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Total Cholesterol and Triglyceride Level in Patients of Chronic Kidney Disease

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Abstract
Background: *The high prevalence of total cholesterol and triglyceride level in chronic kidney disease (CKD) patients reveals significant association between CKD and dyslipidemia.*
Objectives: *The aim of study the total cholesterol and triglyceride levelin patients of CKD and study the correlation between total cholesterol, triglycerides and severity of renal diseases.*
Materials and Methods: *A cross-sectional study were conducted among CKD patients attending OPD and admitted in Medicine department of GSVM Medical College, Kanpur from January 2018 to October 2019 to investigate thyroid function and lipid profile in CKD stage 3–5. A total of 100 newly diagnosed and known CKD cases (stage 3 to stage 5) would be included in the study.*
Result: *Correlation between triglycerides of case and control where mean of control group is99.05±18.93, and case group is 180.61±89.77 where p value is 0.0001.correlation between serum total cholesterol of case and control group where mean of control group is 139.58±20.84, and case group is 167.49±18.24, where p value is 0.0001.*
Conclusion: *The correlation of Total Cholesterol and Triglycerides in CKD patients is found to be highly significant.*
Keyword: *Chronic Kidney Disease, Triglycerides, Total Cholesterol.*

Introduction

The lipoprotein metabolism

Lipoproteins are substances formed by the combination of proteins with lipids which are hydrophobic, in order to transport them to various organs. The human plasma lipoproteins can be classified into four groups.

Chylomicrons

Very low density lipoproteins (VLDL) Low density lipoproteins (LDL) High density lipoproteins (HDL).

Digestion of fats

The usual diet contains small quantities of phospholipids, cholesterol and cholesterol esters. The phospholipids and cholesterol esters contain fatty acid and therefore can be considered to be fats themselves. Cholesterol on the other hand is a sterol compound containing no fatty acid but it does exhibit some of the physical and chemical characteristics of fats, it is derived from fatsand it is metabolized similarly to fats. Therefore,

cholesterol considered from a dietary point of view to be a fat.

Digestion of Fats in the Intestine

Triglycerides are water insoluble non swelling lipids. A small amount of short chain triglycerides of butter fat organised digested in the stomach by gastric lipase (tributyrase). Essentially all fat digestion occurs in small intestine as follows:

Emulsification of Fat by Bile Acids

The carboxyl and other polar parts of the bile salt molecule highly soluble in water whereas most of the sterol portion of the bile salt is highly soluble in fat. The lipases are water soluble compounds and can attack the fat globules on their surfaces, consequently it can be readily understood that it is how important the detergent function of bile salts is, for the digestion of fats.

Digestion of fats by pancreatic lipase

By far the most important enzyme for the digestion of fats is pancreatic lipase in the pancreatic juice. However, the epithelial cells of the small intestine also contain a minute quantity of lipase known as enteric lipase. Both of these acts alike to cause hydrolysis of fat as follows;

$$\text{Tristearin} \xrightarrow{\text{lipase}} \text{2Monoglyceride + Stearicacid}$$

Hydrolysis of Neutral fat catalysed by lipase end products

End products of fat digestion

Most of the triglycerides of the diet are split into free fatty acids and 2-monoglycerides. However, small portions are not digested at all remain in the di glyceride state.

$$\text{Emulsified fat} \xrightarrow{\text{PANCREATIC LIPASE}} \text{Fatty acids and 2-Monoglycerides}$$

The hydrolysis of triglycerides is a highly reversible process; therefore, accumulation of monoglycerides and free fatty acids in the vicinity of digesting fats quickly blocks further digestion. Fortunately, the bile salts play an important role in removing the monoglycerides and free fatty acids from the vicinity of the digesting fat globules.

Digestion of cholesterol esters and phospholipids

Cholesterol esters and the phospholipids are hydrolysed by lipases in the pancreatic secretion, thatfree the fatty acids - the enzyme cholesterol ester hydrolase to hydrolyse the cholesterol ester and phospholipase A2 to hydrolyse the phospholipid.

Absorption of fats

In the presence of an abundance of bile acids, approximately 97 percent of the fat is absorbed, in the absence of bile acids, only 50 to 60 percent is normally absorbed.

The mechanism for absorption of the mono glycerides and fatty acids through the brush border is based entirely on the fact that both these substances are highly lipid soluble. Therefore, they become dissolved in the membrane and simply diffuse to the interior of the cell.

After entering the epithelial cell, the fatty acids and monoglycerides are taken up by the smooth endoplasmic reticulum and here they are mainly recombined to form new triglycerides. However, a few of the monoglycerides are further digested into glycerol and fatty acids by an epithelial cell lipase. Then, the free fatly acids are reconstituted by the smooth endoplasmic reticulum into triglycerides.

