



Study of Lipid Profile in Non Diabetic CKD Patients

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Abstract

Background: Chronic Kidney Disease (CKD) is a worldwide health problem and one of the major health burden in developing countries like India. Dyslipidemia due to alteration in lipoprotein metabolism was considered as a complication of end stage renal disease (ESRD) but these changes can be present in early stages of CKD. Over the last decade it is established that Cardio-Vascular Disease is the major cause of mortality with mild to moderate and ESRD. The present study focused on finding an approximate prevalence of dyslipidemia, type of alteration in lipid fractions in non diabetic CKD populations and the association with staging.

Methods: The study was conducted in VIMSAR, Burla during NOV 2017 to OCT 2019 with an objective to study the lipid profile in non diabetic CKD patients. Patients with CKD admitted to Dept. of Gen. Medicine And Nephrology who had given consent for the study were the source of data. History, clinical examination with supporting biochemical and radiological evidences of 150 cases were taken for diagnosis of CKD. 75 numbers of age and sex matched healthy individuals were taken as control. MDRD equation was used to calculate eGFR. Staging of CKD is as per KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management Of Chronic Kidney Disease.

Results: Among a total of 150 patients with mean age of 52.92 ± 11.41 , the prevalence of dyslipidemia in CKD was found to be about 78.67%. There is significant increase in serum TG with the increase in severity of the disease. Most common abnormality is fall in the serum HDL cholesterol in 59.33% of patients followed by a rise in serum triglyceride concentration 51.33% in patients suffering from CKD.

Conclusion: The high prevalence of lipid abnormalities in CKD may accelerate the progression of Cardio Vascular Disease and increase the mortality of patients. Hence it is worthwhile to early diagnose and manage accordingly to reduce morbidity and mortality.

Introduction

Chronic kidney disease (CKD) encompasses a spectrum of different patho-physiologic processes associated with abnormal kidney function and a progressive decline in Glomerular Filtration Rate (GFR)

CKD is a worldwide health problem. In the 2015 Global Burden of Disease Study, kidney disease

was the 12th most common cause of death, accounting for 1.1 million deaths worldwide. Overall CKD mortality has increased by 31.7% over the last 10 years.¹

The prevalence of CKD was observed to be 17.2% with ~6% have CKD stage 3 or worse.²

Patients with altered renal function exhibit significant alteration in lipoprotein metabolism.³

Lipid abnormalities were originally considered as complications of ESRD but these changes can be present in early stages of CKD and its prevalence increases with increase in severity of disease.^{4,5}

Dyslipidemia actively participate in the pathogenesis of serious complications such as arthero sclerotic vascular diseases.⁶

Over the last decade it was established that Cardio-Vascular Disease is the major cause of mortality with mild to moderate and end stage renal disease.^{6,7}

The nature of dyslipidemia is influenced by factors like Nephrotic range proteinuria, Diabetes mellitus, Hereditary disorder of lipid metabolism, ingestion of drugs like steroid.⁴

According to several prospective studies the most common quantitative lipid abnormality in pre dialysis CKD patients are hyper triglyceridemia, increase concentration of triglyceride rich lipoprotein, reduced HDL-cholesterol.³

There is lack of sufficient evidence when it comes to the prevalence of dyslipidemia in patients suffering from CKD in the India and the pattern of altered lipid fractions due to the variations in the dietary habits and lifestyle differences from the western counterparts.

Indian studies on lipid abnormalities in CRF have varied from no abnormalities at all to significant abnormalities as described in western literature.⁹

The study by Sumathi M.E, Manjunath M showed serum TGL,TC, have significantly increased in conservatively managed patients than in haemodialysis patient.⁸

Another study by Ganta V et al shows that, the prevalence of dyslipidemia in CKD was about 65% and it increases with increase in severity of disease.⁵

The present study is undertaken to explore the pattern and prevalence of lipid abnormalities in different stages of CKD.

Aims and Objectives

General Objective

To find out the prevalence of dyslipidemia in non Diabetic CKD patients.

Specific Objective

To study the alteration in lipid fractions and prevalence of dyslipidemia in relation to the severity of CKD.

Methodology

Place of Study: Patients admitted in the Dept. of General Medicine and Nephrology. VIMSAR, Burla.

Period of Study: November 2017 to October 2019

Study Design: It is an analytical, Observational cross sectional study.

Study Population: Non Diabetic CKD Patients admitted in dept. of Gen Medicine and Nephrology, VIMSAR, Burla.

Sample Size: 150 number of cases and 75 numbers of healthy age and sex matched individuals taken as control.

Sampling Techniques: Convenience Sampling

Selection Criteria

Inclusion Criteria

1. All the patients admitted with clinical, biochemical, sonologic evidences of CKD.
2. Age:- >14 yrs.

Exclusion Criteria

CKD Patients with

1. Diabetes mellitus
2. Maintenance dialysis
3. Hypothyroidism and severe liver disease
4. Diagnosed dyslipidemia in medical management
5. Nephrotic range proteinuria

Operational Definitions

Diagnosis of CKD was done by clinical, biochemical and sonologic evidences of CKD

National kidney foundation defined CKD as:

1. Kidney damage for ≥ 3 months as defined by structural or functional abnormalities of kidney, with or without decreased GFR.

Or

2. $GFR < 60 \text{ ml/min/1.73 m}^2$ for ≥ 3 months with or without kidney damage.

eGFR calculated by MDRD formula i.e

□ Estimated GFR (mL/min per 1.73 m²) = 175 x (S.Cr)^{-1.154} x (age)^{-0.203} (IDMS Traceable MDRD)

Multiply by 0.742 for women multiply by 1.21 for African Americans

Staging of CKD is based on KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management Of Chronic Kidney Disease.

