilateral contracted kidneys in ultrasonography of the abdomen i.e., if the kidneys in long axis are less than 9 cm and a serum creatinine ≥ 2 mg/dl.

EXCLUSION CRITERIA FOR BOTH CASES AND CONTROLS

Exclude patients who are obese, with diabetes mellitus, those on beta - blockers & oral contraceptive pills, pregnant patients, patients

with a history of smoking and chronic alcohol intake.

1. Diabetes mellitus is ruled out by fasting and post-prandial blood sugar. Patients are excluded if they have FBS ≥ 100mg/dl & PPBS ≥140 mg/dl.
2. Protein-to-creatinine ratio in early morning urine sample is used to exclude nephrotic proteinuria. Urine protein in mg and urine creatinine in mg is noted & their ratio is calculated. Cases were excluded if the ratio was >3.5 (correlates with 3.5 gm protein/24 hrs urine sample)[9]. There is a high degree of correlation between 24-hour urine protein excretion and protein-to-creatinine ratios in random, single-voided urine samples.
3. Obese patients are excluded since they have high VLDL & reduced HDL[10]. Obesity classification was based on Body Mass Index (BMI) which takes into account the weight and height of the patient. BMI = wt in kg / ht in m^2. If BMI was ≥ 25 kg/m^2, patients were excluded.
4. Pregnant patients were excluded since VLDL is elevated in pregnancy[10].
5. Those on OCPs were excluded, since the oestrogen component increases HDL[10].
6. Beta blockers elevate VLDL & reduce HDL[10], hence patients consuming it were excluded.
7. A subject was classified as a non-smoker if he/she had smoked fewer than 100 cigarettes in his/her lifetime and had stopped smoking at least 1 year back[11]. A non-drinker was classified as one who had never consumed alcoholic beverages[11]. Alcohol elevates HDL & VLDL, while smoking reduces HDL[10], hence they were excluded. Estimated - GLOMERULAR FILTRATION RATE (e-GFR) was calculated using the Cockroft and Gault formula: e-GFR (ml/min)= [(140-age in yrs) x weight in kg] / (72 x s. creatinine) multiply by 0.85 if female[12]Both the cases and controls elected were matched for age and sex. Data was entered in Microsoft excel spread sheet and analyzed statistically using SPSS (Statistical Package for the Social Science) system. Significance testing of the difference between means was done by unpaired 2 – tailed student't' test, and correlations were assessed by Pearson coefficient. Significance was considered, if the 'p' value was below 0.05.

RESULTS

1. Comparison of BMI, Urea, Creatinine & Creatinine clearance among Study and Control population

CRITERIA	CONTROL			STUDY			MEAN DIFFERENCE	SE DIFFERENCE	P VALUE	
	n	Mean	S.D	n	Mean	S.D				
BMI	80	22.44	1.74	80	21.26	2.35	1.18	0.32	.0001	Sig
UREA (mg/dl)	80	28.40	5.04	80	106.49	41.23	78.09	4.64	.0001	Sig
CREATININE (mg/dl)	80	0.91	0.11	80	5.61	3.33	4.71	0.373	.0001	Sig
CREATININE CLEARANCE (ml/min)	80	68.07	8.44	80	13.79	7.31	54.28	1.24	.0001	Sig

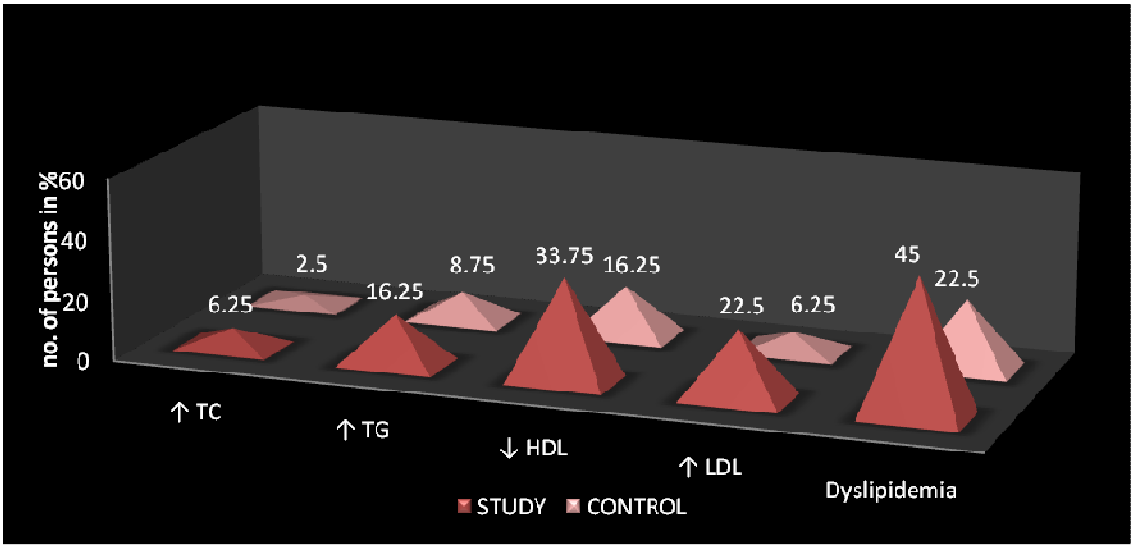
Both the cases and controls were matched which was significant.

