

A DISSERTATION  
ON  
**"STUDY OF FASTING AND POST-PRANDIAL LIPID  
ABNORMALITIES IN TYPE-2 DIABETES MELLITUS IN  
CORRELATION WITH INCREASED  
CARDIOVASCULAR MORBIDITY AND MORTALITY"**

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THE TAMILNADU DR. M. G. R UNIVERSITY  
CHENNAI

In partial fulfilment of the regulations  
for the award of  
M.D DEGREE IN GENERAL MEDICINE  
BRANCH I



GOVERNMENT MOHAN KUMARAMANGALAM  
MEDICAL COLLEGE, SALEM  
APRIL 2016

**Government Mohan Kumaramangalam Medical College Hospital**



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I hereby declare that this dissertation titled "**STUDY OF FASTING AND POST-PRANDIAL LIPID ABNORMALITIES IN TYPE-2 DIABETES MELLITUS IN CORRELATION WITH INCREASED CARDIOVASCULAR MORBIDITY AND MORTALITY**"

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## LIST OF ABBREVIATIONS

ADA	American Diabetes Association
Apo-E	Apolipoprotein E
CAD	Coronary Artery Disease
CE	Cholesteryl ester
CETP	Cholesteryl ester transfer protein
DM	Diabetes mellitus
FFA	Free fatty acid
HDL	High density lipoprotein
HL	Hepatic lipase
IDL	Intermediate density lipoprotein
IHD	Ischemic heart disease
LCAT	Lecithin cholesterol acetyl transferase
LDL	Low density lipoprotein
LDLR	Low density lipoprotein receptor
Lp(a)	Lipoprotein(a)
LPL	Lipoprotein lipase
PL	Phospholipid
SR-BI	Class B, type I scavenger receptor
TC	Total cholesterol
INR	International normalised ratio
TG	Triglyceride

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## **ABSTRACT**

### **BACKGROUND AND OBJECTIVES**

Type 2 diabetes mellitus is associated with the development of premature atherosclerosis and a higher cardiovascular morbidity and mortality. Diabetic dyslipidaemia is believed to play an important role in the pathogenesis of accelerated atherosclerosis in this condition. It is being increasingly believed that atherosclerosis is a postprandial phenomenon as at least with respect to lipids, we are in the postprandial phase for most of the day. High postprandial triglycerides have shown a strong and independent association with CAD. Hence this study is being carried out to assess the characteristics of post prandial dyslipidaemia in types 2 diabetes mellitus in comparison with the fasting lipid levels in diabetics and controls.

### **METHODOLOGY**

This was an observational study which included the patients admitted in The Government Mohan kumaramangalam Medical college Hospital, Tamil Nadu. The study included 50 patients with type 2 diabetes mellitus meeting the inclusion criteria and were compared with 50 age and sex matched healthy controls, fulfilling the inclusion and exclusion criteria.

## **METHOD OF COLLECTION OF DATA**

Data for the proposed study was collected in a pretested proforma . Detailed history and physical examination of all the cases and controls was done. Fasting and Post prandial lipid levels were estimated in all the cases and controls. Blood was collected from patients after an overnight (12-hour) fast and six hour postprandial (after a standard meal) for lipid profile measurements.

## **RESULTS**

The majority of cases and controls were in the age group of 61-70 years. All the cases in the fasting state had a raised triglyceride (mean  $172.92 \pm 75.51$ mg/dL) level, raised VLDL-C (mean  $37.76 \pm 20.01$ mg/dL) level, decreased HDL-C (mean  $33.44 \pm 11.99$ mg/dL) level, normal total cholesterol (mean  $176.36 \pm 52.43$ mg/dL) level and normal LDL-C (mean  $101.16 \pm 38.17$ mg/dL) levels compared to the control group.

In the post prandial state the diabetics had a significant increase in the post prandial triglyceride level (mean  $232.52 \pm 105.08$ mg/dL), decrease in the HDL-C level (mean  $30.96 \pm 11.15$ mg/dL) compared to the fasting state whereas in the control group there was no significant increase in the post prandial lipid levels compared to the fasting state.

## **CONCLUSION**

The dyslipidemia of Type 2 DM is characterised mainly of raised triglyceride levels, raised VLDL-C Levels and decreased HDL-C levels. In the post prandial state there was significant hyper-triglyceridaemia and decreased HDL-C level in diabetics when compared to that of the controls.

# INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders characterised by the distinct phenotype of hyperglycemia. Various distinct types of DM are due to the complex interaction of the environmental and the genetic factors.

Based on the etiology of the DM, factors responsible for hyperglycemia are reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation seen in DM is responsible for secondary pathophysiologic changes in multiple organ systems which results in tremendous burden on the individual suffering from diabetes as well as on the health care system.

DM is classified based on the the pathogenic process responsible for hyperglycemia, as opposed to earlier criteria based on age of onset or type of therapy.

The two broad categories of DM are designated as type 1 diabetes and type 2 diabetes. Both types of diabetes are preceded by the period of abnormal glucose homeostasis . Type 1 DM occurs because of complete or near-total insulin deficiency. Type 2 DM is a heterogeneous group of disorders and the

factors responsible for hyperglycemia include variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. Distinct genetic and metabolic defects in insulin action and/or secretion is responsible for the common phenotype of hyperglycemia in type 2 DM and have important potential therapeutic implications based on which the pharmacologic agents are available to target specific metabolic derangements.

Type 2 DM is preceded by a phase of abnormal glucose homeostasis defined as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT).

Dyslipidemia that is associated with type 2 diabetes plays a vital role in the pathogenesis of accelerated atherosclerosis in that population. The most important features of this dyslipidemia include an elevated very low density lipoproteins (VLDL) and total triglycerides (TGs) and a decreased high density lipoproteins (HDL) concentration in the serum. While fasting hypertriglyceridemia plays an important role in atherosclerosis, particularly in people with diabetes mellitus, this association has been less consistent and fasting HDL-C appears to be a far more significant determinant of atherosclerosis. However, when TGs are analysed in the postprandial state, they emerge as an independent and stronger coronary risk factors than HDL-C.

Postprandial hypertriglyceridemia is shown to be associated with asymptomatic and symptomatic macro vascular disease in both normo- and hypertriglyceridemic groups and such abnormalities have been reported in people with type 2 diabetes and hence the increased risk of atherosclerosis among them, might therefore be correlated to the higher degree of postprandial triglyceridemia.

Earlier studies clearly demonstrate the presence of hypertriglyceridemia in the postprandial state among the diabetic subjects, irrespective of whether fasting triglyceride levels were high or low.

It is not clearly known whether the patients with type 2 diabetes with macro vascular disease have greater abnormalities of the triglyceride metabolism in the post prandial state than those without.

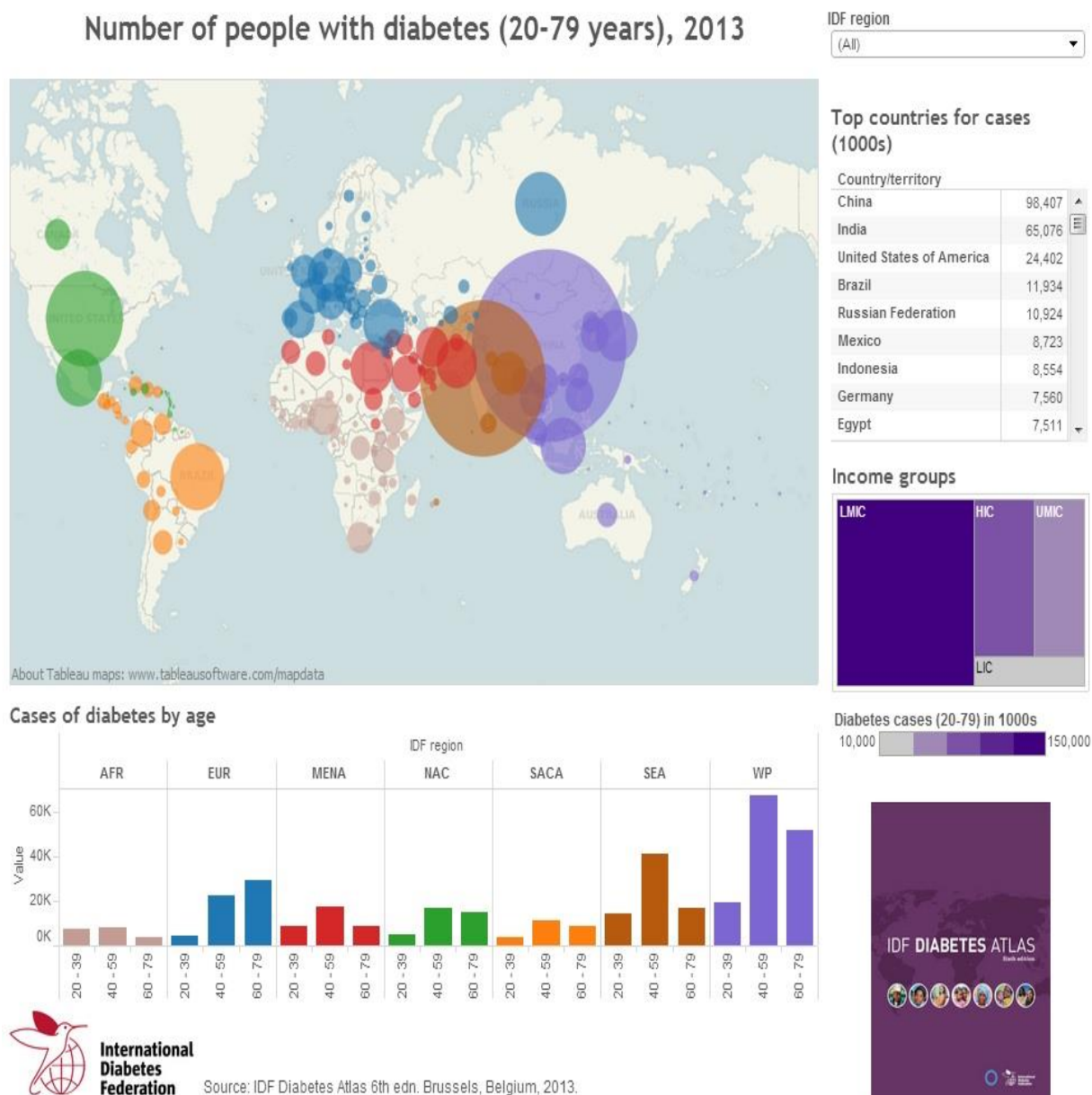
## **AIMS AND OBJECTIVES**

1. To study the post-prandial lipid abnormalities in patients with type 2 Diabetes Mellitus.
2. To compare the relationship between fasting and post-prandial lipids in Diabetics and Non Diabetics

# REVIEW OF LITERATURE

The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 382 million in 2013. Based on the current trends, the International Diabetes Federation projects that 592 million will have diabetes by 2035. Although the prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalence of type 2 DM is rising much more rapidly, presumably because of increasing obesity, reduced activity levels as countries become more industrialized, and the ageing of the population.<sup>(1)</sup>

In 2013, the prevalence of diabetes in individuals from age 20-79 ranged from 23 to 37% in the 10 countries with highest prevalence. The countries with the greatest number of individuals with diabetes in 2013 are China ( 98.4 million), India (65.1 million), United States (24.4 million), Brazil (11.9 million) and the Russian federation (10.9 Million). DM increases with aging. In 2012, the prevalence of DM in the United States was estimated to be 0.2% in individuals aged <20 years and 12% in individuals aged >20 years. In individuals aged >65 years, the prevalence of DM was 26.9%. The prevalence is similar in men and women throughout most age ranges.<sup>(1)</sup>



**Fig. 1 Worldwide Prevalence of diabetes in 2013**

# LIPIDS AND LIPOPROTEINS

The lipids are a heterogeneous group of compounds that are important dietary constituents not only because of their high energy value, but also because of the fat-soluble vitamins and the essential fatty acids contained in the fat of natural foods. <sup>1</sup>

They are found in cell membranes, which maintain cellular integrity and allow the cytoplasm to be compartmentalized into specific organelles. Lipids function as a major form of stored nutrients (triglycerides), as precursors of adrenal and gonadal steroids and bile acids (cholesterol), and as extracellular and intracellular messengers (e.g., prostaglandins, phosphatidylinositol). <sup>2</sup>

Combinations of lipid and protein (lipoproteins) are important cellular constituents, occurring both in the cell membrane and in the mitochondria, and serving also as the means of transporting lipids in the blood. <sup>1</sup>

## Classification of lipids <sup>1</sup>

**1. Simple lipids:** Esters of fatty acids with various alcohols.

a. **Fats:** fatty acids + glycerol

b. **Waxes:** fatty acids + higher molecular weight monohydric alcohols

**2. Complex lipids:** Esters of fatty acids containing groups in addition to an alcohol and a fatty acid.

a. **Phospholipids:** fatty acids + alcohol + a phosphoric acid residue.

Eg. glycerophospholipids , sphingophospholipids

b. **Glycolipids (glycosphingolipids):** Lipids containing a fatty acid, sphingosine, and carbohydrate.

c. **Other complex lipids:** eg. Sulfolipids, aminolipids, Lipoproteins.

**3 . Precursor and derived lipids:** These include fatty acids, glycerol, steroids, other alcohols, fatty aldehydes, and ketone bodies , hydrocarbons, lipid-soluble vitamins, and hormones.

# **LIPOPROTEINS**

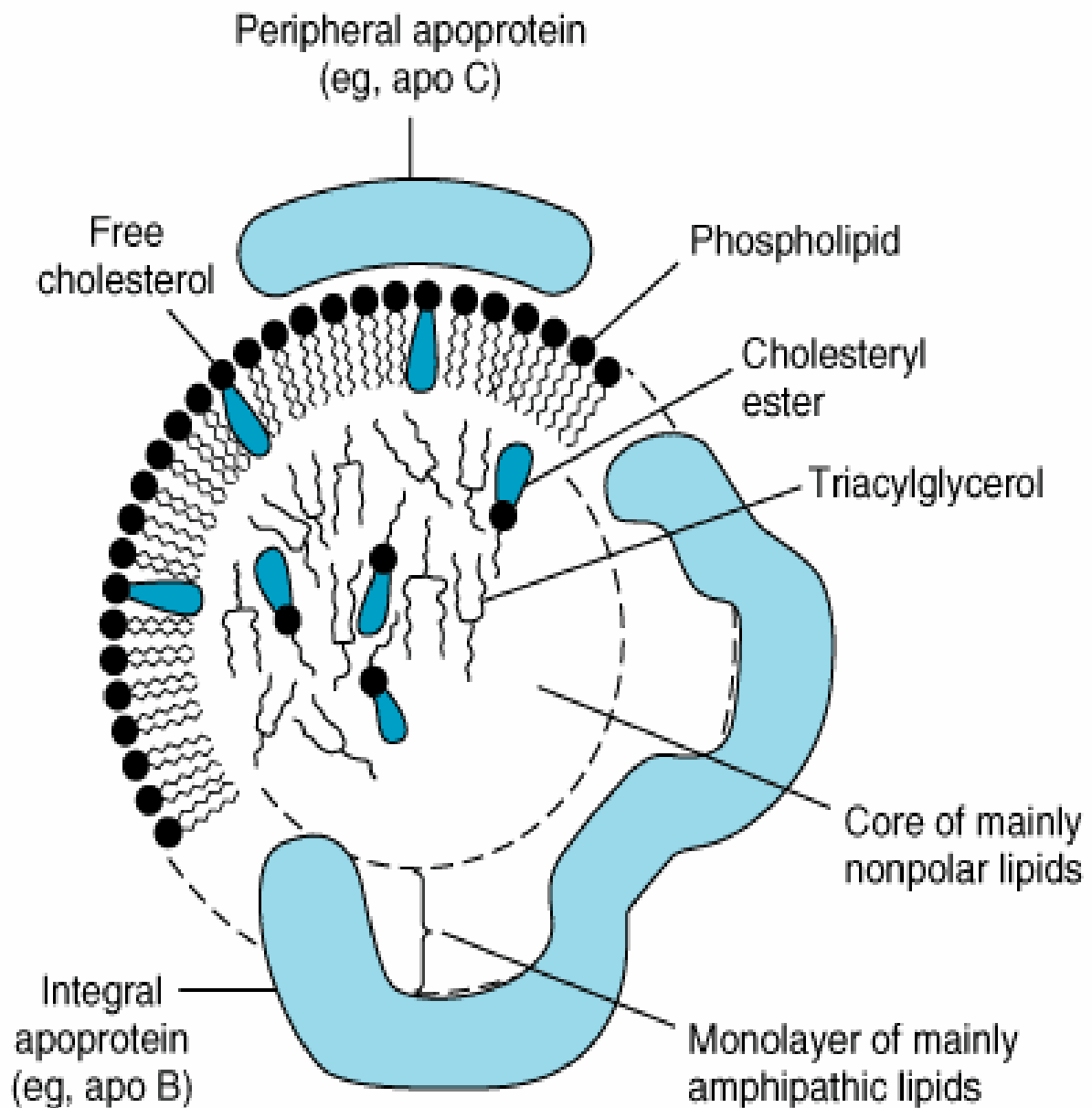
Lipoproteins are microemulsions composed of lipids (cholesterol, cholesteryl ester, triglyceride, and phospholipid) and proteins (apoproteins). Their function is to transport non-water-soluble cholesterol and triglycerides in plasma.<sup>3,4,5</sup>

## **Structure of a plasma lipoprotein.<sup>1</sup>**

Lipoproteins consist of a nonpolar lipid core made up of mainly triacylglycerol and cholesteryl ester and is surrounded by a single surface layer of amphipathic phospholipid and cholesterol molecules. The protein moiety of a lipoprotein is known as an apolipoprotein or apoprotein.