Statistical Analysis

Observed data were collected, compiled and analysed with appropriate statistical methods. Mean and standard deviations of lipid fractions were compared with control group by Independent Student t test. Pearsons Chi- square test is used to assess the association of different study parameters. Differences were considered statistically significant if p value < 0.05.

Implications of Outcome

Diagnosis and management of lipid abnormality in early stages of CKD will decrease the morbidity and mortality due to Cardio Vascular Diseases.

Table 1 Age and Sex Distribution of Study Group

Age	Male	Female	Total	Percentage (%)
21-30	2	2	4	2.66
31-40	16	3	19	12.67
41-50	18	25	43	28.67
51-60	24	27	51	34
>60	18	15	33	22
Total	78(52%)	72(48%)	150	100%

In this study out of 150 CKD patients 52% are male and 48% were female. Age of patients varies from 22 yrs to 80 yrs and majority 68.67% of the patients were in 41-60 yrs age group.

Graph 1: Age and Sex Distribution of Study Gro

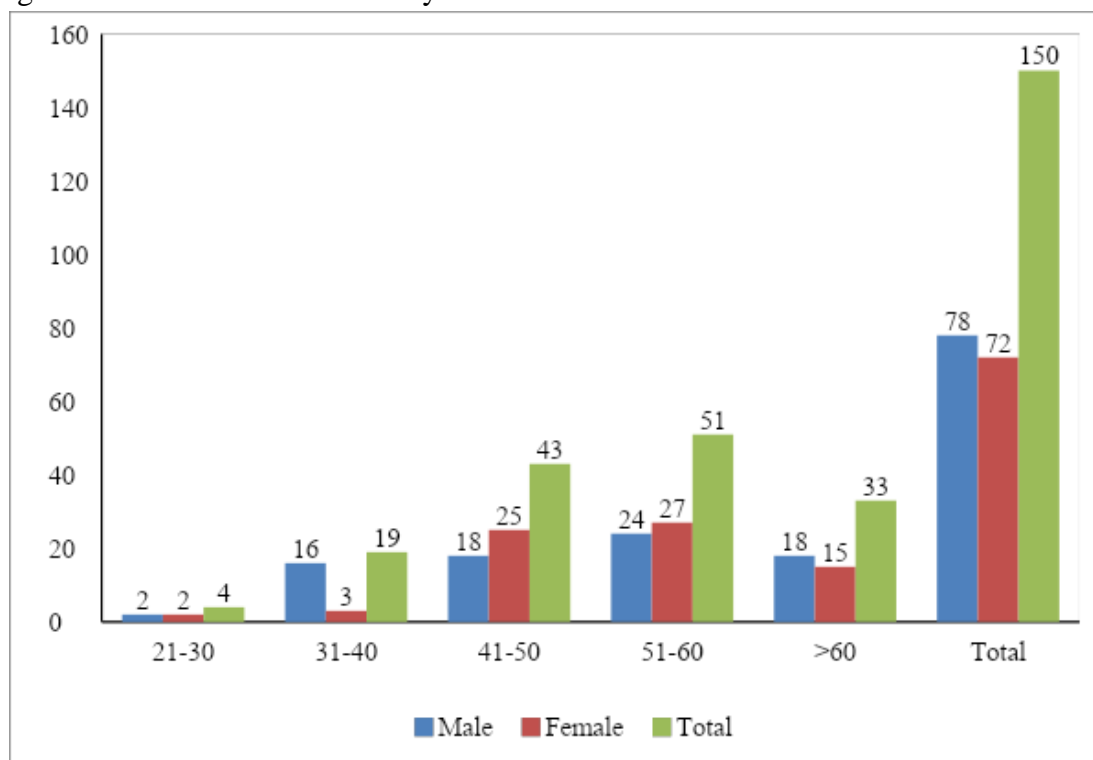


Table 2 Staging of Chronic Kidney Disease (CKD) in the study population

CKD Stage	Number	Percentage (%)
Gr 3	20	13.33
Gr 4	37	24.67
Gr 5	93	62
Total	150	100%

In the present study it was found that all the patients were suffering from Stage 3, 4, and 5 of CKD. Most of the patients were in Stage 5 CKD

constituting 62% of cases. Stage 3 and 4 patients represents 13.33% and 24.67% of total study populations respectively.

Graph 2: Staging of Chronic Kidney Disease (CKD) in the study population

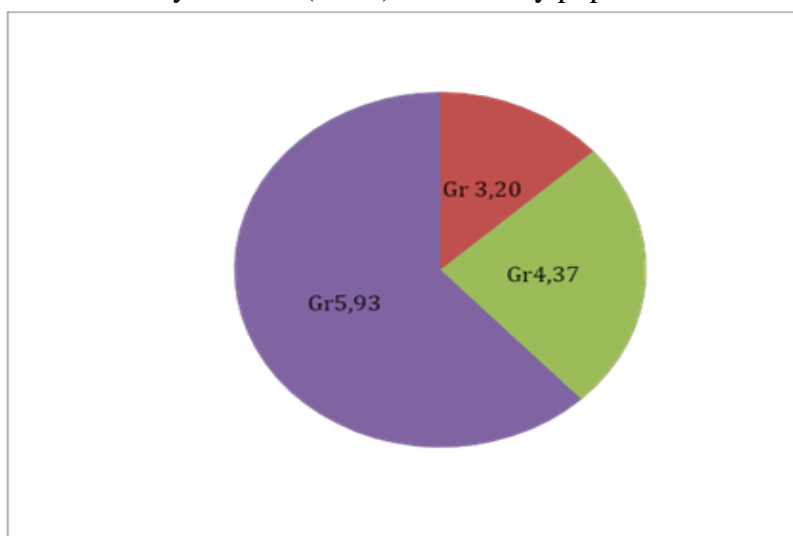


Table 3: Lipid Abnormality in Study Group

Type of Lipid Disorder	Number Of Patient (N=150)	Percentage (%)
Increased TC	9	6
Increased TG	77	51.33
Decreased HDL	89	59.33
Increased LDL	5	3.33
Total Lipid Abnormality	118	78.67

In our study the prevalence of dyslipidemia was found in 78.67%. Most common abnormality in this study was decreased HDL (59.33%), followed

by increased TG in 51.33% of cases. Increased T.Ch & LDL were seen in 6% and 3.33% of patients respectively.