2. Distribution of Lipid abnormalities among Study & Control group

LIPID ABNORMALITY	STUDY		CONTROL		ODDS RATIO	95% CI
	NO	%	NO	%		
↑ TC	5	6.25	2	2.5	2.60	0.49 - 13.81
↑ TG	13	16.25	7	8.75	2.02	0.76 – 5.37
↓ HDL	27	33.75	13	16.25	2.62	0.18 – 0.81
↑ LDL	18	22.50	5	6.25	4.36	1.53 – 12.40
Dyslipidemia	36	45	18	22.5	2.82	-

In the study group, there was an increase in the total cholesterol, triglycerides & LDL and decrease in HDL when compared with the control population and the difference was significant by Odds ratio (Odds ratio > 1). Dyslipidemia (defined as presence of one or more lipid abnormalities) was present in 36 of the study group (45%) and 18 in the control group (22.5%) which was also significant by Odds Ratio (2.82).

Dyslipidemia distribution in Study & Control group



2. Comparison of Total Cholesterol, Triglycerides, HDL, TC/HDL, LDL-C & VLDL among Study and Control population

CRITERIA	CONTROL			STUDY			MEAN DIFFERENCE	STD. ERROR DIFFERENCE	P VALUE	
	N	Mean	S.D	n	Mean	S.D				
TC	80	155.43	27.51	80	170.80	46.54	15.38	6.04	.012	Sig
TG	80	136.80	30.00	80	154.15	67.58	17.35	8.26	.037	Sig
HDL	80	38.50	3.579	80	37.15	4.93	1.35	0.68	.049	Sig
TC/HDL	80	4.08	0.88	80	4.71	1.52	0.63	0.19	.002	Sig
LDL-C	80	89.68	26.46	80	101.60	44.41	11.93	5.78	.041	Sig
VLDL	80	27.25	6.02	80	30.21	12.58	2.96	1.56	.059	Not sig

When compared with the control group, the study population had significantly increased total cholesterol (p=0.012), triglycerides (p=0.037), LDL-C (p=0.041) and TC/HDL ratio (p=0.002) and the decrease in the HDL-C was also significant (p=0.049) when compared with the control group. Whereas, there was an increase in VLDL-C in the study population when compared with the control group, but this increase was not significant (p=0.059).

4. Analysis of Lipid abnormalities among Study and Control population

CRITERIA	CONTROL			STUDY			MEAN DIFFERENCE	STD. ERROR DIFFERENCE	P VALUE	
	n	Mean	S.D	n	Mean	S.D				
↑ TC	2	242.00	.000	5	293.40	52.28	51.40	39.12	0.246	Not Sig
↑ TG	7	214.71	11.87	13	272.85	73.46	58.13	28.30	0.015	Sig
↓ HDL	13	33.31	0.95	27	31.70	1.88	1.60	0.55	0.006	Sig
↑ LDL-C	5	149.40	13.61	18	162.88	41.98	13.49	19.33	0.493	Not Sig

On considering only the dyslipidemia population in both the study and control group, 36 in the study group (45%) had dyslipidemia and 18 in the control group (22.5%) had dyslipidemia. On analysing the above population alone, there was an increase in the prevalence of ↑TC & LDL-C but this increase was not statistically significant (p>0.05).But the decrease in HDL-C and increase in TGs in the study group were statistically significant when compared with the controls (p=0.006 & p=0.015, respectively).