Apolipoproteins carry out several roles:

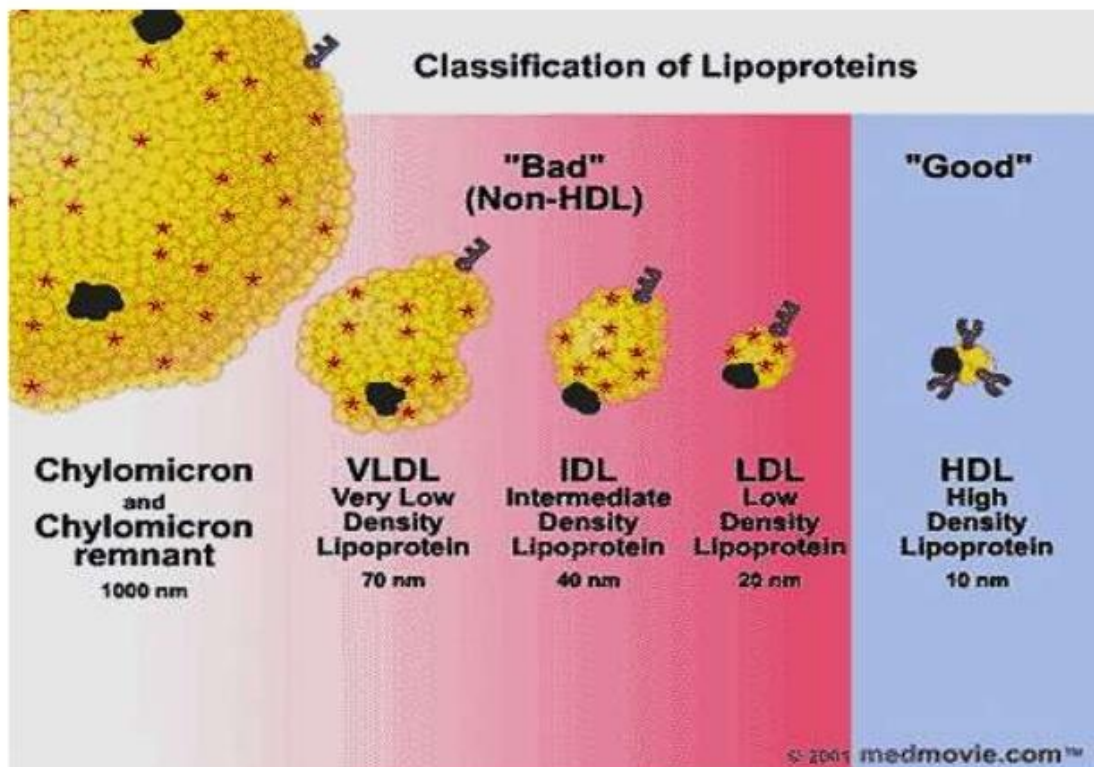
- (1) They can form part of the structure of the lipoprotein,
- (2) They are enzyme cofactors, and
- (3) They act as ligands for interaction with lipoprotein receptors in tissues.



**Fig. 2 : Structure of a plasma lipoprotein**

## Classification<sup>3</sup>

Lipoproteins have been classified on the basis of their densities during ultracentrifugation.



**Fig. 3 : Classification of plasma lipoproteins**

**Table 1 : Major classes of plasma lipoproteins <sup>2</sup>**

Type	Density (g/mL)	Electrophoretic Mobility	Site of Origin	Major Lipids	Major Apolipoproteins
Chylomicrons	< 0.95	Origin	Intestine	85% Triglyceride	B48, AI, AIV (E, CI, CII, CIII—by transfer from HDL)
Chylomicron Remnants	<1.006	Origin	Intestine	60% Triglyceride, 20% cholesterol	B48, E
VLDL	<1.006	Pre-β	Liver	55% Triglyceride, 20% cholesterol	B100, E, CI, CII, CIII
IDL	1.006-1.019	B	Derived from VLDL	35% Cholesterol, 25% triglyceride	B100, E
LDL	1.019-1.063	B	Derived from IDL	60% Cholesterol, 5% triglyceride	B100
HDL	1.063-1.21	A	Liver, intestine, plasma	25% Phospholipid, 20% cholesterol, 5% triglyceride (50% protein)	AI, AII, CI, CII, CIII, E
Lp(a)	1.05-1.09	A	Liver	60% Cholesterol, 5% triglyceride	B100, apo(a)

## **LIPOPROTEIN METABOLISM**

### **Chylomicrons :**

Chylomicrons are the largest of the plasma lipoproteins and are composed of 98% to 99% lipid (85%-90% triglyceride) and 1% to 2% protein. They contain several apolipoproteins, including apo-B48, apo-AI, apo-AIV, apo-E, and the C apolipoproteins .<sup>6, 7, 8</sup>

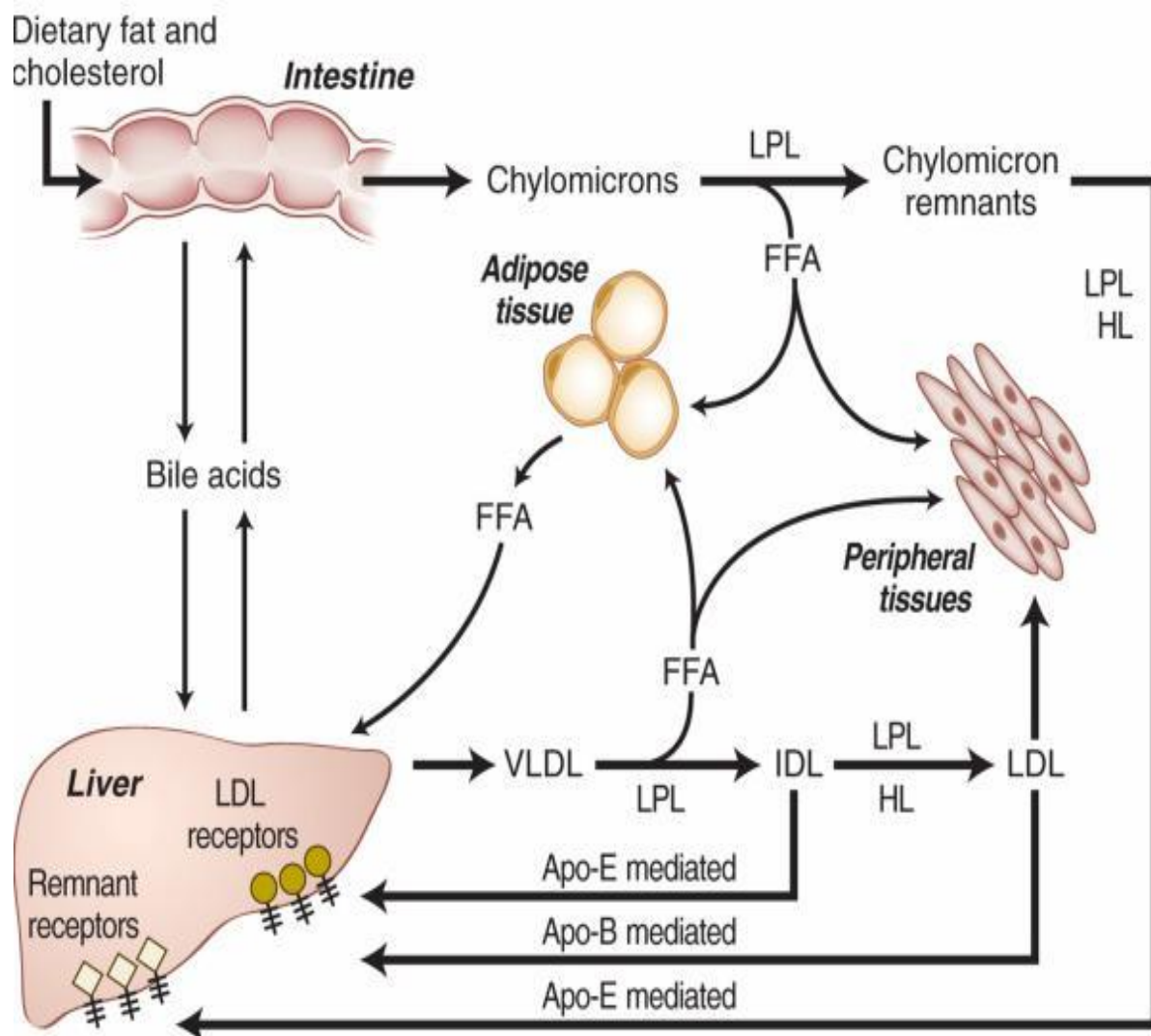
### **Origin :**

Chylomicrons are produced by the epithelial cells of the small intestine (duodenum and proximal jejunum) when dietary fat and cholesterol are presented to the brush border of the epithelial cell membranes as bile acid micelles. Triglycerides, phospholipids, and cholesterol (absorbed or synthesized by the intestinal cells) are used for chylomicron formation in the Golgi apparatus, where some of the apolipoproteins undergo final carbohydrate processing, and the chylomicrons are secreted into the space along the lateral borders of the intestinal cells. From there, they enter the mesenteric lymph and proceed through the thoracic duct lymph to the general circulation. Newly synthesized chylomicrons possess apo-B48, apo-AI, and apo-AIV (intestinally synthesized apolipoproteins); they acquire apo-E and C apolipoproteins in the lymph and blood, primarily from HDL.<sup>2</sup>

**Metabolic Fate :**

In the circulation, LPL catalyzes the release of FFAs from chylomicron triglycerides and converts them into triglyceride-poor, cholesterol enriched chylomicron remnants. Chylomicron remnants are cleared rapidly from the plasma by the liver.<sup>9, 10, 11</sup>

**Function :** Major carrier of exogenous (dietary) triglycerides.<sup>1</sup>



**Figure 4 : General scheme summarizing the major pathways involved in the metabolism of chylomicrons synthesized by the intestine and VLDL synthesized by the liver.** <sup>12</sup>

## **Very-Low-Density Lipoproteins**

**Characteristics :** VLDLs are made up of 85% to 90% lipid (about 55% triglyceride, 20% cholesterol, and 15% phospholipid) and 10% to 15% protein. The distinctive apolipoprotein is apo-B100, the hepatic form of apo-B. VLDLs also contain apo-E and C apolipoproteins. <sup>6, 13</sup>

**Origin :** VLDLs are synthesized by the liver, and their production is stimulated by increased delivery of FFAs to the hepatocytes, either from a high intake of dietary fat or from the mobilization of fatty acids from adipose tissue with fasting or uncontrolled diabetes mellitus. Triglycerides and phospholipids to be used in the formation of VLDL are synthesized in the liver, whereas VLDL cholesterol can be synthesized de novo or reused from LDL cholesterol. <sup>14</sup>

**Metabolic Fate :** VLDL triglycerides are hydrolyzed by the actions of LPL and hepatic lipase. They are converted to smaller and smaller particles that become increasingly rich in cholesterol. The products of VLDL catabolism are IDLs. IDLs are processed to LDLs. <sup>2</sup>

Approximately half of VLDLs are converted to LDLs, and the remainder are cleared directly by the liver as VLDL remnants (small VLDL) and IDLs. <sup>15, 16, 17</sup>

**Function :** Major carrier of endogenous triglycerides. <sup>1</sup>

## **Intermediate-Density Lipoproteins**

**Characteristics :** IDLs are normally present in low concentrations in the plasma and are intermediate in size and composition between VLDL and LDL. Their primary proteins are apo-B100 and apo-E. <sup>13, 15</sup>

**Metabolic fate :** They are precursors of LDLs and represent metabolic products of VLDL catabolism in the plasma by the action of lipases. IDLs may be further processed by hepatic lipase or removed from the plasma by the LDL receptor.<sup>2</sup>

**Function :** IDLs are often considered to be VLDL remnants and to be atherogenic.<sup>2</sup>

## **Low-Density Lipoproteins**

**Characteristics :** LDLs are the major cholesterol-carrying lipoproteins in the plasma; about 70% of total plasma cholesterol is in LDL. LDLs are composed of approximately 75% lipid (about 35% cholesteryl ester, 10% free cholesterol, 10% triglyceride, and 20% phospholipid) and 25% protein. Apo-B100 is the principal protein in these particles, along with trace amounts of apo-E. <sup>13, 18</sup>

**Origin :** LDLs are the end products of lipase-mediated hydrolysis of VLDLs. <sup>2</sup>

**Metabolic Fate :** About 75% of LDL is taken up by hepatocytes. Other tissues take up smaller amounts of LDL. Approximately two thirds of the uptake is mediated by the LDL receptor, and the remainder is mediated by a poorly defined process that does not involve receptors. LDLs are considered to be atherogenic. <sup>2</sup>

**Function :** Transports cholesterol from liver to peripheral tissues. <sup>2</sup>

## **High-Density Lipoproteins**

**Characteristics :** HDLs are small particles (70-120 Å in diameter) which contain about 50% lipid (25% phospholipid, 15% cholesteryl ester, 5% free cholesterol, and 5% triglyceride) and 50% protein. Their major apolipoproteins are apo-AI (65%), apo-AII (25%), and smaller amounts of the C apolipoproteins and apo-E . Apo-E is a minor component of a subclass of HDL referred to as HDL1. HDLs serve as a reservoir for apo-E and the C apolipoproteins to be distributed to other lipoproteins when they enter the plasma (e.g., chylomicrons, VLDLs). <sup>18, 19, 20</sup>

They are divided into two major subclasses :

1. HDL2 ( $d = 1.063\text{-}1.125$  g/mL)
2. HDL3 ( $d = 1.125\text{-}1.21$  g/mL).

**Origin :** HDLs originate from three major sources.

1. The liver secretes an apo-AI-phospholipid disc called nascent or precursor HDL (pre- $\beta$  HDL).
2. The intestine directly synthesizes a small apo-AI-containing HDL particle.
3. HDLs are derived from surface material (primarily apo-AI and phospholipid) that comes from chylomicrons and VLDLs during lipolysis.