Graph 3: Lipid Abnormality in Study Group

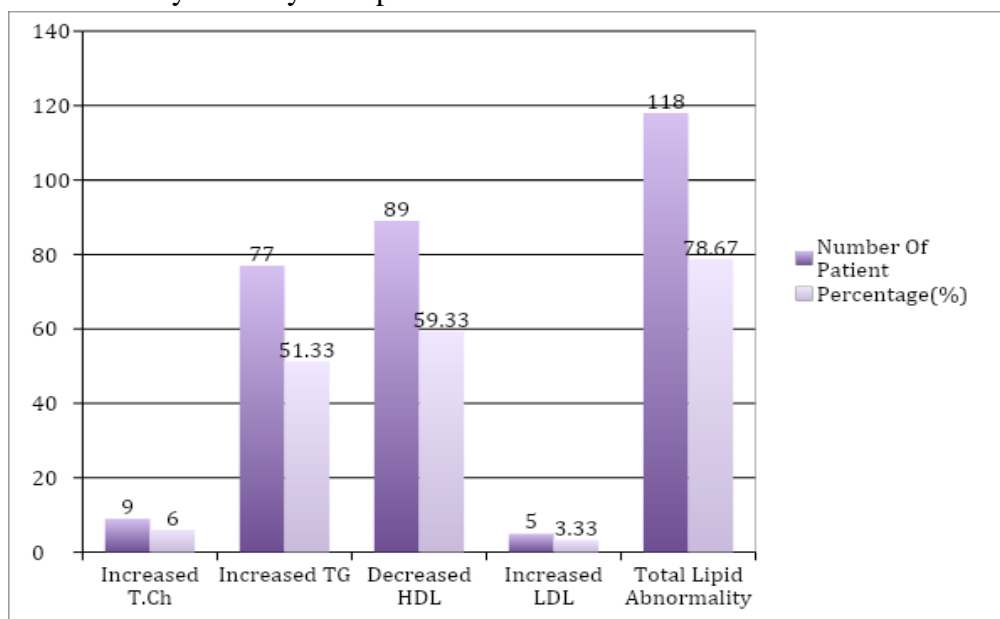


Table 4 Prevalence of Dyslipidemia Vs. Stages of CKD.

Lipid Profile	CKD III	CKD IV	CKD V	P value/Chi
Abnormal	15 (75%)	27 (73%)	76 (81.7%)	P=0.28 Chi sq= 2.49 df=2
Normal	5 (25%)	10 (27%)	17 (18.3%)	
Total	20 (100%)	37 (100%)	93 (100%)	

Comparing the dyslipidemia with staging of CKD, it was found that lipid abnormality in Stage III, IV and V were 75%, 73% and 81.7% respectively.