5. CKD Stage wise analysis of Lipid abnormalities

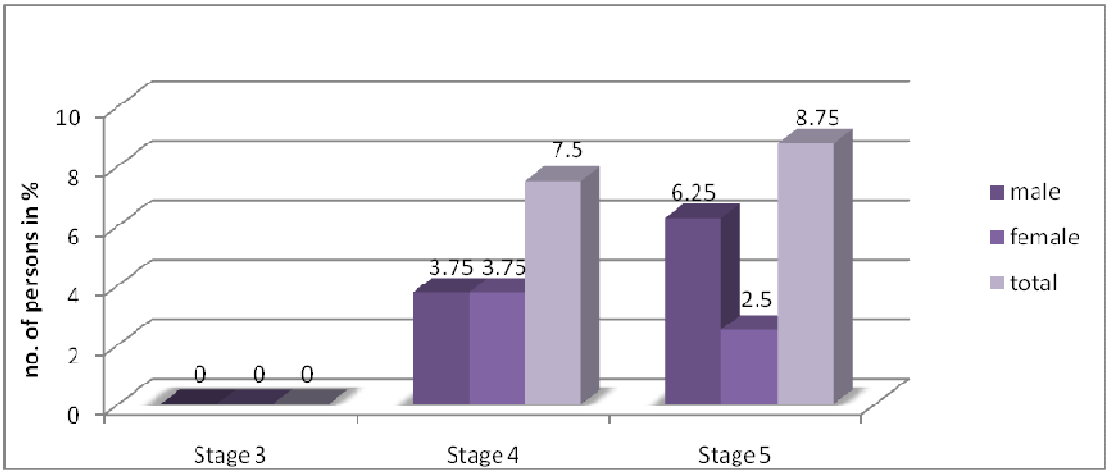
CRITERIA	STAGE 3	STAGE 4	STAGE 5
↑ TC	0 %	0%	6.25%
↑ TG	0%	7.5%	8.75%
↓ HDL-C	0%	12.5%	21.25%
↑ LDL-C	0%	6.25%	16.25%
DYSLIPIDEMIA	0%	46.15%	47.06%

In stage 3 CKD, no lipid abnormalities were noticed. In stage 4 & 5, dyslipidemia (defined as presence of one or more lipid abnormalities) was 46.15% and 47.06% respectively. Total cholesterol was within the normal limits in stage 4 CKD group, whereas it was elevated in stage 5. The increase in TGs & LDL-C and decrease in HDL-C were higher in stage 5 when compared with stage 4.

6. Distribution of Triglycerides among different Stages of CKD

CKD-STAGE	MALE		FEMALE		TOTAL	
	NO	%	NO	%	NO	%
3	0	0	0	0	0	0
4	3	3.75	3	3.75	6	7.5
5	5	6.25	2	2.5	7	8.75

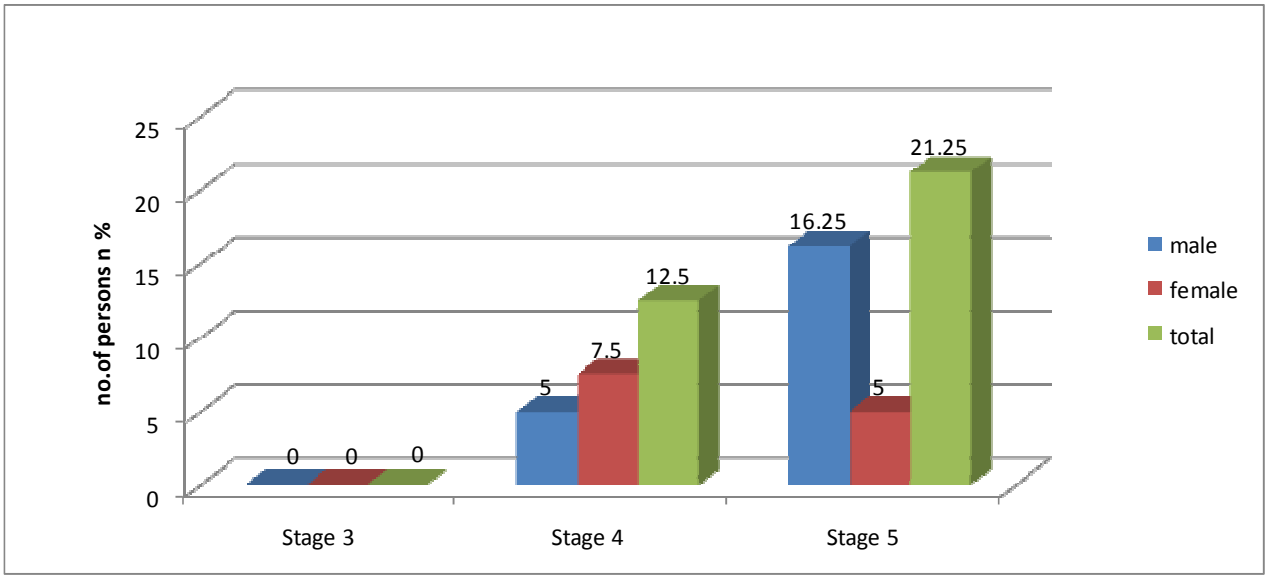
Sex & CKD Stage wise distribution of Triglycerides