This provides an electrically charged surface that makes these globules miscible with the fluids of the cell In addition small amounts of B-lipoprotein also synthesized by the endoplasmic reticulum, coat part of the surface of the each globule. In this form the globule diffuse to the side of the epithelial cell and is excreted by the process of cellular exocytosis into the space between the cells, from there it passes into the lymph in the central lacteal of the villus. These globules are then called chylomicrons.

Transport of the Chylomicrons in the Lymph

From the sides of the epithelial cells the chylomicrons wend their way into the central lacteals of the vii and from here are propelled along with thelymph, by the lymphatic pump upward through the thoracic duct to be emptied into the great veins of the neck. Between 80 to 90 percent of all fat absorbed from the gut is absorbed in this manner and is transported to the blood by way of the thoracic lymph in the form of chylomicrons.

Direct Absorption of Fatty Acids into the Portal blood

Small quantities of short chain fatty acids such as those from butter fat are absorbed directly into the portal blood rather than being converted in to triglycerides and absorbed into the lymphatics. The cause of this difference between short and long chain fatty acid absorption is that the shorter chain fatty acids are more water soluble and are reconverted into triglycerides. This allows direct diffusion of these fatty acids from the epithelial cells into capillary blood of the villus.

Rate Limiting Steps of Fat Absorption

Miscellar solubilization

Permeation across the unstirred water layer.

Intracellular uptake

Secretion of lipoprotein For the diffusion process the unstirred water layer is implicated as the rate limiting step for large molecular structure such as Micelles. Whereas lipid membrane limits diffusion of smaller molecules.

APO Lipoproteins

Apo-lipoproteins play a key role in metabolism and may be important factor in the development of atherosclerosis. Each class of lipoprotein has a variety of Apo lipoproteins in differing proportions, with the exception of LDL which predominantly contain only Apo B. Apolipoprotein A is the major protein in HDL.

Apolipoprotein A

Apo lipoprotein AI and All constitute about 90% of total HDL. Apolipoprotein AI has two major sites of synthesis, primarily the intestine and liver. The intestinally derived Apo AI enters the circulation associated with chylomicron but is rapidly transferred to HDL particle during lipase hydrolysis of chylomicrons. Hepatic Apo Al probably enters circulation associated with HDL particles. Because Apo AI binds lipid and is the major protein constituent of HDL, it follows that Apo AI must be an important structural component of lipoproteins. The major site of synthesis of Apo AII is liver. Apo AII might inhibit LCAT enzymes and activate the hepatic lipase enzyme.

APO B

Apo lipoprotein is a heterogeneous protein and exists primarily as two forms, Apo B-100 and Apo B-48. The majority of Apo B present in fasting plasma consists of apo-B-100. This protein is present in LDL and VILDL. Apo B-100 is synthesized in liver. It is suggested that there is single molecule of apo-B-100 per LDL particle. Apo lipoprotein B-48 is neither the product nor the precursor of Apo B-100. Apo B-48 is found in chylomicrons. Both Apo B-100 and B-48 play an important role in regulating cholesterol synthesis and degradation.

Apolipoprotein C

The Apo C consists of three major low molecular weight proteins, Apo CI, CII, CIII. Liver is the major site for the synthesis of the Apo C proteins while intestine contributes just a minor portion. Apolipoprotein CI, the smallest of the C Apolipoproteins, is reported to activate LCAT in vitro. Apo CIII plays an important role in the metabolism of triglyceride rich lipoprotein (VLDL) and chylomicrons. It activates the lipoprotein lipase (LPL) enzyme that hydrolyses the triglyceride in the lipoproteins liberating fatty acids. Apo CII the most abundant of the C Apolipoproteins, exist in at least three polymorphic forms.

APO E

Apolipoprotein E is a constituent of chylomicrons VLDL and HDL. The major site of synthesis of Apo E is the liver.

In addition, it has been demonstrated that macrophages produce this protein. Apolipoprotein E plays a central role in the metabolism of triglyceride rich lipoproteins. It regulates and facilitates cholesterol uptake through the interaction of chylomicron remnants with specific Apo E receptors on hepatic and extra hepatic cellular membranes.

Lipid Abnormalities in CKD

Progressive renal failure especially when associated with proteinuria is accompanied by abnormalities of lipoprotein transport. Typically, the dyslipidaemia is reflected predominantly in

increased serum levels of triglycerides with high levels of VLDL, Apo B and pre ß HDL and low levels of HDL and of Apo A. Cholesterol levels may be very high in proteinuric patients.