Graph 4: Prevalence of Dyslipidemia Vs. Stage of CKD

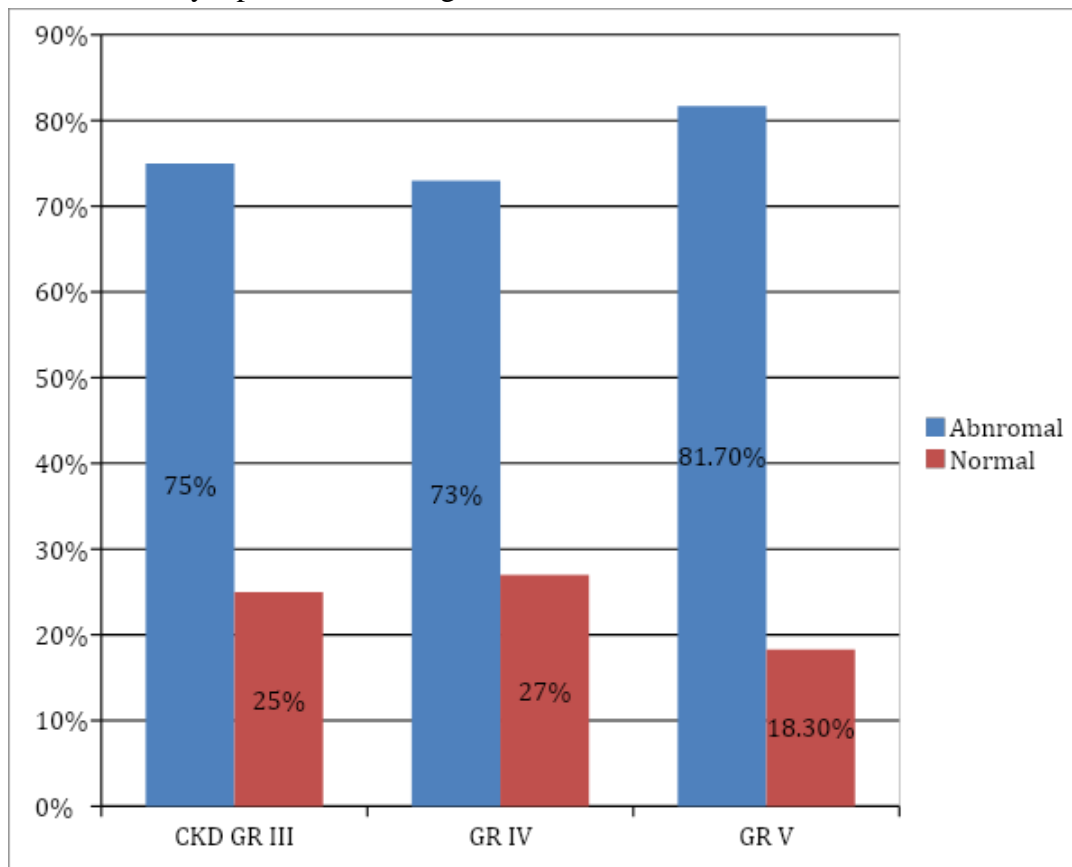


Table 5 Correlation between Lipid Fractions and Stage of CKD

LIPID FRACTION	Stage III n=20	Stage IV n= 37	Stage V n = 93
↑ TC	1	3	5
↑ TG	9 (45%)	12 (32.43%)	56 (60.21%)
↓ HDL	10 (50%)	18 (48.64%)	61 (65.59%)
↑ LDL	0	2	3

In this study decreased HDL was the most frequent abnormality which was found in 65.59% of patients in Stage V .In Stage III and Stage IV

population decreased HDL was 50% & 48.64% respectively. Increased TG found in Stage III, IV & V were 45%, 32.43% and 60.21% respectively.

Graph 5: Correlation between Lipid Fractions and Stage of CKD

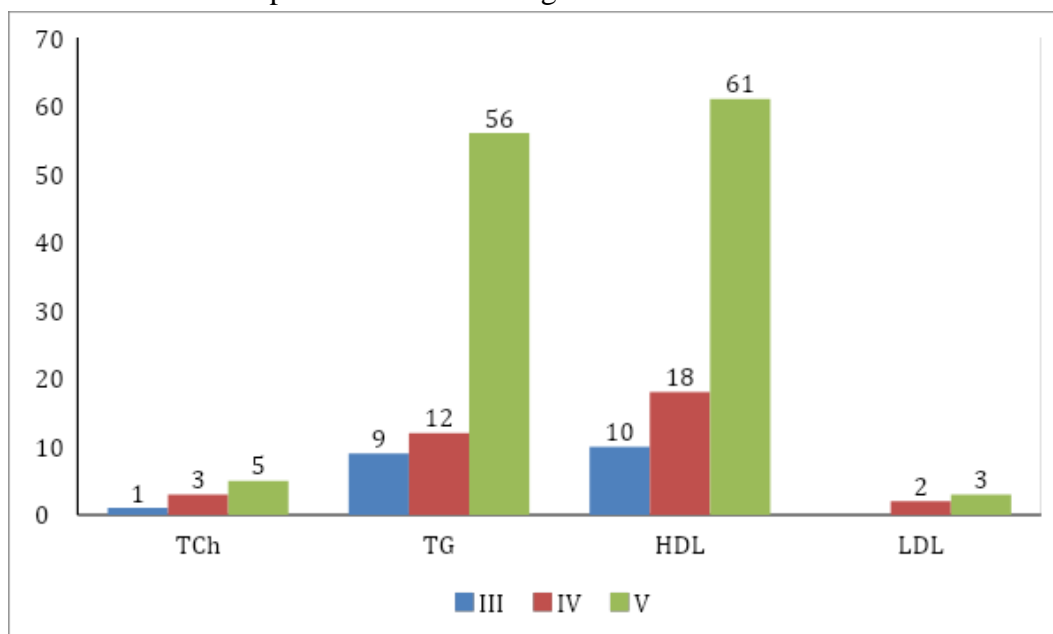


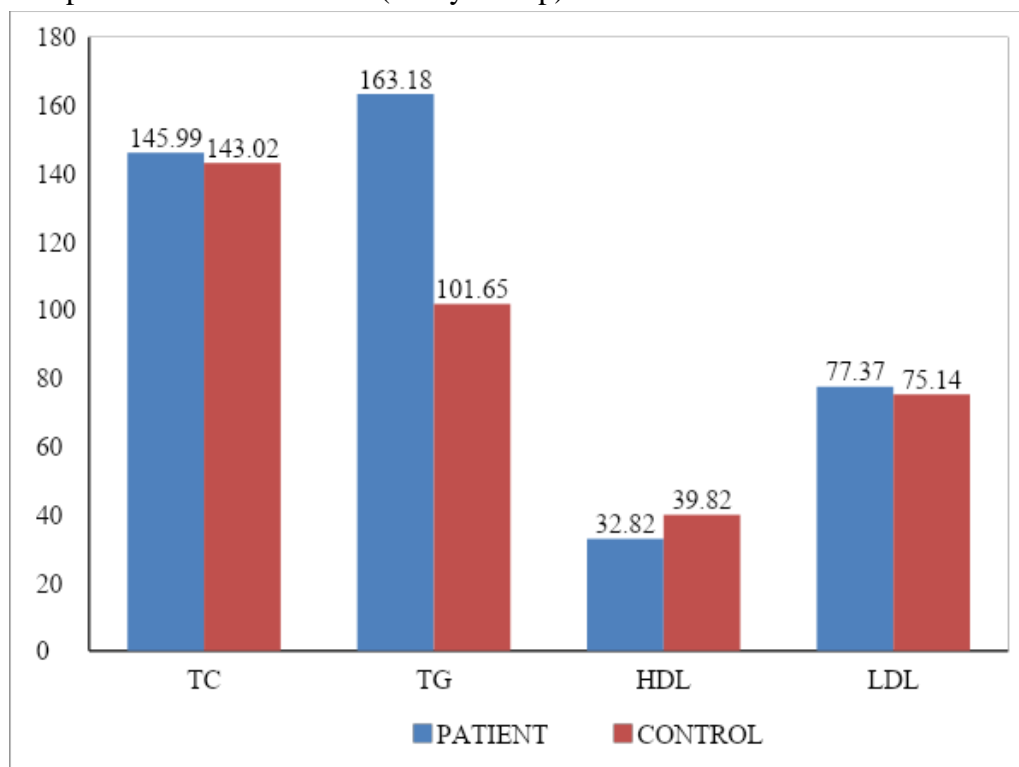
Table 6: Lipid fraction of Patients (Study Group) Vs Control

LIPID FRACTION	PATIENT(n=150)	CONTROL(n=75)	P Value
TC	145.99±40.79	143.02±30.72	0.57
TG	163.18±83.53	101.65±20.71	<0.05
HDL	32.82±14.01	39.82±8.21	<0.05
LDL	77.37±35.78	75.14±22.22	0.6

Comparing the mean values of different lipid fractions we found statistically significant

($p < 0.05$) difference in TG and HDL levels between study and control groups.