7. Sex - wise distribution of HDL-C among different stages of CKD

CKD-STAGE	MALE		FEMALE		TOTAL	
	NO	%	NO	%	NO	%
3	0	0	0	0	0	0
4	4	5	6	7.5	10	12.5
5	13	16.25	4	5	17	21.25

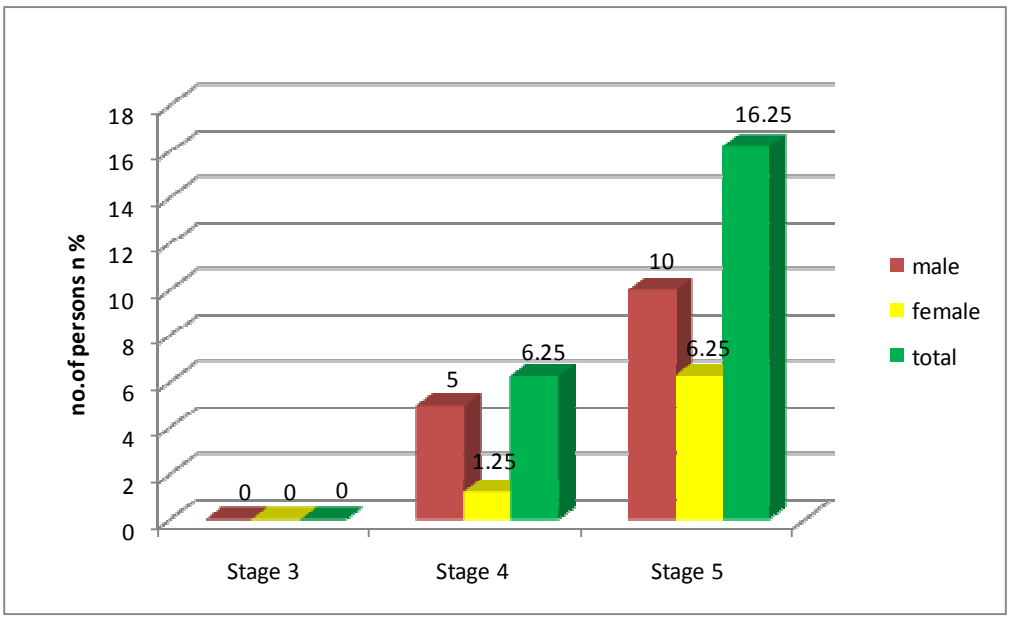
Sex & CKD Stage-wise distribution of HDL-C



8. Sex - wise distribution of LDL-C among different stages of CKD

CKD-STAGE	MALE		FEMALE		TOTAL	
	NO	%	NO	%	NO	%
3	0	0	0	0	0	0
4	4	5	1	1.25	5	6.25
5	8	10	5	6.25	13	16.25

Sex & CKDStage-wise distribution of LDL- C



DISCUSSION

CKD is a worldwide health problem and one of the growing, silent epidemic of non-communicable diseases. For a long time, dyslipidemia in CKD patients was an underestimated problem. Diabetes, nephrotic syndrome, thiazide diuretics and many