### **Maturation of High-Density Lipoproteins.** <sup>19, 20</sup>

The nascent or precursor HDL particles exist as apo-AI-phospholipid discs.

Designated pre- $\beta$ 1, pre- $\beta$ 2, and pre- $\beta$ 3, these discs are excellent acceptors of free cholesterol from cells with excess cholesterol or from other lipoproteins forming small, spherical, mature HDL particles (HDL3) . (HDL3) accepts more free cholesterol and increases in size, forming HDL2.

HDL1 can also arise from a precursor particle that displays  $\gamma$ -electrophoretic mobility and is called  $\gamma$ Lp-E. This particle is approximately 80% protein and 20% lipid (primarily sphingomyelin and phosphatidylcholine, with some free cholesterol). The  $\gamma$ Lp-E is a good acceptor of free cholesterol from cells and appears to be converted to the larger HDL1.

**Function :** Is a main transporter of cholesterol from peripheral tissue to liver.

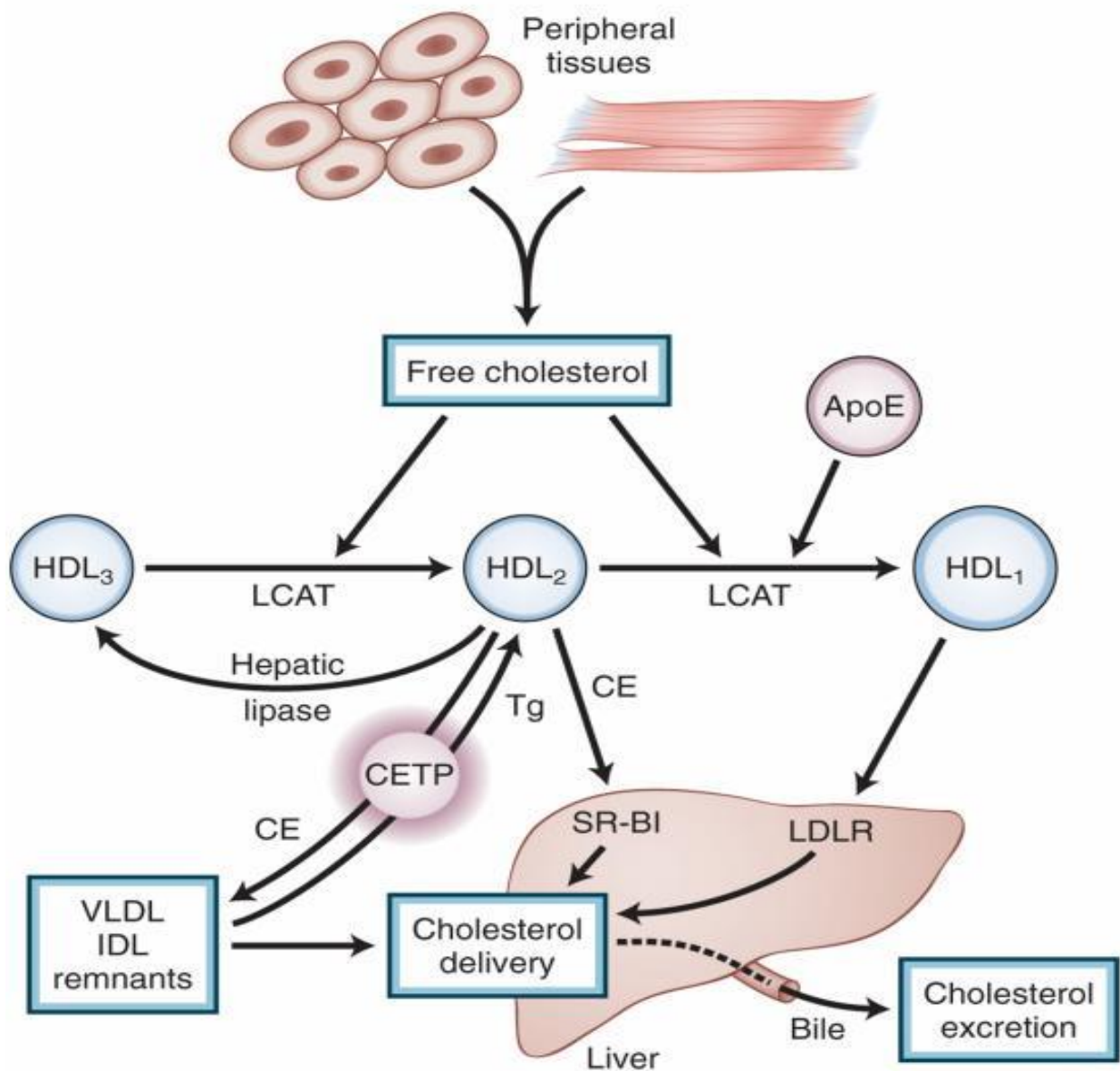
### **Acquisition of Cholesterol by High-Density Lipoproteins**

HDL, especially HDL3, precursors of mature HDL, and lipid-poor apo-AI, can acquire cholesterol from cells by two mechanisms. aqueous transfer from cells and transport facilitated by a cell-surface binding protein.<sup>21, 22</sup>

### **Metabolic Pathways Involving High-Density Lipoproteins**

HDLs function in the redistribution of lipids among lipoproteins and cells by a process called reverse cholesterol transport.<sup>19, 20, 22</sup>

HDLs acquire cholesterol from cells and transport it to the liver for excretion or to other cells that require cholesterol. The scheme is shown in Fig. 4.



**Figure 5 : <sup>2</sup> Role of high-density lipoprotein (HDL) in the redistribution of Lipids from cells with excess cholesterol to cells requiring cholesterol or to the liver for excretion.**

A second pathway of cholesterol redistribution involves CETP ( Fig. 4) CETP transfers cholesteryl ester from HDL2 to VLDL, IDL, LDL, and remnants. The cholesterol is thus delivered indirectly to the liver through VLDL and chylomicron remnant pathways. In exchange for transfer of the cholesteryl ester, CETP transfers triglyceride from VLDL, IDL, LDL, and remnants to HDL2, which becomes enriched with triglycerides. The CETP pathway is the major route for the transport and delivery of cholesteryl esters from HDL to the liver in humans.<sup>23, 24</sup>

A third pathway involves SR-BI ( Fig. 4). Cholesteryl esters are removed from the particle by selective uptake and preferentially delivered to the liver, adrenal glands, and gonads. The SR-BI can facilitate the transfer of cholesteryl esters from HDL to cells without the lipoprotein particle's entering the cell or being degraded. The SR-BI appears to function by transferring cholesteryl ester through a hydrophilic channel formed in the cell membrane.<sup>25</sup>

#### **HDL<sub>2</sub> Is Reconverted to HDL<sub>3</sub> to Regenerate These Cholesterol Acceptors.<sup>26</sup>**

HDL<sub>2</sub> particles are partially depleted of cholesteryl esters and enriched in triglycerides by the action of CETP. Hepatic lipase can then act on the large, triglyceride-enriched HDL<sub>2</sub> to hydrolyze the triglycerides (and possibly excess phospholipids), converting HDL<sub>2</sub> to HDL<sub>3</sub>. HDL<sub>3</sub> serves as an acceptor of free cholesterol, thus perpetuating the HDL<sub>2</sub>-HDL<sub>3</sub> cycle (Fig 4)

## **High-Density Lipoproteins as Anti-atherogenic Lipoproteins**

Numerous studies have demonstrated that high levels of HDL-C are associated with a lower incidence of CHD. Conversely, low levels of HDL-C are associated with a higher incidence of CHD.<sup>27</sup> The protective mechanism involving HDL may be related to its role in reverse cholesterol transport, which results in redistribution of cholesterol away from the artery wall. Other potentially protective roles for HDL include inhibition of monocyte adhesion and antioxidative activity that could prevent LDL oxidation.<sup>2</sup>

## LIPOPROTEIN ALTERATIONS IN TYPE2 DIABETES

**Table 2 : Lipoprotein alterations in type 2 diabetes.** <sup>3</sup>

Lipoprotein	Alterations
VLDL ↑	<p>Increased production of triglyceride and apoB,</p> <p>Decreased clearance of triglyceride and apoB,</p> <p>Abnormal composition</p>
LDL ↑→	<p>Increased production of LDL apoB,</p> <p>Decreased receptor-mediated clearance,</p> <p>Triglyceride enrichment,</p> <p>Smaller (more dense) particle distribution,</p> <p>Glycation,</p> <p>Oxidation</p>
HDL ↓	<p>Increased clearance of apoA,</p> <p>Decreased proportion of large HDL,</p> <p>Triglyceride enrichment,</p> <p>Glycation,</p> <p>Diminished reverse cholesterol transport</p>
Chylomicron	Delayed clearance; remnant accumulation

## **Alterations in Triglycerides and VLDL**

The most common alteration of lipoproteins in type 2 diabetes is hypertriglyceridemia caused by an elevation in VLDL concentrations. It is clear, however, from population-based studies<sup>28, 29</sup> that type 2 diabetes generally is associated with only a 50% to 100% elevation in the plasma levels of total and VLDL triglycerides. Thus, it is likely that subjects with type 2 diabetes who have concentrations of total triglycerides greater than 350 to 400 mg/dL also have genetic defects in lipoprotein metabolism, the expression of which may be exacerbated by hyperglycemia.<sup>30</sup>

### **Metabolic Determinant**

One of the determinants of diabetic hypertriglyceridemia is the overproduction of VLDL triglyceride, which is most likely due to the increased flow of substrates, particularly glucose and free fatty acids, to the liver. In addition, individuals with type 2 diabetes appear to have a defect in clearance of VLDL triglyceride that parallels the degree of hyperglycemia. Overproduction of VLDL apoB and decreased fractional catabolic rate for VLDL apoB also occurs in type 2 diabetes.<sup>31, 32, 33</sup>

The alterations in VLDL metabolism in type 2 diabetes are related in part to insulin resistance. Hyperinsulinemia and the central obesity that typically accompanies insulin resistance also are thought to lead to overproduction and impaired catabolism of VLDL.

In addition to increases in the amount of VLDL, individuals with diabetes, especially those with severe hyperglycemia, may have larger triglyceride-rich VLDL. Subfractions of VLDL have been found to be enriched in the proportion of cholesterol-rich particles. These compositional changes may have implications for the increased propensity for atherosclerosis among people with type 2 diabetes, because cholesterol-enriched VLDL may be atherogenic.<sup>35, 36</sup>

Triglyceride elevations in type 2 diabetes may also be due to delayed clearance of postprandial particles.<sup>34</sup>

### **Alterations in Low-Density Lipoprotein Cholesterol**

Studies examining plasma concentrations of total and LDL cholesterol in type 2 diabetes vary by population, with some showing higher and some showing lower levels in type 2 diabetes than in control subjects.<sup>36</sup>

## **Metabolic Determinant**<sup>3,37</sup>

The composition of LDL in type 2 diabetes is altered, with an increase in the proportion of small, dense, triglyceride-enriched LDL and these changes also contribute significantly to abnormal metabolism and atherosclerosis. The small, dense LDL have increased oxidative susceptibility and are more rapidly oxidized. Oxidized LDL particles are believed to play a major role in stimulating the atherosclerotic process because of their recognition by macrophage receptors.

Increased plasma triglyceride levels, low HDL levels, and small, dense LDLs usually occur together in a lipoprotein pattern often referred to as atherogenic dyslipidemia.

The transfer of LCAT-synthesized cholesteryl esters to VLDL and LDL is inhibited, with a concomitant increase in their transfer to HDL; this abnormal metabolic pattern is reversed by insulin therapy. The block in cholesteryl ester transfer activity in patients with type 2 diabetes is correlated with an increase in free cholesterol content of both LDL and VLDL. Therefore, in type 2 diabetes, this abnormal cholesteryl ester transfer may be related to an increased risk for atherosclerosis.

## **Alterations in High-Density Lipoprotein Cholesterol**

In individuals with type 2 diabetes decreased concentrations of HDL cholesterol has been observed.<sup>3</sup>

### **Metabolic Determinant**

Individuals with type 2 diabetes have an increased rate of HDL clearance. Elevated hepatic lipase activity also contribute to the decrease in HDL concentrations in type 2 diabetes.<sup>38</sup>

In type 2 diabetes an increased proportion of triglyceride in HDL has been observed. These compositional changes appear to be related to the activity of adipose tissue LPL, because LPL deficiency may be a factor responsible for the altered distribution of HDL particles in untreated type 2 diabetes. Nonenzymatic glycation of HDL appears to interfere with HDL receptor binding.<sup>39</sup> Thus, glycation of HDL may also play a role in the lower levels of HDL observed in diabetes. Finally, abnormalities in HDL composition have been noted even in individuals with optimal glycemic control.<sup>40</sup>

All of these alterations in HDL composition may impair the role of HDL in reverse cholesterol transport.

## DIABETIC DYSLIPIDEMIA

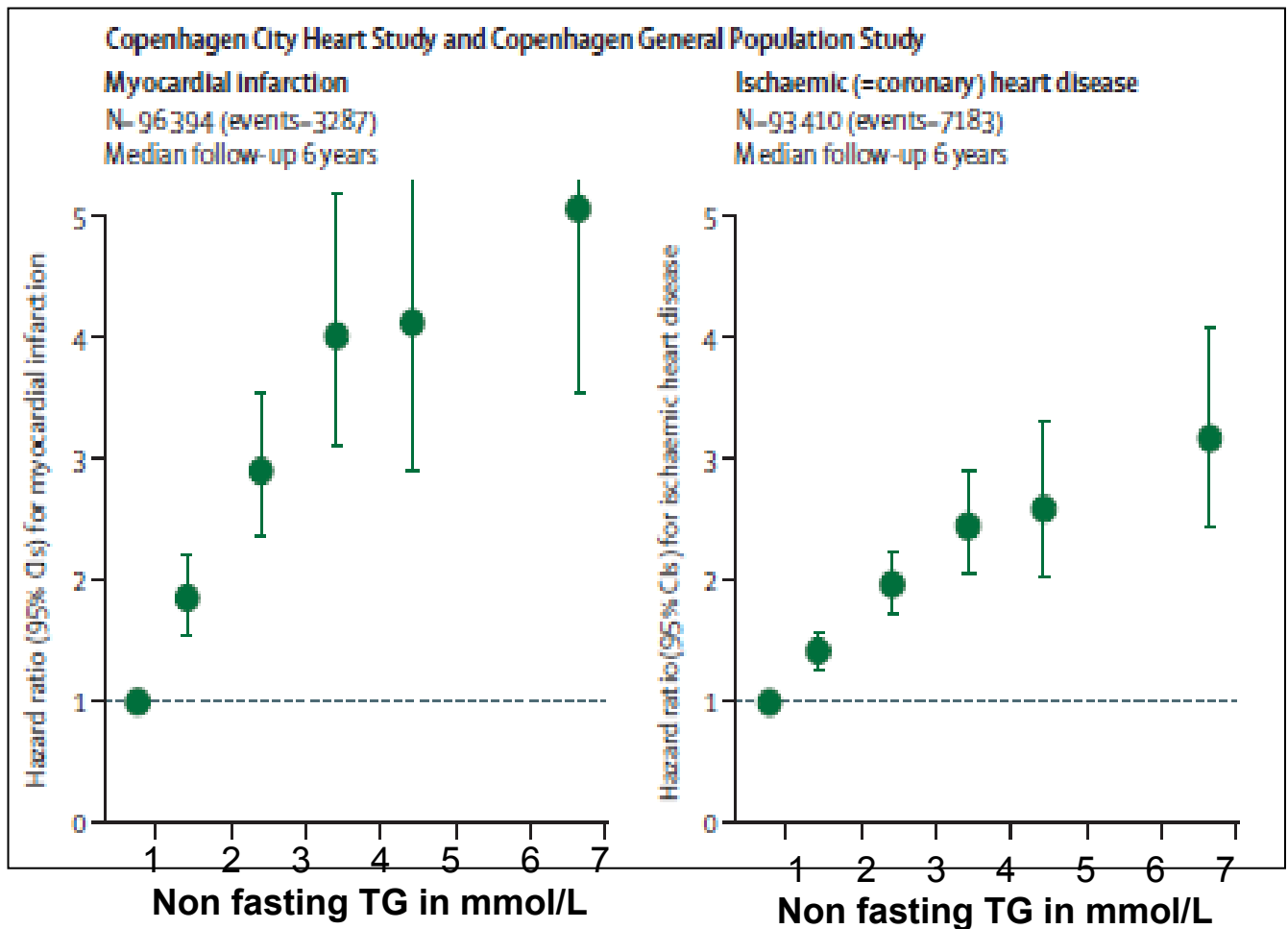
The dyslipidemia associated with type 2 diabetes and insulin resistance typically consists of elevated triglycerides and decreased HDL cholesterol level. The frequently mild abnormality in LDL cholesterol concentration associated with diabetes belies a qualitative abnormality in the LDL structure, i.e., decreased size and increased density of the LDL particle.<sup>41</sup> LDL appears to be a very potent contributor to the development of CHD