Graph 6: Mean Lipid fractions of Patients (Study Group) Vs Control



Lipid Fractions in Relations to Stages of CKD

Table 7 Total Cholesterol Vs Stage of CKD

TC	Stage III (n=20)	Stage IV(n=37)	Stage V(n=93)	P value
Abnormal(↑)	1	3	5	$P=0.823$
Normal	19	34	88	Chi Sq=0.39

Total Cholesterol level in Stage III, IV and V of CKD in our study was found to be abnormal in 1, 3 and 5 number of patients respectively. We found

no significant relationship ($p=0.823$) between TC level and stages of CKD in our study.

Graph 7: Total Cholesterol Vs Stage of CKD

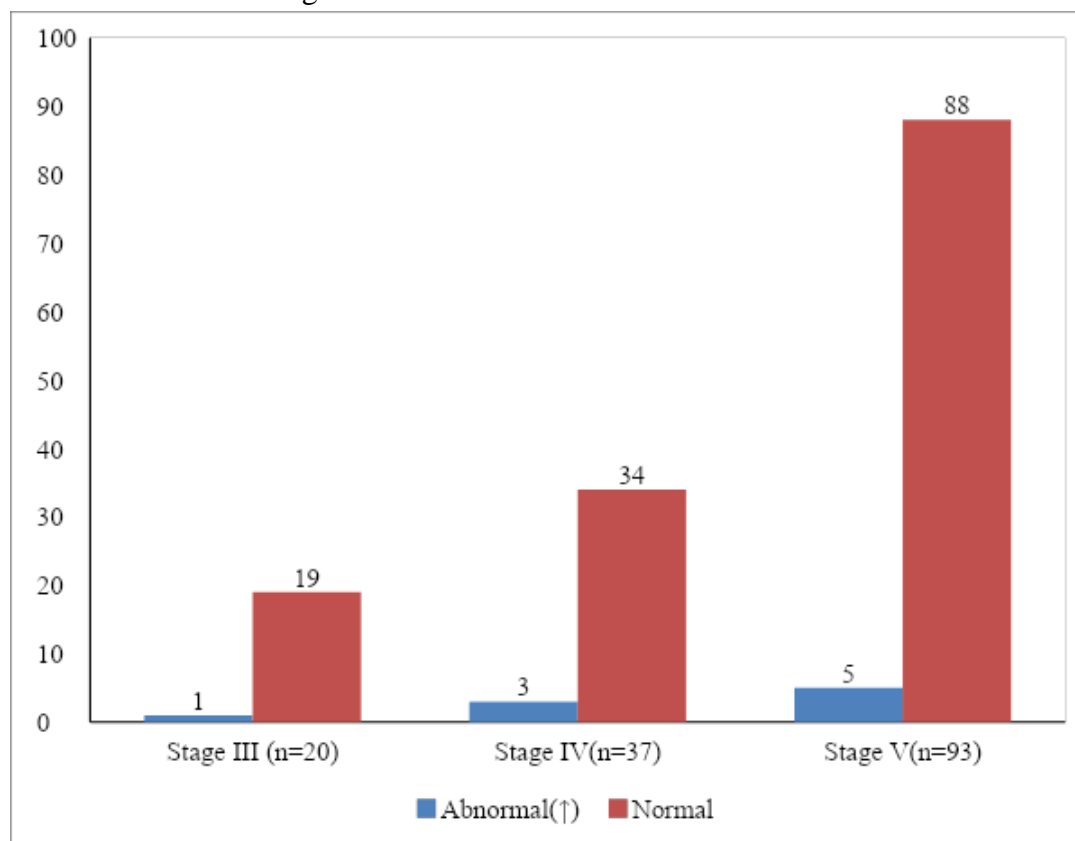


Table – 8 TG Vs Stage of CKD

TG	Stage III (n=20)	Stage IV(n=37)	Stage V(n=93)	P value
Abnormal(↑)	9	12	56	$P=0.013$
Normal	11	25	37	Chi Sq=3.98

Triglyceride fraction in Stage III, IV and V of CKD in this study was found to be abnormal in 9, 12 and 56 number of patients respectively. There

was statistically significant ($p=0.013$) increase in TG level in relation to increased severity of CKD in our study.