Urinary protein loss stimulates an increased LDL synthesis by the liver. It is likely that proteinuria with the resultant hypoalbuminemia leads to an up regulation of 3-hydroxy-3-methyglutaryl CoA reductase with a consequent hypercholesterolemia. Lipoprotein lipase (P) is the rate-limiting enzyme in lipolysis of chylomicrons and VLDL. LPL binds to heparan sulphate proteoglycans on the cell surface of endothelium. In proteinuric renal diseases, a down regulation of LPL protein and enzymatic activity was found. These events are largely responsible for profound abnormalities in lipoprotein metabolism in nephrotic syndrome and chronic kidney disease there by rendering these lipoproteins more atherogenic.

The existence of a link between dyslipidaemia and oxidative stress in the pathogenesis of renal damage was shown in nephrectomised rats, in glomerular and tubulointerstitial infiltration and aggravated glomerulosclerosis. Oxidative stress, with the resultant increased reactive oxygen species generation, contributed significantly to these chronic degenerative processes.

.This is also supported by the study done in patients with metabolic syndrome who were found to have a higher prevalence of CKD. Thus dyslipidaemia is not only the consequence of chronic renal disease but it also increases the progression of the disease condition. The uremic dyslipoproteinemia has been linked to alarming incidence of cardiovascular complications. Cardiovascular disease has been the leading cause of death in patients who are on chronic haemodialysis therapy.

Material and Method

Study Design

A cross-sectional study conducted among CKD patients attending OPD and medicine emergency of Medicine department of GSVM Medical College, Kanpur from January 2018 to October 2019. A total of 200 patients with 100 newly diagnosed and100 known CKD cases (stage 3 to stage 5) were included in the study. CKD will be defined on the basis of National Kidney Foundation guidelines of having an estimated glomerular filtration rate (EGFR) < 60 ml/min/1.732 m^2 for more than 3 months. The Modification of Diet in Renal Disease study (MDRD) equation used to calculate eGFR. eGFR between 30-60 ml/min considered as moderate CKD (Stage 3) and eGFR< 30 ml/min considered as severe CKD (Stage 4 & 5) in the present study. The study protocol was approved by the Institutional Review Board of Ethics Committee GSVM Medical College, Kanpur and consents would be obtained from each patient.

Sample Size: 100 cases and 100 controls of age and gender matched of Age group 20-70 years was taken.

Selection of Study Subjects

Inclusion Criteria

- Patients between Age 20 -70 years of either sex.
- All patients diagnosed with moderate to severe CKD.

Exclusion Criteria

- Age <20 years and >70 yrs.
- Patients with history of hyper or hypothyroidism.
- CKD patients who were or underwent previous dialysis.
- Obesity
- Nephrotic Syndrome.
- Patients on estrogens, corticosteroids, anti-thyroid drugs, dietary supplements, lipid lowering drugs.
- Pregnant Woman
- Acutely ill patients

Investigation

Hb, Total leukocyte count ,KFT, LFT, Platelet count, TSH, FT3,FT4, Lipid Profile (TC, TG, LDL, HDL, VLDL), Hba1c

Results

In our study total 200 patients were taken in which 100 were in case group and 100 in control group. Age group of patients were in between 20 to 70 years in both case group and control group.