Unlike LDL-C, which is well-established as a major predictor for CVD in global populations, the independent relationship of TG on predicting CVD has long been controversial.<sup>42</sup>

Although some previous studies like UKPDS did not favour hypertriglyceridemia as an independent risk factor for CVD, two recent metaanalysis studies have suggested that TG is independently associated with myocardial infarction, CHD, CVD and CVD death.<sup>43, 44, 45, 46</sup>

Asian studies have shown that increased serum TG levels have been an independent risk factor for CHD and TG appeared to play an important role in the development of CHD.<sup>47, 48</sup>

The Copenhagen city heart study has shown significant increase in the hazard ratio with increasing non fasting triglycerides level



**Fig. 6 : Copenhagen heart study result**

## **RATIONALE FOR THERAPY FOR LIPID ABNORMALITIES IN DIABETES**

Atherosclerotic macrovascular disease is the leading cause of morbidity and mortality in patients with diabetes mellitus. Both men and women with diabetes have a significantly increased risk of myocardial infarction (MI), stroke, and peripheral gangrene.<sup>49, 50</sup> The risk for developing coronary heart disease (CHD) begins prior to the development of type 2 diabetes. By the time the diagnosis of type 2 diabetes is made, more than half of all diabetic individuals already have clinical CHD.<sup>51</sup> In addition, patients with diabetes have an increased rate of MI-associated pre hospital mortality, as well as increased morbidity and mortality during and after hospitalization.<sup>52</sup>

These data provide a strong rationale for treating cardiovascular risk factors in diabetic patients as aggressively as in nondiabetic patients with clinical CHD. Thus, diabetes confers a risk that is equivalent to that of known CHD. The ADA and the American Heart Association consider type 2 diabetes a CHD equivalent.<sup>53</sup>

Various Randomized controlled clinical trials demonstrate that people with diabetes benefit from cholesterol-lowering therapy, with improvements in lipoprotein values and reduced CVD events.

**Table 3 : Results of Controlled Clinical Trials of Lipid Lowering in Individuals with Diabetes**

Study	LDL cholesterol	HDL cholesterol	Triglycerides	Clinical outcomes
<b>CARE</b> <sup>33</sup>	Decreased 27%	Increased 5%	Decreased 14%	25% risk reduction ( $P = 0.05$ )
<b>4S</b> <sup>34,35</sup>	Decreased 36%	Increased 8%	Decreased 10%	55% risk reduction ( $P = 0.002$ )  42% on later analysis ( $P = 0.001$ )
<b>VA-HIT</b> <sup>36</sup>	No change	Increased 6%	Decreased 31%	24% decrease in CVD death or nonfatal myocardial infarction ( $P = 0.05$ )
<b>DAIS</b> <sup>37</sup>	Decreased 10%	Increased 6%	Decreased 29%	40% reduction in progression of localized atherosclerotic lesions ( $P = 0.02$ )
<b>AFCAPS/ TexCAPS</b> <sup>38</sup>	Decreased 25%	Increased 6%	Decreased 15%	33% reduction in CVD events  (NS)
<b>HPS</b> <sup>39</sup>	Decreased 29%	Increased 3%	Decreased 14%	26% reduction in first CVD event (data incomplete)

## **MATERIALS AND METHODS**

This was an observational study which included the patients admitted in The Government Mohan kumaramangalam Medical college Hospital, Tamil Nadu.

The study included 50 patients with type 2 diabetes mellitus meeting the inclusion criteria and were compared with 50 age and sex matched healthy controls, fulfilling the inclusion and exclusion criteria.

### **The study period :**

From August 2014 to July 2015

### **INCLUSION CRITERIA**

Patients diagnosed with type 2 diabetes mellitus on the basis of revised American Diabetic Association Criteria (Fasting plasma glucose  $\geq 126$  mg/dl and 2 hour postprandial plasma glucose  $\geq 200$  mg/dl), aged more than 30 years.

## **EXCLUSION CRITERIA**

- Type 1 diabetes mellitus
- Inherited disorder of lipid metabolism
- Liver disease
- Endocrine diseases affecting lipids (hypothyroidism, cushing's syndrome)
- Renal disease
- Smoking and
- Patients on medication affecting lipid metabolism

## **Method of collection of data**

A detailed proforma was filled up for each patient, which included age, sex, IP number, detailed history, past and personal history, medication history. A detailed clinical examination was done. Laboratory parameters including fasting and postprandial blood glucose, renal function tests, liver function tests, ECG and routine urine examination

Fasting and Post prandial lipid profile which included serum total cholesterol, serum triglycerides, LDL cholesterol, HDL cholesterol and VLDL were estimated in all the cases and controls. Blood was collected from patients after an overnight (12-hour) fast and six-hour postprandial (after a standard meal) for lipid profile measurements.

## **Statistical Analysis**

The following statistical methods were employed

1. Descriptive statistics
2. T test – Independent samples
3. T test pair samples
4. Repeated measure ANOVA
5. Product-moment correlation

Using SPSS for windows

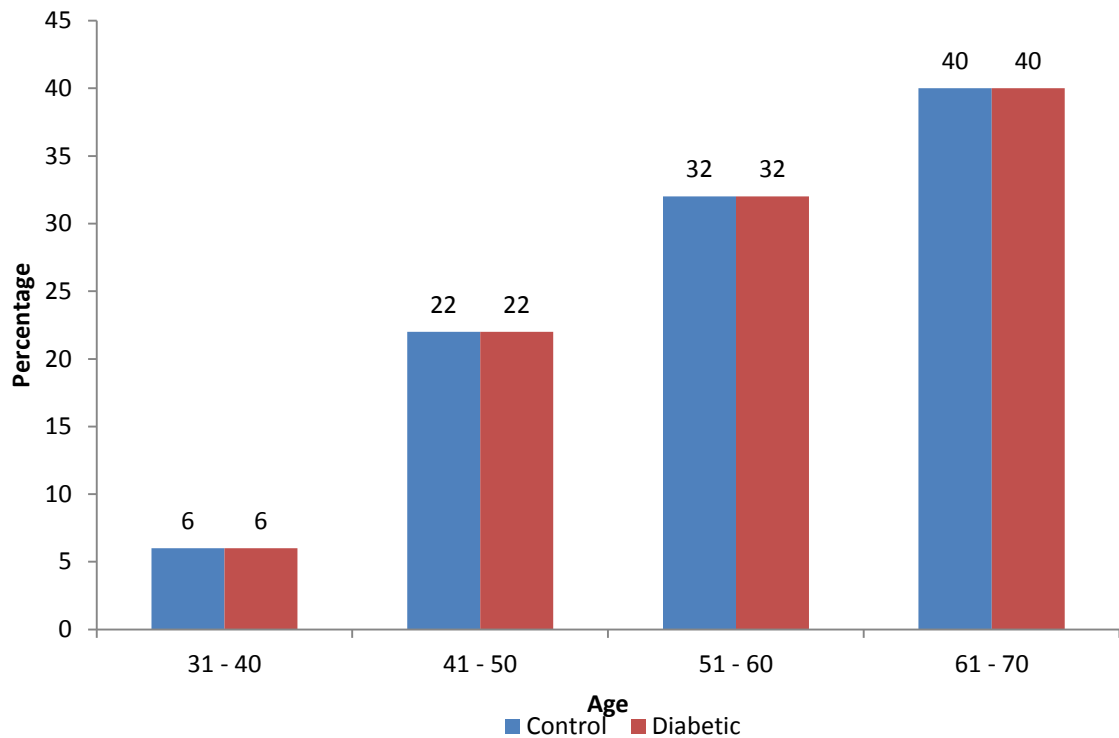
## RESULTS

In this study, fasting and post prandial lipid profile was done in 50 patients with type 2 diabetes mellitus and was compared with the fasting and post prandial lipid profile in 50 healthy controls, age and sex matched.

**Table 4: Age distribution of the cases and controls**

Age	Control		Diabetic		Total
	N	%	N	%	
31 - 40	3	6	3	6	6
41 - 50	11	22	11	22	22
51 - 60	16	32	16	32	32
61 - 70	20	40	20	40	40
Total	50	100	50	100	100

**Graph 1 : Showing the age distribution of the cases and controls**



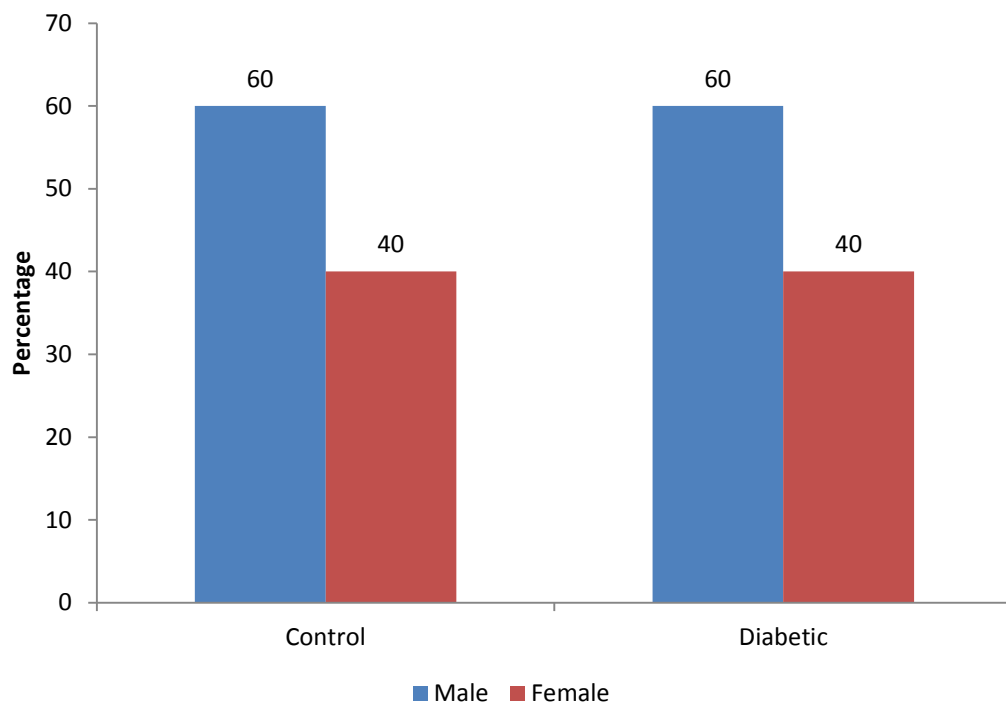
In this study, the study group constituted cases between the age 31 to 70 years.

The majority of cases and controls were in the age group of 61-70 years which constituted 40% of the total; followed by persons in the age group 51-60 years who constituted 32% of the total study.

**Table 5 : Sex wise distribution of the cases and controls**

Sex	Control		Diabetic		Total
	N	%	N	%	
Male	30	60	30	60	60
Female	20	40	20	40	40
Total	50	100	50	100	100

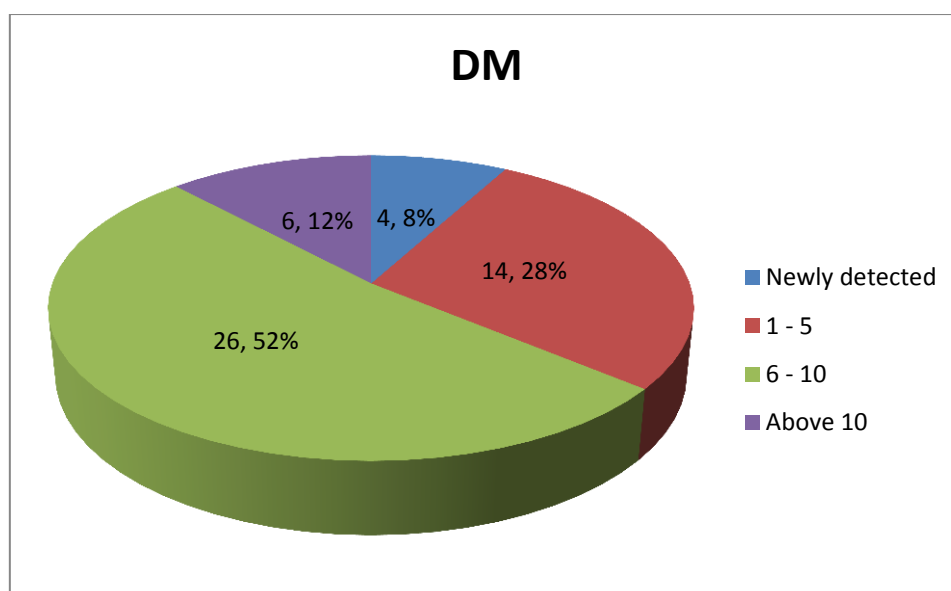
**Graph 2 : Showing the sex wise distribution of the cases and controls**



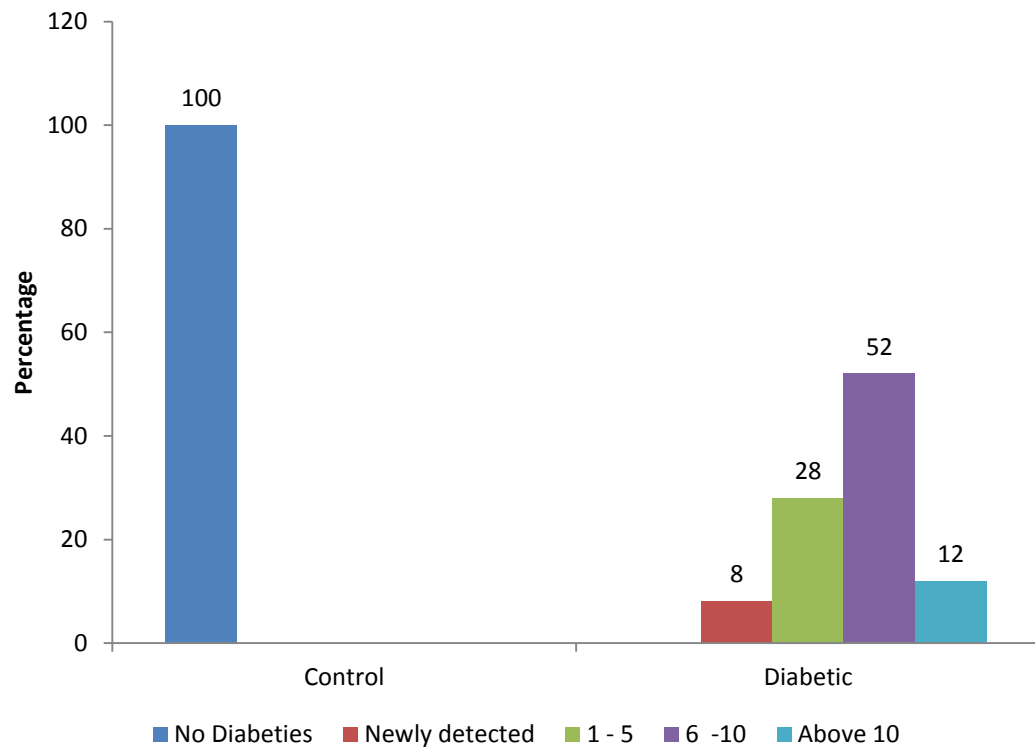
In this study, 60 percent were males and 40 percent were females, in both the groups.