Graph 8: TG Vs Stage of CKD

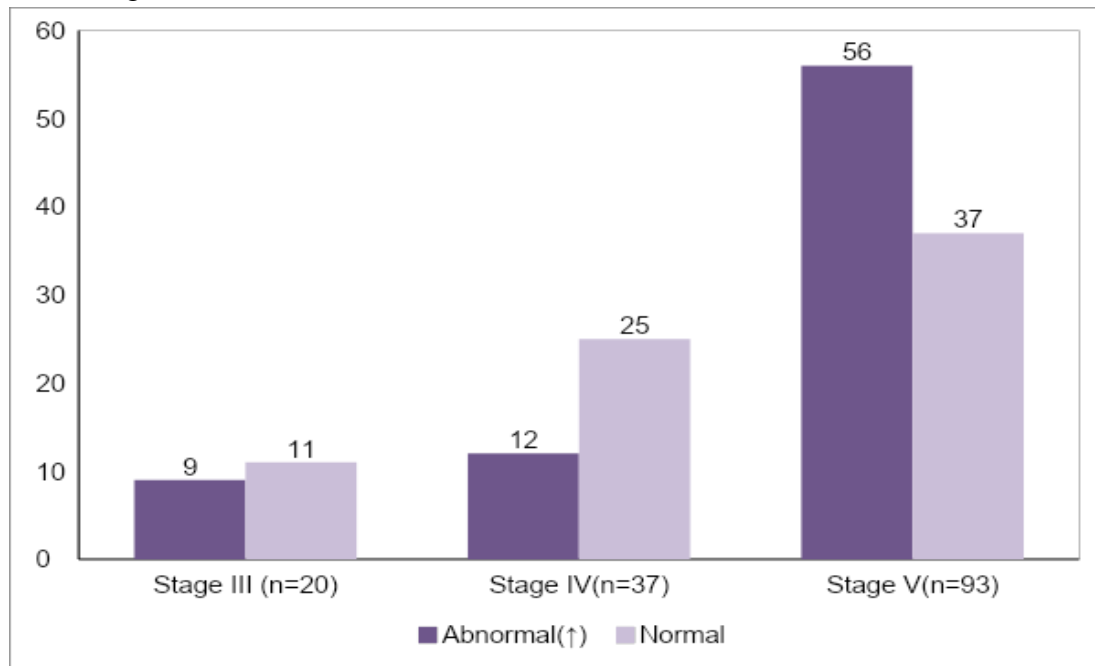


Table 9 HDL Vs Stage of CKD

HDL	Stage III (n=20)	Stage IV (n=37)	Stage V (n=93)	P value
Abnormal(↓)	10	18	61	$P=0.136$
Normal	10	19	32	Chi Sq=3.98

HDL level in Stage III, IV and V of CKD in this study was found to be abnormal in 10, 18, and 61 number of patients respectively. There was no

statistically significant ($p=0.136$) decrease in HDL level in relation to increased severity of CKD in our study.