secondary causes of dyslipidemia are well known to us and obviously CKD due to the above disorders (diabetes being the most common etiology) will have dyslipidemia. This study was hence undertaken to look, whether chronic kidney disease per se, possess a risk of dyslipidemia (without the above secondary causes of dyslipidemia) by excluding obesity, diabetes, patients with nephrotic range of proteinuria, those on beta-blockers & OCPs, pregnant patients, patients with history of smoking and chronic alcohol intake. 80 such CKD patients were selected (who satisfied the above exclusion & inclusion criteria) and 80 age and sex matched, hospital based controls were also chosen and lipid profile was done on a fasting sample. The results obtained were statistically analysed. In this study of 80 patients, males predominated (72.5%) compared to females (27.5%). Majority of the males were in the age group of 60-79 yrs, whereas females were in the age group of 50-69 yrs. The mean BMI of the study group was significantly lower (21.26) than that of the control group (22.44) (p=0.0001). This may be probably due to malnourishment of the CKD patients. The mean blood urea level in the study group was 106.49 mg/dl & that in the control was 28.4 mg/dl, which is a significant difference (p=0.0001). The mean creatinine in the study group was 5.61 mg/dl& that in the control was 0.91 mg/dl and this difference is also significant (p=0.0001). The mean creatinine clearance in the study group was 13.79 ml/min& that in the control was 68.07 ml/min, which again was significant. In the study group the creatinine clearance was below 39 ml/min and most of them had it less than 19 ml/min. In the control population it was above 50 ml/min and most of them had above 60 ml/min. The CKD patients were staged according to Kidney Disease Outcomes Quality Initiative (KDOQI 2002) guidelines. Only 3.75% of them were in stage 3; 32.5% were in stage 4 & majority (63.75%) in stage 5. This distribution was maintained both in males &females. There was an increase in the prevalence of total cholesterol abnormality (6.25% in study group Vs 2.5% in controls), triglyceride abnormality (16.25% Vs 8.75%), LDL-C abnormality (22.5% Vs 6.25%) & HDL-C abnormality (33.75% Vs 16.25%) in the study group, when compared with the control group (odds ratio > 1). Dyslipidemia (defined as presence of one or more lipid abnormalities) was present in 36 of the study group (45%) and 18 in the control group (22.5%) (Odds ratio=2.46). Comparing this data with the Data from National Health and Nutrition Examination Survey (NHANES) III and the Framingham Offspring Study, Data from multiple observational studies kasiske[13]& Study in Singapore General Hospital conducted by CM Chan, Department of Renal Medicine reported in Ann Acad Med[14], the prevalence of all the lipid abnormalities in this study were higher in the CKD population than the controls, themost significant being increased prevalence of total cholesterol & LDL-C. In the above NHANES III study, the prevalence of LDL-C abnormality in CKD population was lower than that in the control group and the main abnormality was increased TGs. Comparing this study with the NHANES III study, the prevalence of total cholesterol and LDL-C abnormality is much lower in our population, even in the control group. The prevalence of increased triglycerides is half that of western population in the normal control group, whereas the prevalence of HDL-C abnormality is slightly higher than that of the western population. (NHANES) III and the Framingham Offspring Study:

	TC >240 mg/dl	LDL-C >130 mg/dl	HDL-C <35 mg/dl	TG >200 mg/dl
Control-NHANES III	20%	40%	15%	15%
Control-this study	2.5%	6.25%	16.25%	8.75%
CKD without nephrotic syndrome-conservative mgmt-NHANES III	30%	10%	35%	40%
CKD without DM &Nephrotic proteinuria-conservative mgmt-this study	6.56%	27.87%	34.43%	16.39%
HD-NHANES III	20%	30%	50%	45%
HD-this study	5.26%	5.26%	31.58%	15.79%