Table 1: Gender Wise Distribution of Case

GENDER	NUMBER
MALE	71
FEMALE	29

Table 2: Gender Wise Distribution of Control Group

GENDER	NUMBER
MALE	66
FEMALE	34
TOTAL	100

Table 3 Mean Value of Triglyceride of Case And Control Group

MEAN	CONTROL	CKD
	99.05±18.93	180.61±89.77

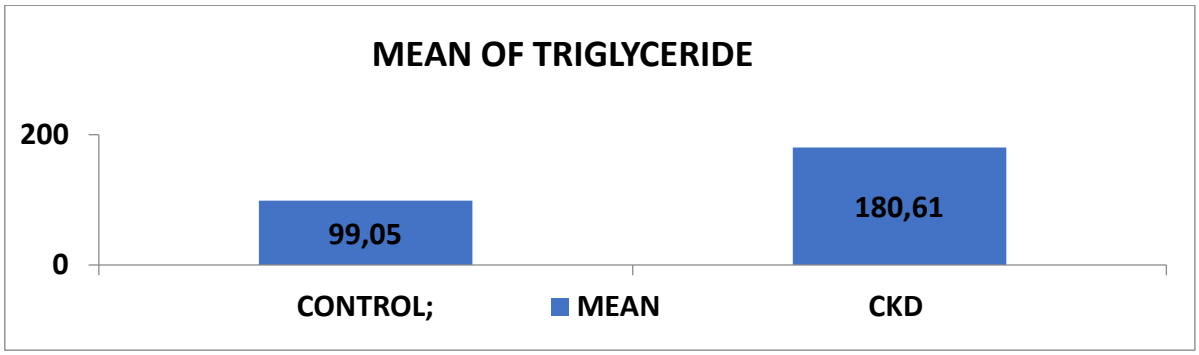

Figure 3 Correlations between Triglyceride of Case and Control Group

Correlation between Triglyceride of case and control group where mean of control group is 99.05±18.93 and case group is 180.61±89.77 where p value is 0.0001 with confidence interval of 63.46 to 99.65 with t value of 8.89.

Table 4 Mean Value of Serum Total cholesterol

MEAN	CONTROL	CKD
	139.58±20.84	167.49±18.24

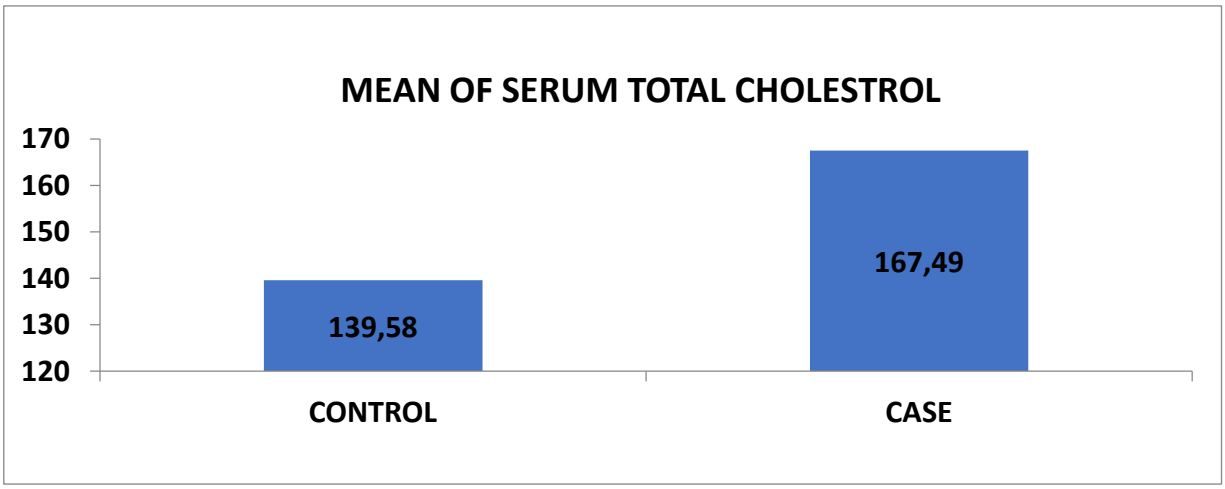

Figure 4 Correlations between Serum Total Cholestrol of Case and Control Group

Correlation between Serum cholesterol of case and control group where mean of control group is 139.58±20.84 and case group is 167.49±18.24 where p value is 0.0001with confidence interval of 22.44 to 33.37 with t value of 10.07.

Discussion

Chronic kidney disease (CKD) is a serious health problem and the no. Of people with impaired renal function is rapidly increasing. Progression of CKD is associated with having a number of complications, including thyroid dysfunction, dyslipidaemia and CVD.

We studied 200 patient which are between the age of 20 years to 70 years and diagnose as CKD in which 100 were in case group and 100 were in control group and patient were investigated for thyroid profile in which we are investigating for serum Triglyceride leveland serum total cholesterol level group in biochemistry department laboratory of GSVM medical college, and compared with control.

First we discuss the Total cholesterol level in case group and control group and we found that mean value of Total Cholesterol was 167.49 mg/dl and standard deviation was 18.24 and the mean value of Total cholesterol in control group was 139.58 mg/dl and the standard deviation was 20.84. And the mean of Total Cholesterol of case group and control group were compares and found that the value Total cholesterol was higher in case group and was highly significant and this was also found in many studies so these patient needs early treatment.

We also discuss the Triglyceride level in case group and control group and we found that mean value of Triglyceride was 180.61 mg/dl and standard deviation was 89.77 and the mean value of Triglyceride in control group was 99.05 mg/dl and the standard deviation was 18.93. And the mean of Triglyceride of case group and control group were compares and found that the value of Triglyceride was higher in case group and was significant and these patient should be treated.

Conclusion

In our study we found that level of total cholesterol and triglycerides has highly significant correlation with chronic renal failure. (p value is 0.0001)

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