Graph 9: HDL Vs Stage of CKD

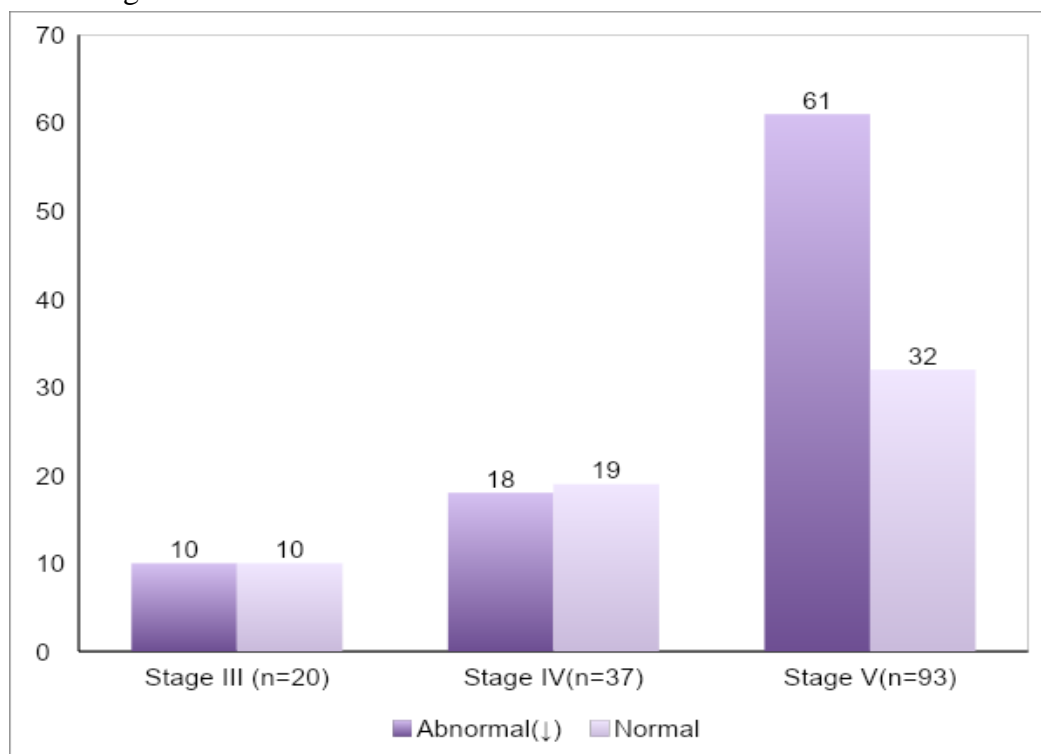


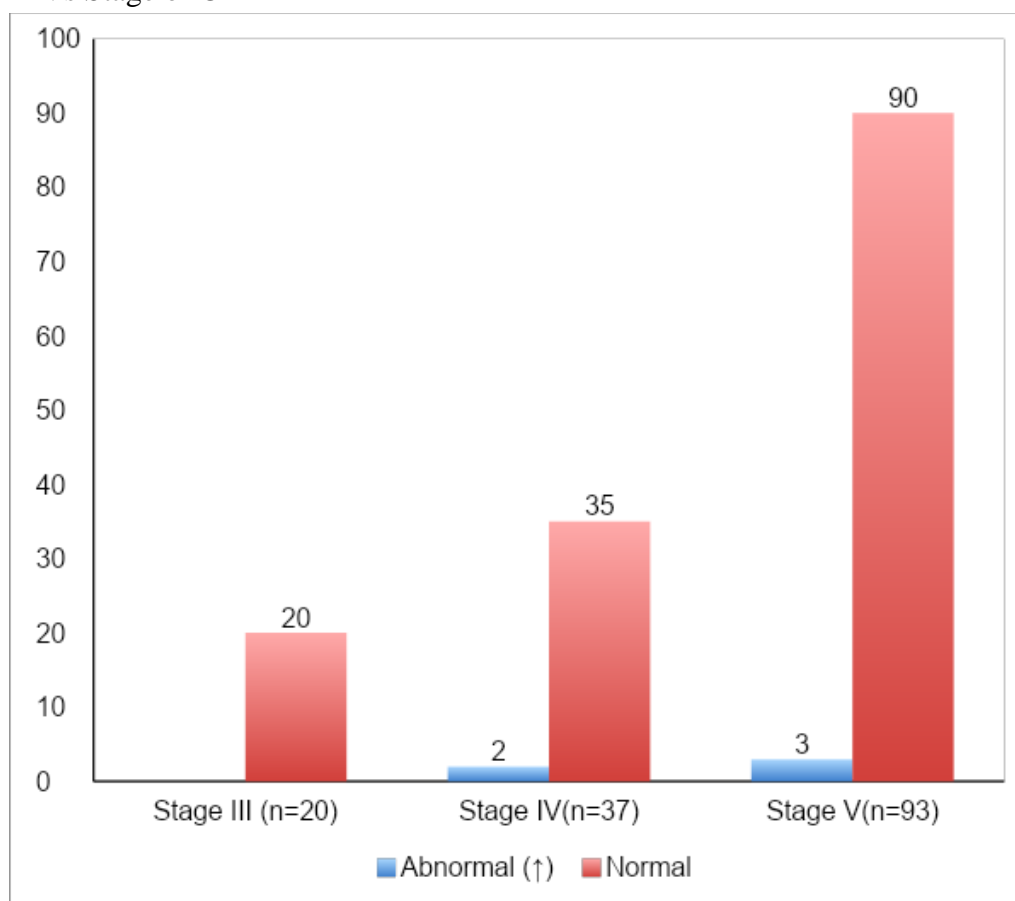
Table 10 LDL Vs Stage of CKD

LDL	Stage III (n=20)	Stage IV(n=37)	Stage V(n=93)	P value
Abnormal (↑)	0	2	3	P=0.55
Normal	20	35	90	Chi Sq=0.34

LDL level in Stage III, IV and V of CKD in this study was found to be abnormal in 0, 2, and 3 number of patients respectively. There was no

statistically significant (p=0.55) increase in LDL level in relation to increase severity of CKD in our study.

Graph 10: LDL Vs Stage of CKD



Discussion

Chronic kidney disease (CKD) results in profound lipid disorders, which stem largely from dysregulation of high-density lipoprotein (HDL) and triglyceride-rich lipoprotein metabolism. Specifically, maturation of HDL is impaired and its composition is altered in CKD.

In addition, clearance of triglyceride-rich lipoproteins and their atherogenic remnants is impaired, their composition is altered, and their plasma concentrations are elevated in CKD. Impaired maturation of HDL in CKD is primarily due to down regulation of lecithin cholesterol acyltransferase (LCAT) and, to a lesser extent,

increased plasma cholesteryl ester transfer protein (CETP). Triglyceride enrichment of HDL in CKD is primarily due to hepatic lipase deficiency and elevated CETP activity.

The CKD-induced hypertriglyceridemia, abnormal composition, and impaired clearance of triglyceride-rich lipoproteins and their remnants are primarily due to down regulation of lipoprotein lipase, hepatic lipase, and the very-low-density lipoprotein receptor, as well as, upregulation of hepatic acyl-CoA cholesterol acyltransferase (ACAT). In addition, impaired HDL metabolism contributes to the disturbances of triglyceride-rich lipoprotein metabolism. These

abnormalities are compounded by downregulation of apolipoproteins apoA-I, apoA-II, and apoC-II in CKD. Together, these abnormalities may contribute to the risk of arteriosclerotic cardiovascular disease and may adversely affect progression of renal disease and energy metabolism in CKD.

Hyperlipidemia accelerates progression of renal disease by several mechanisms. Reabsorption of fatty acids, phospholipids, and cholesterol contained in the filtered proteins by tubular epithelial cells can stimulate tubulointerstitial inflammation, foam cell formation, and tissue injury.^{14,15} Accumulation of lipoproteins in glomerular mesangium can promote matrix production and glomerulosclerosis.¹⁶⁻¹⁸ In this context, native and oxidized lipoproteins, particularly LDL, stimulate production of matrix proteins by cultured mesangial cells and promote generation of proinflammatory cytokines, which can lead to recruitment and activation of circulating and resident macrophages.^{19,20,21}

In addition, impaired HDL-mediated reverse cholesterol transport can further contribute to tissue injury by limiting the unloading of the excess cellular cholesterol and phospholipid burden. In fact, low plasma HDL has been identified as an independent risk factor for progression of renal disease.^{22,23} Moreover, hereditary LCAT deficiency, which is associated with a marked reduction in HDL cholesterol and impaired HDL-mediated reverse cholesterol transport, results in progressive renal disease.²⁴

The present study consisted of 150 patients of non diabetic chronic kidney disease. These patients satisfied the criteria laid by the National kidney foundation kidney disease outcome quality initiatives (NKF-KDOQI) for diagnosing CKD.

Age and Sex Distribution

In this study age of the patients varies from 22 yrs to 80 yrs and majority 68.67% of the patients are in 41-60 yrs age group. Maximum number of CKD cases are in there 5th to 6th decades of life. Mean age of the patients in our study is $52 \pm$

11.41 and this is consistent with the observation made by Rajapurkar et al.¹¹. In this study 52% of patients were male and 48% were female which is similar to the observation made by Agarwal SK, Dash SC et al¹² but differs from the study of Rajapurkar et al in which male to female ratio was found 2.33: 1.