**Table 6 : Duration of diabetes among the study group**

DM	Control		Diabetic		Total
	N	%	N	%	
No Diabetes	50	100			
Newly detected			4	8	54
1 - 5			14	28	14
6 - 10			26	52	26
Above 10			6	12	6
Total	50	100	50	100	100



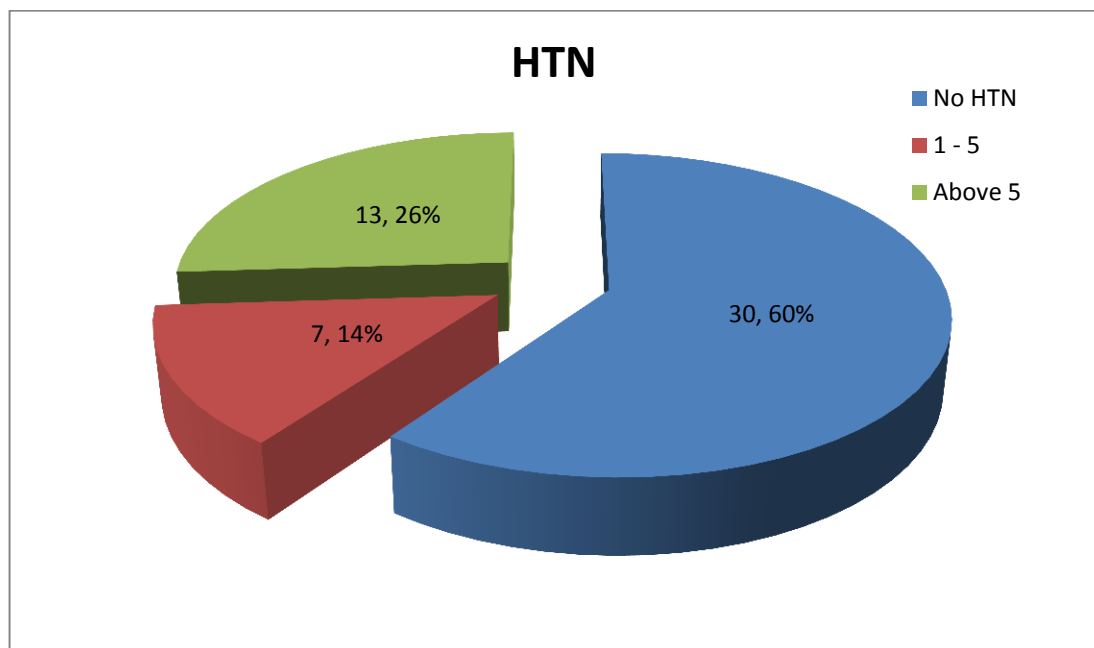
**Graph 3 : Graph showing the duration of diabetes among the study group**



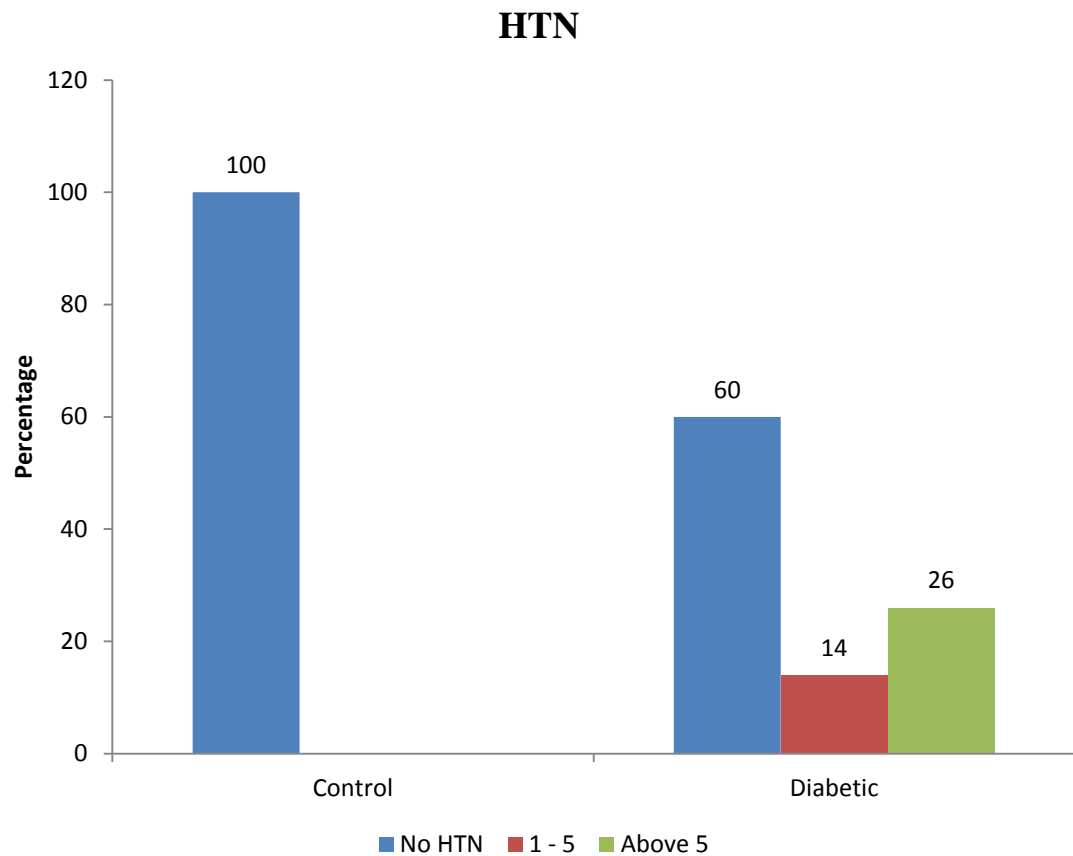
In this study 8% of the cases were newly detected type 2 diabetics, whereas 28% of the cases had diabetes for 1 - 5 years, 52% had diabetes for 6 – 10 years and 12 % had diabetes for more than 10 years. In the control group none of the patients had type 2 diabetes mellitus.

**Table 7 : Duration of hypertension among the study group**

HTN	Control		Diabetic		Total
	N	%	N	%	
No HTN	50	100	30	60	80
1 - 5			7	14	7
Above 5			13	26	13
Total	50	100	50	100	100



**Graph 4 : Graph showing the duration of hypertension among  
the study group**



In this study, 40 % of diabetics had hypertension whereas 60 % of diabetics were normotensive. None of the controls, were found to have hypertension.

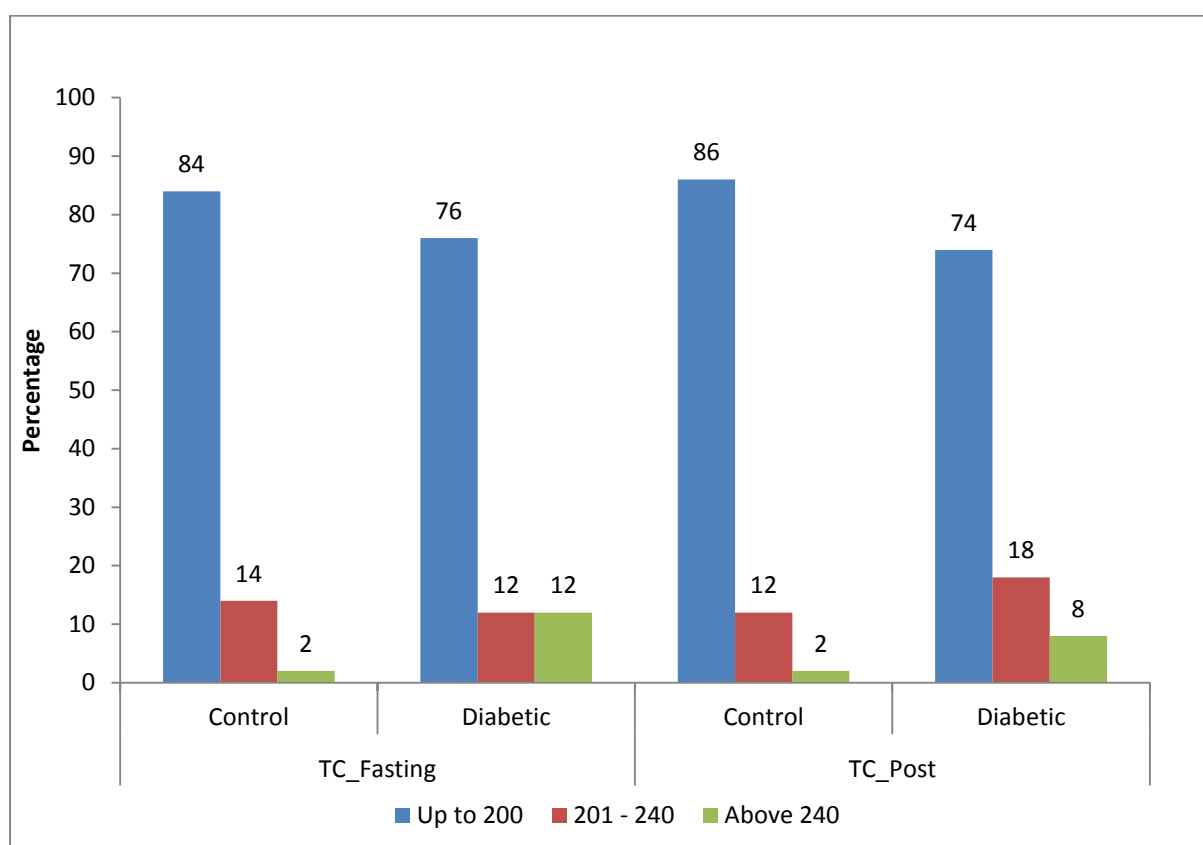
**Table 8a : Fasting Total Cholesterol levels among the cases and controls**

TC _ Fasting	Control		Diabetic		Total	Chi square	p
	N	%	N	%			
Up to 200	42	84	38	76	80	3.85	0.146
201 - 240	7	14	6	12	13		
Above 240	1	2	6	12	7		
Total	50	100	50	100	100		

**Table 8b: Post prandial Total Cholesterol levels among the cases and controls**

TC_ Post	Control		Diabetic		Total	Chi square	p
	N	%	N	%			
Up to 200	43	86	37	74	80	2.85	0.241
201 - 240	6	12	9	18	15		
Above 240	1	2	4	8	5		
Total	50	100	50	100	100		

**Graph 5 : Fasting and post prandial Total Cholesterol levels among  
the cases and controls**



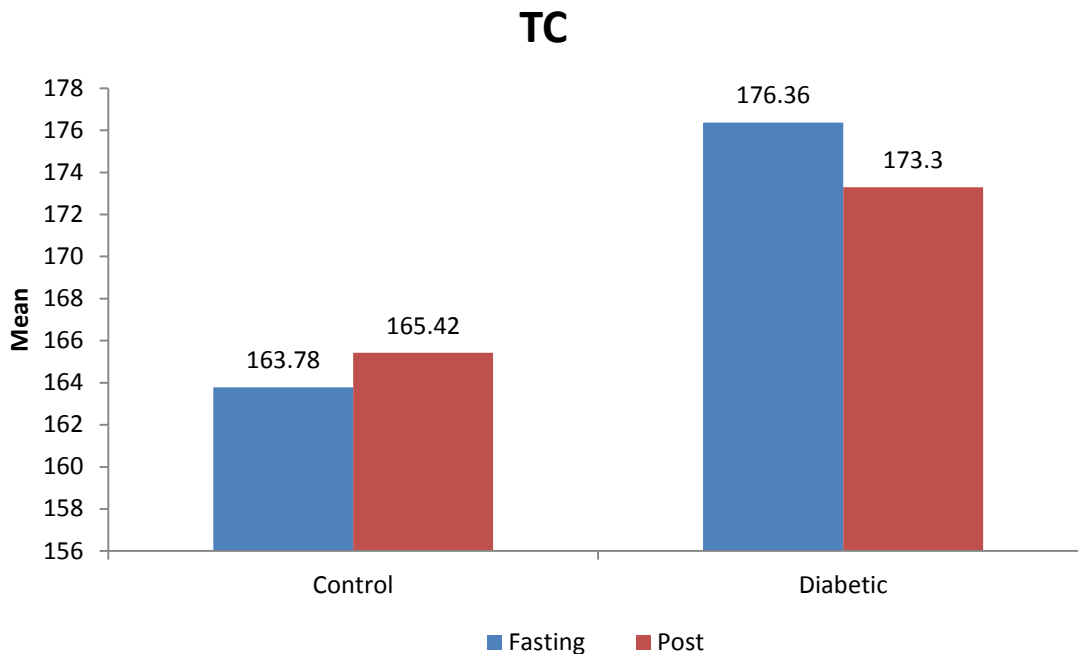
In this study, in the fasting state, 24% of cases had total cholesterol levels of >200 mg/dl as compared with the control group wherein 16% of them had total cholesterol of >200 mg/dl.

In the post prandial state, 26% of cases had total cholesterol levels of >200 mg/dl, but when compared with that of controls only 14% of them had total cholesterol levels of >200 mg/dl.

**Table 9 : Comparison of the mean fasting and post prandial Total Cholesterol levels among the cases and controls**

		TC							
Group	N	Fasting				Post			
		Mean	SD	t	p	Mean	SD	t	p
Control	50	163.78	36.29	1.4	0.166	165.42	35.36	0.99	0.323
Diabetic	50	176.36	52.43			173.3	43.56		

**Graph 6 : Comparison of the mean fasting and post prandial Total Cholesterol levels among the cases and controls**



In this study, the mean TC level in the cases was  $176.36 \pm 52.43$  mg/dl in the fasting state and  $173.3 \pm 43.56$  mg/dl in the post prandial state. The controls had a mean TC level of  $163.78 \pm 36.29$  mg/dl in the fasting state and  $165.42 \pm 35.36$  mg/dl in the post prandial state.