When compared with the control group, the study population had significantly increased total cholesterol (p=0.012), triglycerides (p=0.037), LDL-C (p=0.041) andTC/HDL ratio (p=0.002) and the decrease in the HDL-C was also significant (p=0.049) when compared with the control group. Whereas there was an increase in VLDL-C in the study population when compared with the control group, but this increase was not significant (p=0.059). In addition , in our study, TC/HDL ratio was higher in the study group (4.71) than the controls (4.01) which was significant (p=0.002). VLDL-C was also elevated in the study group but not significant (p=0.059). In stage 3 CKD, no lipid abnormalities were noticed. The prevalence of increase in TGs & LDL-C and decrease in HDL-C were higher in stage 5 when compared with stage 4. In stage 4 & 5, dyslipidemia (defined as presence of one or more lipid abnormalities) was 46.15% and 47.06% respectively. Comparing our study with the 'Study of Abnormal Lipids and Apolipoprotein-B composition in Diabetic and Non-diabetic Chronic Renal Failure patients' by Dr.Meera Shivashekar[15], plasma triglyceride concentrations were significantly increased in both diabetic and non-diabetic CRF patients compared to controls. Total and LDL cholesterol were elevated in both groups of CRF patients. CRFpatients had higher total and LDL cholesterol levels than controls. In CRF patients the levels of Total cholesterol, Triglycerides, LDL and VLDL showed statistically significant (P<0.001) increase compared to controls. But in diabetic CRF patients the levels of Total Cholesterol, Triglycerides, LDL and VLDL levels were significantly elevated than the non-diabetic CRF patients. Non-diabetic CRFpatients showed significant raise in Total cholesterol, Triglycerides, LDL and VLDL levels when compared to the controls. Apo-B levels in diabetic CRF patients were significantly increased compared to non-diabetic CRF patients and healthy controls. The levels of Apo-B containing lipoproteins were increased in both diabetic and non-diabetic CRF patients compared to controls. There is a significant correlation between LDL cholesterol and Apo-B in all groups. The levels of Apo-B were high in the diabetic renal failure patients compared to non-diabetic CRF patients. According to a study conducted by A. Madhusudhana Rao, et al., on lipid abnormalities, lipoprotein(a) and apoprotein pattern in non-dialyzed patients with CKD[16], TGs were high in CKD stage 1-4 (p<0.05), whereas VLDL-C was significantly high (p<0.05) in all the groups when compared to controls. However, LDL-C was significantly low in stage 5 only as compared to control group (P<0.05). Though total cholesterol levels in stage 1 & 2and LDL levels in stage 1-4 were higher than controls, the values attained were not statistically significant (P>0.05). HDL-C was lower in stage 5 CKD, but not significant. Prevalence of dyslipidemia, by guideline definitions, was 82%, predominantly manifested by elevated triglycerides (52%) and VLDL (52%) and decreased HDL (51%), with less frequent elevations of LDL (40%) and total cholesterol (24%), according to a study by Pennell P, et al., Division of Nephrology and Hypertension (R-126), Miller School of Medicine, University of Miami in University of Miami[17]. In all of the above studies, CKD group was selected irrespective of the etiology. No exclusion for diabetes was made. In one study from Department of Hemodialysis and Renal Tansplantation, Victor Babes University of Medicine and Pharmacy, Timisoara[18], the increase in TGs & decrease in HDL-C was noticed in diabetic CKD as opposed to non - diabetic CKD. LDL-C was increased in non diabetic CKD. Diabetic patients without CKD had a higher TG & lower HDL-C when compared with non-diabetic CKD, which means diabetes possess higher dyslipidemic potency when compared with CKD per se. Concluding, hypertriglyceridemia and elevated total cholesterol was the main abnormality in CKD patients in other studies, whereas this study shows significant elevation of total cholesterol, triglycerides, LDL-C and decreased HDL-C. So chronic kidney disease per se, excluding the other causes of secondary dyslipidemia, possess lipid abnormalities.

CONCLUSION

This case - control study was aimed at finding out the prevalence and type of dyslipidemia in chronic kidney disease excluding the secondary causes of dyslipidemia like obesity, diabetes, nephrotic syndrome, beta-blocker intake, pregnant patients, etc., and comparing it with the age & sex matched controls. On

analysis, a) There was an increase in the prevalence of dyslipidemia (elevated total cholesterol, LDL-C, triglycerides, VLDL-C & TC/HDL ratio and decreased HDL-C), as defined by the National Cholesterol Program (NCEP) Adult Treatment Panel (ATP) III guidelines. b) The major lipid abnormalities in the CKD population were elevated total cholesterol, triglycerides &LDL-C and decreased HDL-C. c) No lipid abnormality was noted in stage 3 CKD. In stage 4, there was an increase in triglycerides & LDL-C and decrease in HDL-C, while in stage 5 there was an increase in total cholesterol, triglycerides & LDL-C and decrease in HDL-C. Concluding, chronic kidney disease per se, excluding the other causes of secondary dyslipidemia, possess lipid abnormalities, thus imposing higher risk for cardiovascular events. Hence dyslipidemia should be treated from early stages of CKD to prevent the secondary complications.