Staging of Chronic Kidney Disease (CKD) in the Study Population

In the present study it was found that all the patients were suffering from Stage 3, 4, 5 of CKD. Most of the patients were in Stage 5 i.e 62% of cases. Stage 3 and 4 patients represents 13.33% and 24.67% of total study populations respectively and none in Stage 1 and 2 Which was similar to the finding of Sathyan et al.¹³ Majority of the patients are in Stage 4 and 5.

Dyslipidemia in CKD

The results of this study on the lipid profile in patients with chronic kidney disease show that there are significant alteration in lipid profiles of these patients.

Prevalence of Dyslipidemia

In the study population the prevalence of dyslipidemia was found 78.67% which is consistent with the findings of Ganta V et al (65.5%), P Mohanraj, G. Anbazhagan, S. Kalaivalli (74%). Most common abnormality in this study is decreased HDL 59.33% followed by increased TG in 51.33% of cases. Increased T.Ch & LDL are seen in 6% and 3.33% of patients respectively. The prevalence of dyslipidemia in Stage III, IV and V were 75%, 73% and 81.7% respectively. In our study we found no significant relationship ($p=0.28$, $\chi^2=2.49$) between prevalence of dyslipidemia with severity of CKD but Ganta V et al have noted significant relationship. This may be due to the variation in sample size in different stages of chronic kidney disease. When individual fractions of lipid profile were compared with the stages of CKD, decreased HDL is the most frequent abnormality which was found in 65.59% of patients in Stage V. In Stage III and Stage IV population decreased HDL was

50% & 48.64% respectively. Increased TG found in Stage III, IV & V were 45%, 32.43% and 60.21% respectively. Abnormality in serum TG level was found statistically significant ($p=0.013$) in relation to severity of CKD but rest of the fractions shown no significant association.

Decreased HDL Cholesterol

Most common lipid abnormality in our study is decreased HDL levels found in 59.33% of patients. Mean HDL in study and control group are 32.82 ± 14.01 and 39.82 ± 8.21 . There is statistically significant difference obtained between study population and the controls ($p<0.05$). Similar observation has been noted by P. Mohanraj, G. Anbazhagan, S. Kalaivalli in their study but it differs from many studies by Ganta V et al⁵, , Gupta DK²⁵, Das BS²⁶ and Bagdae J²⁷ Diana M Lee LG et al²⁸, where hypertriglyceridemia is the most common lipid abnormality. Study of Rapoport, Aviram, showed there is no decrease in HDL concentration in chronic kidney disease patients.²⁹ Nisha I. Parikh, Shih-Jen Hwang, Marin G. Larson noted low HDL and CKD have a synergistic effects on cardiovascular disease risk.³⁰

Recent study by Bowen B et al, found significant association between low HDL levels and risk of incident CKD and CKD progression.³¹

Elevated Triglycerides

Second most frequent lipid abnormality in our study is Hypertriglyceridemia (\uparrow TG). Mean value of study and control group were 163.18 ± 83.53 and 101.65 ± 20.71 respectively. The present study demonstrates that there was a significant alteration ($p<0.05$) in TG fractions between study population and the control group. CRF is commonly accompanied by lipid abnormality in the form of hypertriglyceridemia. This is similar to the observations made in Western studies and recent Indian studies by P. Mohanraj, G. Anbazhagan, S. Kalaivalli,⁴ Ganta V et al,⁵ Gupta DK,²⁵ Das BS²⁶ and Bagdae J. et al.²⁷

Total Cholesterol and LDL

In this study the total cholesterol level was marginally elevated in 6% and LDL in 3.33% of patients. Shah et al, in their study showed no significant change in levels of total cholesterol.³² Gerald Appel et al., showed normal or decrease in LDL levels.³³

Anderson et al, showed increase in LDL levels which differs from our observation.³⁴

Chronic kidney disease in the absence of heavy proteinuria does not significantly affect gene expressions of either hydroxyl-3-methylglutaryl-CoA reductase (HMG-CoA reductase) which is the rate-limiting enzyme for cholesterol biosynthesis, or that of cholesterol 7 α -hydroxylase which is the rate-limiting enzyme for cholesterol catabolism and conversion to bile acids.³⁵ So CKD in the absence of heavy proteinuria does not alter hepatic LDL receptor gene expression, thereby LDL levels are not elevated. Heavy proteinuria alone or in combination with chronic renal insufficiency results in acquired LDL receptor deficiency, which plays a central role in the genesis of the associated hypercholesterolemia.³⁶.

Conclusion

Predominant lipid abnormalities were reduced HDL and elevated TG levels. Due to the significant association between low HDL levels and risk of incident CKD and CKD progression, Screening of HDL level in CKD patients can be used as a diagnostic tool to detect disease severity. There is statistically significant rise in TG fraction in relation to severity of CKD but prevalence of dyslipidemia in relation to severity of CKD showed no significance

There is minimal increase in serum T.Ch and LDL-Cholesterol level in the study populations.

Lipid abnormalities in chronic kidney disease accelerates the progression of the kidney disease and predisposes to cardio vascular disease risk. Therefore it is worthwhile to detect early and treat dyslipidemia in these patients but a large prospective study is necessary to find the direct

causal relationship between the lipid abnormality in CKD and cardiovascular disease.

Limitations of the Study

- Smoking, alcoholism may alter the lipid pattern in the body. Their influences in the study group also have to be considered.
- Patients on drugs affecting lipid metabolism like beta blockers and oral contraceptive pill have to be considered.
- We had not estimated the lipid abnormalities in patients who underwent dialysis or renal transplantation.
- This is a hospital based study with small study population. Sample size should be more to show the significance of lipid abnormality in relation to CKD severity.

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