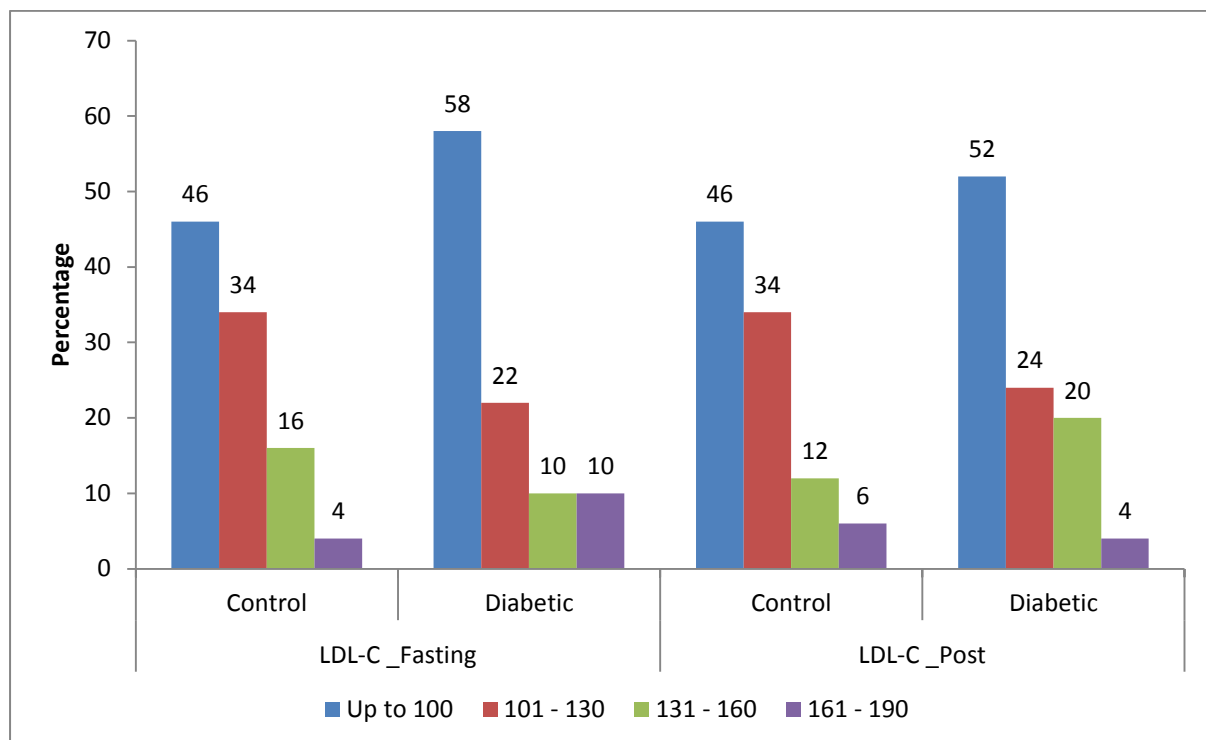
**Table 10a: Fasting LDL-C levels among the cases and controls**

LDL-C Fasting	Control		Diabetic		Total	Chi square	p
	N	%	N	%			
Up to 100	23	46	29	58	52	3.96	0.266
101 - 130	17	34	11	22	28		
131 - 160	8	16	5	10	13		
161 - 190	2	4	5	10	7		
Total	50	100	50	100	100		

**Table 10 b: Post prandial LDL-C levels among the cases and controls**

LDL-C Post	Control		Diabetic		Total	Chi square	p
	N	%	N	%			
Up to 100	23	46	26	52	49	3.25	0.518
101 - 130	17	34	12	24	29		
131 - 160	6	12	10	20	16		
161 - 190	3	6	2	4	5		
Total	50	100	50	100	100		

**Graph 7 : Fasting and post prandial LDL-C levels among the cases and controls**



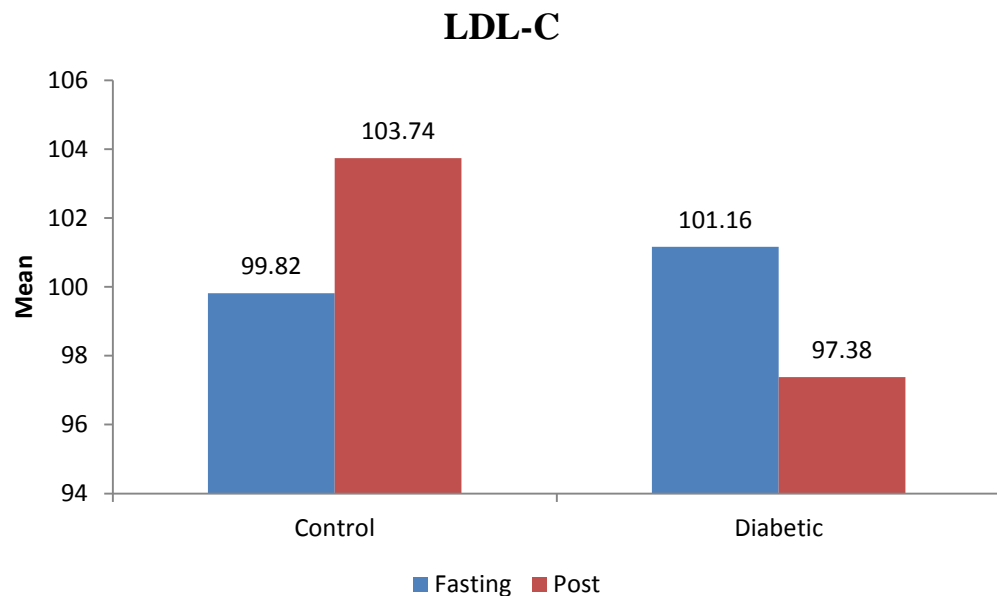
In this study, in the fasting state, 58% of cases had LDL-C levels of <100 mg/dl as compared with that of the control group where 46% of controls had LDL-C of <100 mg/dl.

In the post prandial state, 52% of cases had LDL-C levels of <100 mg/dl as compared with that of control group where 46% of them had LDL-C of <100 mg/dl.

**Table 11: Comparison of the mean fasting and post prandial LDL-C levels among the cases and controls**

		LDL-C							
Group	N	Fasting				Post			
		Mean	SD	t	p	Mean	SD	t	p
Control	50	99.82	36.21	0.18	0.857	103.74	35.6	0.88	0.383
Diabetic	50	101.16	38.17			97.38	36.93		

**Graph 8 : Comparison of the mean fasting and post prandial LDL-C levels among the cases and controls**



In this study, the cases had a mean LDL-C level of  $101.16 \pm 38.17$  mg/dl in the fasting state and  $97.38 \pm 36.93$  mg/dl in the post prandial state. The controls had a mean LDL-C level of  $99.82 \pm 36.21$  mg/dl in the fasting state and  $103.74 \pm 35.6$  in the post prandial state

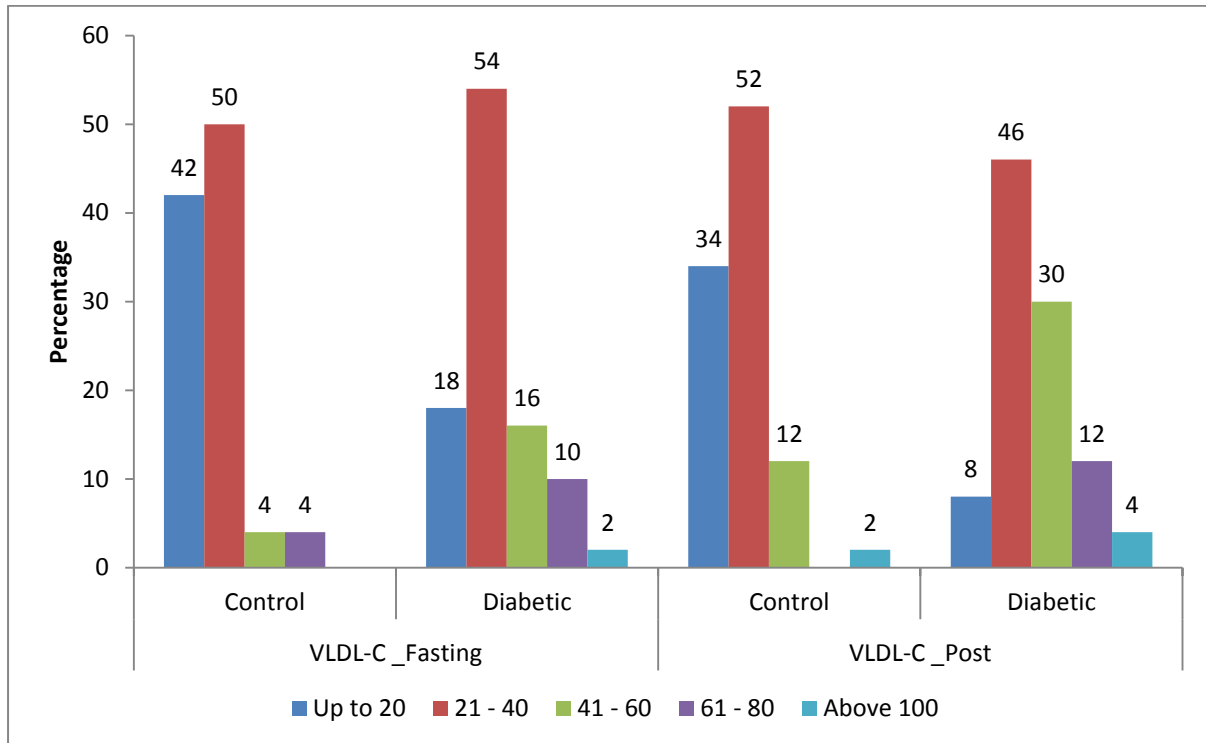
**Table 12 a: Fasting VLDL-C levels among the cases and controls**

VLDL-C Fasting	Control		Diabetic		Total	Chi square	p
	N	%	N	%			
Up to 20	21	42	9	18	30	10.76	0.029*
21 - 40	25	50	27	54	52		
41 - 60	2	4	8	16	10		
61 - 80	2	4	5	10	7		
Above 100			1	2	1		
Total	50	100	50	100	100		

**Table 12 b: Post prandial VLDL-C levels among the cases and controls**

VLDL-C Post	Control		Diabetic		Total	Chi square	p
	N	%	N	%			
Up to 20	17	34	4	8	21	18.42	0.001**
21 - 40	26	52	23	46	49		
41 - 60	6	12	15	30	21		
61 - 80			6	12	6		
81 - 100	1	2	2	4	3		
Total	50	100	50	100	100		

**Graph 9 : Fasting and post prandial VLDL-C levels among the cases and controls**



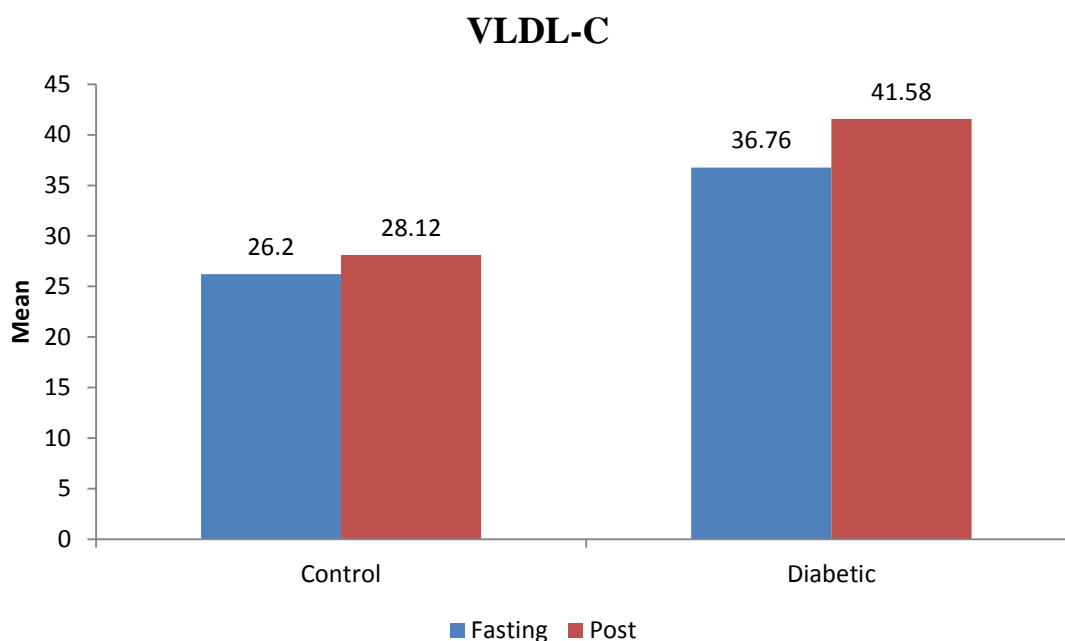
In this study, in the fasting state 28% of cases had total VLDL-C levels of >40 mg/dl as compared with that of the control group where only 8% of them had VLDL-C levels of >40mg/dl.

Similarly, in the post prandial state, 46% of cases had VLDL-C levels of >40 mg/dl as compared with that of control group, where 14% of them had VLDL-C levels of >40 mg/dl.

**Table 13 : Comparison of the mean fasting and post prandial VLDL-C levels among the cases and controls**

		VLDL-C							
Group	N	Fasting				Post			
		Mean	SD	t	p	Mean	SD	t	p
Control	50	26.2	13.41	3.1	0.003	28.12	14	3.92	0.000
Diabetic	50	36.76	20.01			41.58	19.82		

**Graph 10 : Comparison of the mean fasting and post prandial VLDL-C  
among the cases and controls**



In this study, the cases had a mean VLDL-C level of  $36.76 \pm 20.01$  mg/dl in the fasting state and  $41.58 \pm 19.82$  mg/dl in the post prandial state. The controls had a mean VLDL-C level of  $26.2 \pm 13.41$  mg/dl in the fasting state and  $28.12 \pm 14$  mg/dl in the post prandial state.

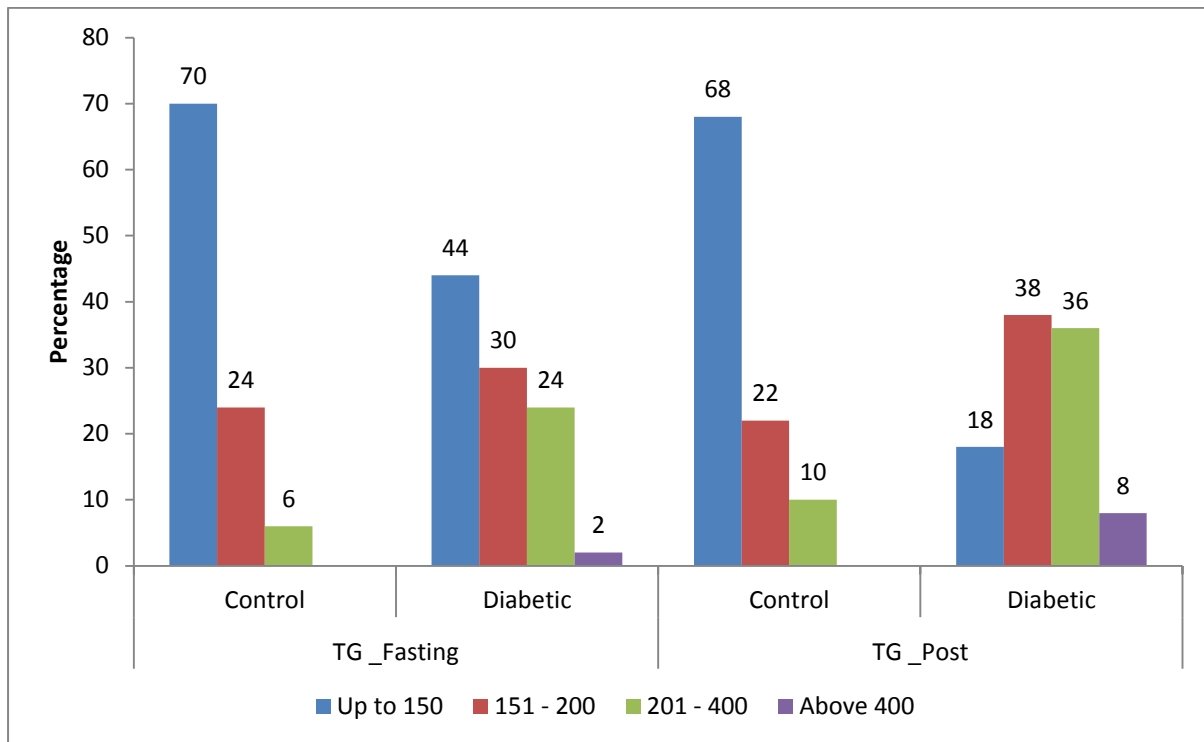
**Table 14a: Fasting Triglyceride levels among the cases and controls**