REFERENCES

1. World Health Organisation - Burden of disease project accessed on September 2006.
2. Bamgboye EL. Hemodialysis: management problems in developing countries, with Nigeria as a surrogate. Kidney Int. 2003; 63(83).
3. Parfrey PS, Foley RN, Harnett JD, Kent GM, Murray D, Barre PE. Outcome and risk factorsof ischemic heart disease in chronic uremia Kidney Int; 1996; 49:1428-1434.
4. Harrison's Principles of Internal Medicine - 17th edition, volume 2, chapter 274 – Chronic kidney disease; pg 1761-1771.
5. Kronenberg F, Kuen E, Ritz E, et al: Lipoprotein(a) serum concentrations and apolipoprotein(a) phenotypes in mild and moderate renal failure. J Am SocNephrol 2000; 11:105-115.
6. Brenner: Brenner and Rector's The Kidney, 8th ed. Section IV –Pathogenesis of Renal Disease, Chapter 22 – Approach to the Patient with Kidney Disease - Ramesh Saxena, Robert D. Toto.
7. Attman PO, Alaupovic P, Samuelsson O: Lipoprotein abnormalities as a risk factor for progressive non-diabetic renal disease. Kidney Int 1999; 56:S14-S17.
8. Toto RD, Vega G, Grundy SM: Cholesterol management in patients with chronic Kidney disease; Brayd H, Wilcox C, ed. Therapy in Nephrology and hypertension, Philadelphiaand New York: Lippincott - Williams &Wilkins; 2003:631-639.
9. Schwab SJ, Christensen L, Dougherty K, Klahr S: Quantification of proteinuria by the use of protein-to-creatinine ratio in single urine samples. Arch Intern Med 1987; 147:943- 944.
10. Harrison's Principles of Internal Medicine - 17th edition, volume 2, chapter 350 – disorders of lipoprotein metabolism; pg 2416-2429.
11. The Association among Smoking, Heavy Drinking, and Chronic Kidney Disease by Anoop Shankar, Ronald Klein and Barbara E. K. Klein andTen year incidence of age related maculopathy and smoking and drinking: The Beaver Dam Eye by Klein R, Klein BE,Tomany SC, et al. Study: Am J Epidemiol 2002; 156: 589-598.
12. Cockcroft DW, Gault MH: Prediction of creatinine clearance from serum creatinine. Nephron 1976; 16:31-41.
13. Managing Dyslipidemia in Chronic Kidney Disease: Prevalence of Dyslipidemia in CKD; Data from National Health and Nutrition Examination Survey (NHANES) III and the Framingham Offspring Study; Data from multiple observational studies Kasiske.Journal of General Internal Medicine 2004; Volume 19; number 10; 1045-1052, DOI:
14. Hyperlipidaemia in Chronic Kidney Disease - CM Chan, Department of Renal Medicine Singapore General Hospital, Singapore; Ann Acad Med Singapore 2005; 35:31-5.
15. Dr.MeeraShivashekar, Mr. Ashok VardhanNandigam, Dr. Ebenezer William and Dr.Padmanabhan, Study of abnormal lipids and apolipoprotein-B composition in diabetic and nondiabetic chronic renal failure patients, Int Journal of Pharma and Bio Sciences, Vol 3/ Issue 2/ April – June 2012.

16. A. Madhusudhana Rao, A. R. Bitla, E. P. Reddy, V. Sivakumar and P. V. L. N. Srinivasa Rao, Departments of Biochemistry and Nephrology, Sri Venkaterswara Institute of Medical Sciences, Tirupati-517507, Chittor, AP; Lipid abnormalities, lipoprotein (a) and apoprotein pattern in non-dialyzed patients with chronic kidney disease; Indian journal of clinical biochemistry; Vol 25, Nov 2010,47-50, DOI: 10.1007/s12291- 010-0010-5.
17. Pennell P, Leclercq B, Delahunty MI, Walters BA., Division of Nephrology and Hypertension (R- 126), Miller School of Medicine, University of Miami, Miami, FL, USA. The utility of non-HDL in managing dyslipidemia of stage 5 chronic kidney disease; Clin Nephrol 2006 Nov; 66(5):336-47.
18. Statin Therapy in Chronic Kidney Disease,Department of Hemodialysis and Renal plantation, Victor Babes University of Medicine and Pharmacy, Timisoarav.