TG Fasting	Control		Diabetic		Total	Chi square	p
	N	%	N	%			
Up to 150	35	70	22	44	57	9.70	0.021*
151 - 200	12	24	15	30	27		
201 - 400	3	6	12	24	15		
Above 400			1	2	1		
Total	50	100	50	100	100		

**Table 14b: Post prandial Triglyceride levels among cases and controls**

TG Post	Control		Diabetic		Total	Chi square	p
	N	%	N	%			
Up to 150	34	68	9	18	43	28.02	< 0.001**
151 - 200	11	22	19	38	30		
201 - 400	5	10	18	36	23		
Above 400			4	8	4		
Total	50	100	50	100	100		

**Graph 11 : Fasting and post prandial Triglyceride levels among the cases and controls**



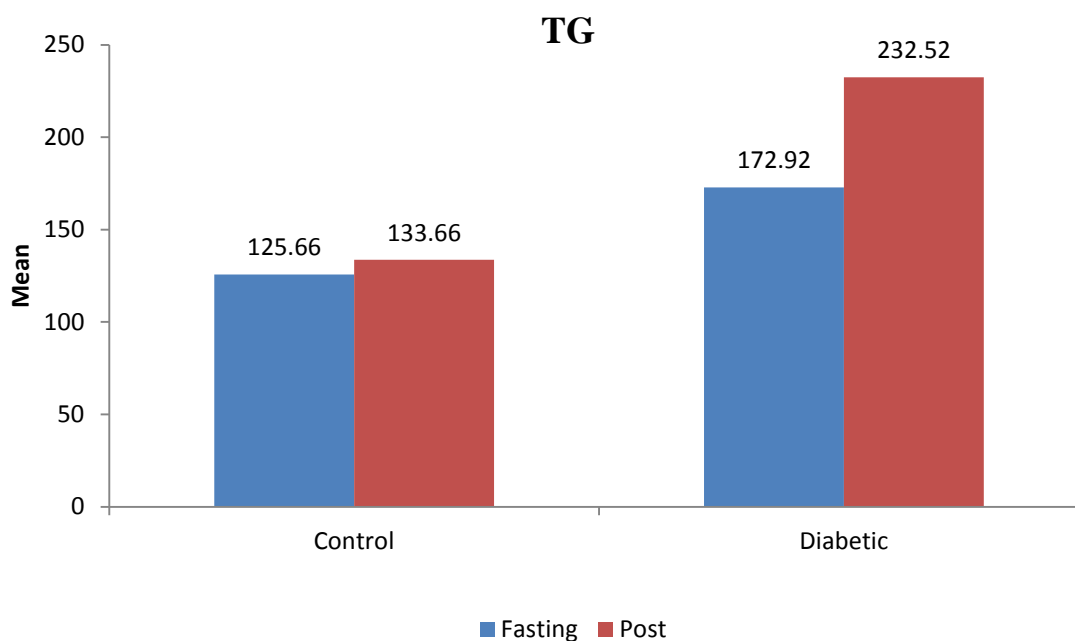
In this study, in the fasting state 56% of the cases had total TG levels of >150 mg/dl as compared with that of control group wherein only 30% of them had TG levels of >150 mg/dl.

Similarly in the post prandial state, 82% of the cases had TG levels of >150 mg/dl as compared with that of control group wherein only 32% of them had TG levels of >150 mg/dl.

**Table 15 : Comparison of the mean fasting and post prandial triglyceride levels among the cases and controls**

		TG							
Group	N	Fasting				Post			
		Mean	SD	t	p	Mean	SD	t	p
Control	50	125.66	49.55	3.7	0.000	133.66	48.79	6.03	0.000
Diabetic	50	172.92	75.51			232.52	105.08		

**Graph 12 : Comparison of the mean fasting and post prandial Triglyceride levels among the cases and controls**



In this study, the cases had a mean TG level of  $172.92.48 \pm 75.51$  mg/dl in the fasting state and  $232.52 \pm 105.08$  mg/dl in the post prandial state. The controls had a mean TG level of  $125.66 \pm 49.55$  mg/dl in the fasting state and  $133.66 \pm 48.79$  mg/dl in the post prandial state

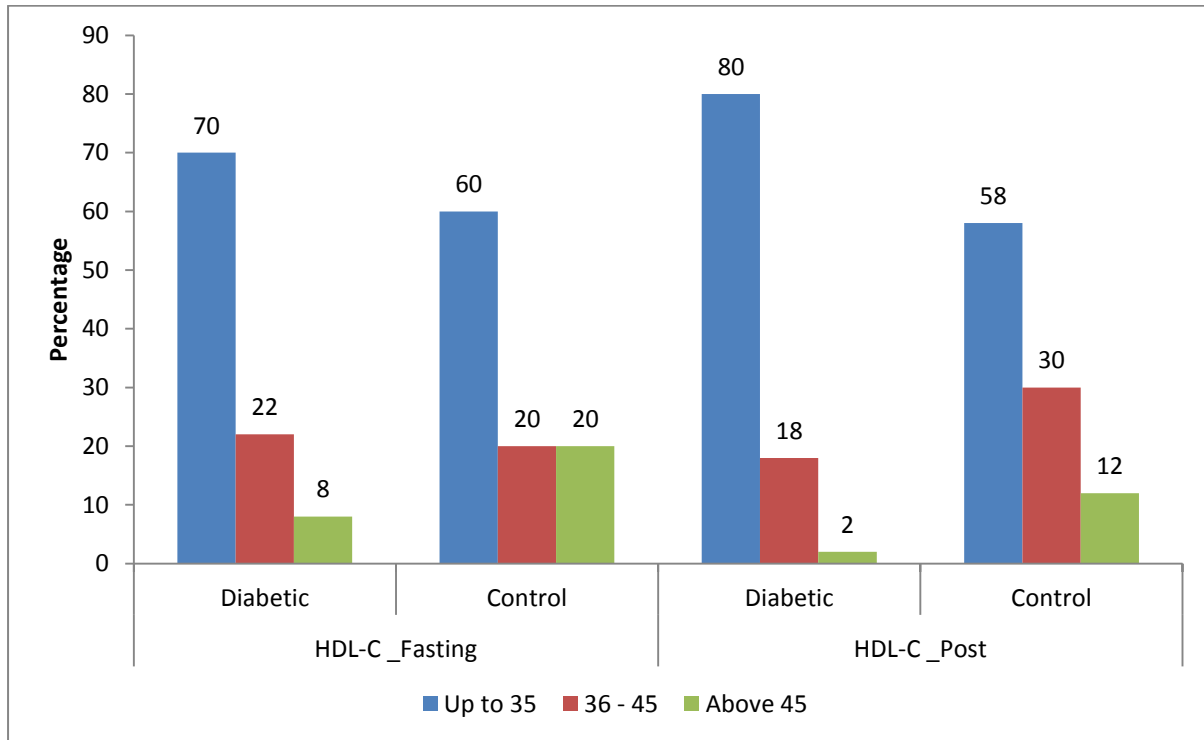
**Table 16a: Fasting HDL-C levels among the cases and controls**

<b>HDL-C Fasting</b>	<b>Diabetic</b>		<b>Control</b>		<b>Total</b>	<b>Chi square</b>	<b>p</b>
	<b>N</b>	<b>%</b>	<b>N</b>	<b>%</b>			
Up to 35	35	70	30	60	65	3.00	0.223
36 - 45	11	22	10	20	21		
Above 45	4	8	10	20	14		
Total	50	100	50	100	100		

**Table 16b: Post prandial HDL-C levels among the cases and controls**

HDL-C Post	Diabetic		Control		Total	Chi square	p
	N	%	N	%			
Up to 35	40	80	29	58	64	9.6	0.04
36 - 45	9	18	15	30	26		
Above 45	1	2	6	12	10		
Total	50	100	50	100	100		

**Graph 13 : Fasting and post prandial HDL-C levels among the cases and controls**



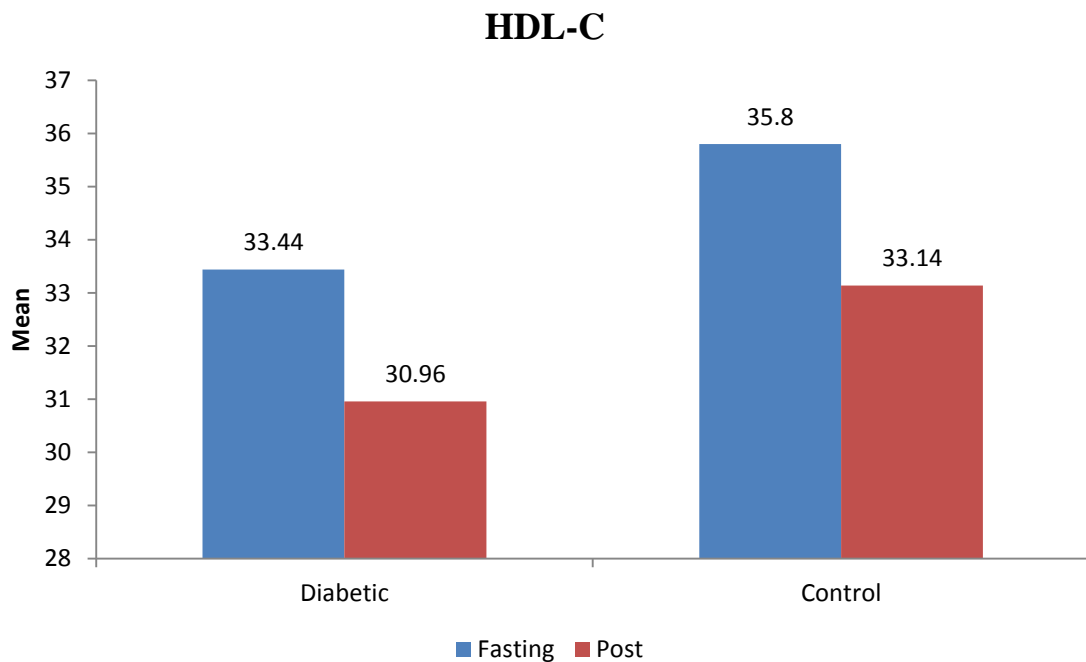
In this study, in the fasting state 70% of the cases had HDL-C levels of < 35 mg/dl as compared with that of control group wherein 60% of them had HDL-C levels of <35 mg/dl.

Similarly in the post prandial state, 80% of the cases had HDL-C levels of <35 mg/dl. as compared with that of control group wherein 58% of them had HDL-C levels of <35 mg/dl.

**Table 17: Comparison of the mean fasting and post prandial HDL-C levels  
among the cases and controls**

		<b>HDL-C</b>					
<b>Group</b>	<b>N</b>	<b>Fasting</b>			<b>Post</b>		
		<b>Mean</b>	<b>SD</b>	<b>p</b>	<b>Mean</b>	<b>SD</b>	<b>p</b>
Diabetic	50	33.44	11.42	0.316	30.96	11.04	0.04
Control	50	35.8	11.99		33.14	11.15	

**Graph 14 : Comparison of the mean fasting and post prandial HDL-C levels among the cases and controls**



In this study, the cases had a mean HDL-C level of  $33.44 \pm 11.42$  mg/dl in the fasting state and  $30.96 \pm 11.04$  mg/dl in the post prandial state. The controls had a mean HDL-C level of  $35.8 \pm 11.99$  mg/dl in the fasting state and  $33.14 \pm 11.15$  mg/dl in the post prandial state

## **DISCUSSION**

In the present study, fasting and post prandial lipid profile was done in 50 patients with type 2 diabetes mellitus and was compared with the fasting and post prandial lipid profile in 50 healthy controls, age and sex matched, fulfilling the inclusion and exclusion criteria.

### **Age distribution of cases and controls**

In the present study, the study group constituted cases from age 31 to 70 years. The majority of cases and controls were in the age group of 61-70 years which constituted 40% of the total; followed by persons in the age group 51-60 years who constituted 32% of the total study. The mean age was  $57.32 \pm 9.13$  years

### **Sex wise distribution of the cases and controls**

In this study, 60% of the study group were males and 40% of the study group were females. Similarly the control group consisted of 60% males and 40% females age matched with the study group

### **Duration of diabetes among the study group**

In this study 8% of the cases were newly detected with type 2 diabetes mellitus.

The duration of diabetes in 28% of cases was between 1 - 5 years, 52% between 6- 10 years and 12% of cases had diabetes for more than 10 years. In the control group none of the patients had diabetes.

### **Prevalence of hypertension among the study group**

In the present study, the prevalence of hypertension among the cases was 40% and among the controls none of them had hypertension.

In the study done by Sumesh raj et al <sup>54</sup> the prevalence of hypertension was seen to be significantly higher in the cases (28%), which is consistent with our study.

**Comparison of the mean fasting and post prandial lipid levels among the  
cases and controls**

		<b>Group</b>	<b>N</b>	<b>Mean</b>	<b>SD</b>	<b>p</b>
<b>FASTING</b>	TC	Control	50	163.78	36.29	0.166
		Diabetic	50	176.36	52.43	
	HDL-C	Control	50	35.80	11.42	0.316
		Diabetic	50	33.44	11.99	
	LDL-C	Control	50	99.82	36.21	0.857
		Diabetic	50	101.16	38.17	
	VLDL-C	Control	50	26.20	13.41	0.003
		Diabetic	50	36.76	20.01	
	TG	Control	50	125.66	49.55	0.000
		Diabetic	50	172.92	75.51	
<b>POST PRANDIAL</b>	TC	Control	50	165.42	35.36	0.323
		Diabetic	50	173.30	43.56	
	HDL-C	Control	50	33.14	11.04	0.04
		Diabetic	50	30.96	11.15	
	LDL-C	Control	50	103.74	35.60	0.383
		Diabetic	50	97.38	36.93	
	VLDL-C	Control	50	28.12	14.00	0.000
		Diabetic	50	41.58	19.82	
	TG	Control	50	133.66	48.79	0.000
		Diabetic	50	232.52	105.08	

## **Total Cholesterol levels among the cases and controls**

In this study, in the fasting state, 24% of cases had total cholesterol levels of >200 mg/dl as compared with the controls where 16% of them had total cholesterol of >200 mg/dl. This association has a p value of 0.146, which is statistically not significant. Hence, the pattern of distribution of patients in different cholesterol levels was found to be similar in both cases and controls. Similar observations were made in the studies done by SV Madhu et al.<sup>55</sup> However, in the study done by Sumesh Raj et al<sup>54</sup> it was found that diabetics had significantly higher levels of TC compared to the controls (p <0.05)

In this study, the cases had a mean TC level of  $176.36 \pm 52.43$  mg/dl in the fasting state and  $176.72 \pm 50.52$  mg/dl in the post prandial state. The controls had a mean TC level of  $163.78 \pm 36.29$  mg/dl in the fasting state and  $165.42 \pm 35.36$  mg/dl in the post prandial state. This association has a p value of 0.323, which is statistically not significant. Hence, there was no significant increase in the post prandial TC level in the cases compared to that of the controls. Similar observations were made in the studies done by SV Madhu et al<sup>55</sup> wherein the cases had a mean TC level of  $209.45 \pm 40.27$  mg/dl in the fasting state and peak mean TC level of  $232.45 \pm 53.13$  mg/dl in the post prandial state. The controls had a mean TC level of  $197.6 \pm 57.13$  mg/dl in the fasting state and peak mean TC level of  $210.35 \pm 54.31$  mg/dl in the post prandial state

## **LDL-C levels among the cases and controls**

In this study, in the fasting state, 58% of cases had LDL-C levels of <100 mg/dl as compared with that of the control group where 46% of controls had LDL-C of <100 mg/dl. This association has a p value of 0.266, which is statistically not significant.

This does not correlate with the study done by sumesh raj et al <sup>54</sup> and SV Madhu et al <sup>55</sup> which showed that LDL-C was higher in the diabetics than in the controls.

In this study, the cases had a mean LDL-C level of  $101.16 \pm 38.17$  mg/dl in the fasting state which is within the normal range. In the Strong Heart Study <sup>56</sup> done by Howard BV et al it was shown that, in American Indians, LDL cholesterol level was the most significant predictor of increased CHD, despite an average LDL cholesterol level of approximately 115 mg/dL in diabetics. In the same study, LDL was a strong predictor of CHD at levels as low as 70mg/dl

In this study, the cases had a mean LDL-C level of  $101.16 \pm 38.17$  mg/dl in the fasting state and  $97.38 \pm 36.93$  mg/dl in the post prandial state. The controls had a mean LDL-C level of  $99.82 \pm 36.21$  mg/dl in the fasting state and  $103.74 \pm 35.6$  in the post prandial state. This association has a p value of 0.383. Hence, statistically insignificant.

In our study though the diabetics had a decreased LDL-C in the post prandial state, it was statistically insignificant. This does not correlate with a study done by Lund et al<sup>57</sup> which showed that in diabetics, LDL-C decreased significantly post prandially ( $p < 0.005$ ).

### **VLDL-C levels among the cases and controls**

In this study, in the fasting state 28% of cases had total VLDL-C levels of  $>40$  mg/dl as compared with that of the control group where only 8% of them had VLDL-C levels of  $>40$ mg/dl. This association has p value of 0.029 which is statistically significant.

Thus cases with diabetes were found to have elevated VLDL-C levels when compared with that of controls. This correlates with the study done by Angela A Rivellesse et al.<sup>58</sup>

Similarly, in the post prandial state, 46% of cases had VLDL-C levels of  $>40$  mg/dl as compared with that of control group, where 14% of them had VLDL-C levels of  $>40$  mg/dl. This association has a p value of 0.001 which is statistically significant.

Thus cases with diabetes were found to have elevated post prandial VLDL-C levels when compared with that of controls .

In this study, the cases had a mean VLDL-C level of  $36.76 \pm 20.01$  mg/dl in the fasting state and  $41.58 \pm 19.82$  mg/dl in the post prandial state. The controls had a mean VLDL-C level of  $26.2 \pm 13.41$  mg/dl in the fasting state and  $28.12 \pm 14$  mg/dl in the post prandial state. ).This association has a p value of 0.000 which is statistically significant.

Hence, there was significant increase in the post prandial VLDL-C levels in diabetics. This does not correlate with the study done by Angela A Rivellesse et al.<sup>58</sup>

### **Triglyceride levels among the cases and controls**

In this study, in the fasting state 56% of the cases had total TG levels of  $>150$  mg/dl as compared with that of control group wherein only 30% of them had TG levels of  $>150$  mg/dl. This association has a p value of 0.021, which is statistically significant.

Thus in the fasting state cases with diabetes were found to have elevated triglyceride levels when compared with that of the controls. This correlates with the studies done by Sumesh raj et al <sup>54</sup>, SV Madhu et al <sup>55</sup>& Angela A Rivellesse et al. <sup>58</sup>

In this study, the cases had a mean TG level of  $172.92.48 \pm 75.51$  mg/dl in the fasting state and  $232.52 \pm 105.08$  mg/dl in the post prandial state. The controls had a mean TG level of  $125.66 \pm 49.55$  mg/dl in the fasting state and  $133.66 \pm 48.79$  mg/dl in the post prandial state. This association has a p value of 0.000. Hence, statistically significant.

Hence, there was a significant increase in the post prandial TG level in the cases compared to that of the controls.

Similar observations were made in the studies done by SV Madhu et al <sup>55</sup> wherein the cases had a mean TG level of  $187.1 \pm 63.45$  mg/dl in the fasting state and peak mean TG level of  $425.2 \pm 204.47$  mg/dl in the post prandial state. The controls had a mean TG level of  $156.85 \pm 76.57$  mg/dl in the fasting state and peak mean TG level of  $283.9 \pm 116.94$  mg/dl in the post prandial state. Similar observations were also made in the studies done by Sumesh raj et al <sup>54</sup> ( $p < 0.01$ ), & Angela A Rivellesse et al. <sup>58</sup>

## **HDL-C levels among the cases and controls**

In this study, in the fasting state 70% of the cases had HDL-C levels of < 35 mg/dl as compared with that of control group wherein 60% of them had HDL-C levels of <35 mg/dl.

This association has a p value >0.05, which is not significant. Hence, there was no significant difference in the HDL-C levels in both the cases and controls in the fasting state.

This correlates with the study done by sumesh raj et al which showed no significant difference in the HDL-C levels in the diabetics and controls. This does not correlate with the study done by SV Madhu et al<sup>58</sup> which showed that diabetics had lower HDL-C levels compared to that of the controls.

In this study, the cases had a mean HDL-C level of  $33.44 \pm 11.42$  mg/dl in the fasting state and  $30.96 \pm 11.04$  mg/dl in the post prandial state. The controls had a mean HDL-C level of  $35.8 \pm 11.99$  mg/dl in the fasting state and  $33.14 \pm 11.15$  mg/dl in the post prandial state.

This association has a p value of 0.04 for post prandial state which is statistically significant. Hence, there was a significant decrease in the post prandial HDL-C level in the cases compared to that of the controls.

Similar observations were made in the studies done by SV Madhu et al <sup>55</sup> in which the cases had a mean HDL-C level of  $35.15 \pm 10.84$  mg/dl in the fasting state and  $28.05 \pm 10.94$  mg/dl in the post prandial state. The controls had a mean HDL-C level of  $42.9 \pm 14.11$  mg/dl in the fasting state and  $37.15 \pm 13.52$  mg/dl in the postprandial state.

## **CONCLUSION**

- The dyslipidemia of Type 2 DM is characterized mainly by raised triglyceride levels, raised VLDL-C Levels and decreased HDL-C levels.
- In the post prandial state there was significant hypertriglyceridaemia and decreased HDL-C levels in diabetics when compared to that of the controls.

## SUMMARY

- Type 2 diabetes mellitus is associated with the development of premature atherosclerosis and a higher cardiovascular morbidity and mortality. Diabetic dyslipidaemia is believed to play an important role in the pathogenesis of accelerated atherosclerosis in this condition.
- The predominant lipid abnormalities seen in diabetes mellitus are an elevated serum triglyceride level and a low HDL-C level.
- The majority of cases and controls in the study group were in the age group of 61-70 years
- There was a high prevalence of hypertension(40%) among the diabetics.
- There was no significant difference in the TC level in the cases compared to that of the controls in both the fasting and post prandial state.
- There was a no significant increase in the LDL-C level among the cases compared to that of the controls in both the fasting and post prandial state

- The cases with diabetes were found to have elevated VLDL-C levels when compared with that of controls in both fasting and post prandial state.
- In the fasting state cases with diabetes were found to have elevated triglyceride levels when compared with that of controls. There was a significant increase in the post prandial TG level in patients with diabetes.
- Though the HDL-C levels in diabetics was low, there was no significant difference in the HDL-C levels in both the cases and controls in the fasting state. In the post prandial state, there was a significant decrease in the HDL-C level in the cases compared to that of the controls.

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## PROFORMA

**Name of the patient** :

**Age** :

**Sex** :

**Address** :

**Occupation** :

**IP No** :

**Date of admission** :

**Date of examination** :

**Chief complaints** :

**History of presenting illness** :

**Past history** :

**Yes No Duration**

Diabetes -

Hypertension -

Hypothyroidism -

Chronic liver disease -

CKD -

**Drug history** :

Whether on any statins, oral contraceptive pills **Yes / No**

Other drugs :

**Personal history** :

**Family history** :

**General examination** :

Pulse :

B P :

Height- weight-

Pallor-

Icterus-

Cyanosis-

Clubbing-

Lymphadenopathy-

Pedal edema-

Markers of Atherosclerosis -

**CVS** :

**RS** :

**P/A** :

**CNS** :

**FUNDUS** :

**Investigations :**

Hb %- gm/dl

TC - cells/cu.mm

DC - N- L- E- M- B

RBS- mg/dl

FBS - mg/dl

PPBS - mg/dl

B.urea- mg/dl

s.creat - mg/dl

**LFT**

T.Bil- mg/dl                      SGOT- U/L

D.Bil- mg/dl                      SGPT- U/L

Alb - gm/dl                      ALP- U/L

**URINE R/E:**

Albumin-

Sugar -

Microscopy -

ECG

**LIPID PROFILE**

**FASTING** (mg/dl)

**Post prandial** (mg/dl)

Total cholestrol

HDL

LDL

VLDL

TRIGLYCERIDES

# MASTER CHART CONTROLS

S NO	NAME	AGE	SEX	IP NO	DM	HTN	RBS	FASTING LIPID PROFILE (mg/dl)					POST PRANDIAL LIPID PROFILE (mg/dl)				
								TC	HDL-C	LDL-C	VLDL-C	TG	TC	HDL-C	LDL-C	VLDL-C	TG
1	MOHAMMED KHAN	50yrs	MALE	98936	-	-	103	181	34	126	19	98	177	31	124	20	103
2	SHANKAR	69yrs	MALE	101032	-	-	100	167	33	59	74	171	188	35	71	81	180
3	ELUMALAI	60yrs	MALE	105314	-	-	130	127	36	70	14	70	129	36	78	14	71
4	SENTHIL	64yrs	MALE	29823	-	-	110	165	27	112	25	129	154	27	100	26	131
5	KUPPAN	55yrs	MALE	107126	-	-	70	130	29	90	10	55	149	29	105	13	79
6	RAMAR	67yrs	MALE	28677	-	-	105	218	65	136	16	81	220	65	137	18	90
7	SELVARAJ	60yrs	MALE	103064	-	-	77	136	26	89	20	102	140	26	92	22	110
8	PALANI	62yrs	MALE	103028	-	-	122	118	35	50	32	163	116	30	50	36	176
9	CHANDRAN	48yrs	MALE	29265	-	-	138	205	40	137	27	136	200	38	134	28	140
10	DURAISAMY	65yrs	MALE	29243	-	-	103	181	34	126	19	98	177	31	124	20	103
11	ARUMUGAM	57yrs	MALE	105028	-	-	99	128	31	60	33	169	130	30	66	34	172
12	JAYARAMAN	55yrs	MALE	105138	-	-	76	122	22	43	57	289	105	16	38	51	256
13	SELVAN	60yrs	MALE	105236	-	-	111	227	29	166	26	130	209	27	140	40	207
14	GANAPATHY	60yrs	MALE	105210	-	-	108	228	30	157	40	203	236	30	166	40	200
15	ADHAVAN ELANGO	48yrs	MALE	105250	-	-	112	110	28	59	33	165	112	30	48	34	170
16	VENGATACHALAM	60yrs	MALE	105298	-	-	115	146	32	95	17	88	133	32	81	18	92
17	CHINNAN	57yrs	MALE	105680	-	-	79	172	24	111	37	185	149	23	76	49	195
18	SENTHIL	43yrs	MALE	29823	-	-	99	124	19	75	29	147	128	28	70	30	150
19	ARUNACHALAM	51yrs	MALE	30223	-	-	135	180	31	132	17	88	184	30	136	18	90
20	CHINNAPPAN	70yrs	MALE	107136	-	-	88	188	30	122	34	174	180	30	114	36	180

21	JAYAPAL	65yrs	MALE	107184	-	-	100	151	38	92	21	106	155	36	97	22	110
22	RAVI	49yrs	MALE	107188	-	-	132	230	49	142	39	198	222	56	122	44	221
23	RAJENDRAN	61yrs	MALE	109112	-	-	136	195	34	41	20	104	200	34	144	22	110
24	ARUMUGAM	61yrs	MALE	109132	-	-	139	160	37	106	17	85	166	36	111	19	96
25	KUPPAN	65yrs	MALE	109318	-	-	116	160	24	124	15	75	180	25	140	14	75
26	MADHU	70yrs	MALE	109332	-	-	85	128	38	70	20	100	142	42	78	22	112
27	RAJI	38yrs	MALE	3100	-	-	70	116	30	70	16	83	130	41	73	60	81
28	RAMASAMY	55yrs	MALE	3782	-	-	109	182	28	132	21	108	176	30	119	26	133
29	JAYARAM	63yrs	MALE	4450	-	-	138	138	30	92	16	87	133	30	86	17	89
30	KRISHNASAMY	46yrs	MALE	4596	-	-	112	141	19	53	62	235	135	16	47	10	246
31	SAROJINI	65yrs	FEMALE	7810	-	-	134	140	87	29	22	112	146	80	42	24	120
32	UMA	38yrs	FEMALE	7812	-	-	125	213	26	105	20	104	220	26	172	22	110
33	REVATHI	37yrs	FEMALE	7866	-	-	123	121	38	50	31	159	130	36	62	32	160
34	CHINNAMMAL	68yrs	FEMALE	8048	-	-	132	104	55	38	9	49	128	50	66	12	63
35	LAKSHMI	50yrs	FEMALE	8768	-	-	122	178	40	118	20	96	180	38	122	20	100
36	MALLIGA	70yrs	FEMALE	8810	-	-	132	173	22	134	16	84	170	22	130	18	90
37	SIVAGAMI	49yrs	FEMALE	8836	-	-	122	164	26	114	22	113	160	24	112	24	120
38	CHITTAYEE	65yrs	FEMALE	8948	-	-	82	162	24	107	30	151	168	22	113	33	164
39	VALARMATHI	55yrs	FEMALE	8942	-	-	101	182	29	127	24	122	180	26	130	24	120
40	RAJESHWARI	45yrs	FEMALE	9348	-	-	110	164	38	102	24	123	168	37	105	26	128
41	KUPPAYEE	52yrs	FEMALE	10980	-	-	131	176	42	110	23	115	180	40	116	24	120
42	KANNAMMAL	64yrs	FEMALE	10992	-	-	96	140	25	90	23	118	146	24	96	26	132
43	SHARADA	50yrs	FEMALE	4058	-	-	136	165	30	111	22	114	170	28	119	23	116
44	BANUMATHI	68yrs	FEMALE	13160	-	-	99	108	24	65	17	89	110	24	68	18	90
45	MYNAVATHI	60yrs	FEMALE	3110	-	-	133	259	32	187	39	195	264	30	192	42	210
46	SOWRIYAMMAL	43yrs	FEMALE	132927	-	-	139	139	33	88	17	87	140	33	89	18	92
47	MANJULA	58yrs	FEMALE	13280	-	-	124	161	38	113	10	47	164	36	114	14	70
48	LAKSHMI	70yrs	FEMALE	15282	-	-	89	217	36	158	22	111	222	34	164	24	120
49	SAVITHRI	60yrs	FEMALE	15427	-	-	113	174	30	86	57	189	170	30	80	60	200
50	VIJAYA	65yrs	FEMALE	16312	-	-	136	195	35	122	36	183	200	34	128	38	190

# MASTER CHART CASES

S NO	NAME	AGE	SEX	IP NO	DM	HTN	RBS	FASTING LIPID PROFILE (mg/dl)					POST PRANDIAL LIPID PROFILE (mg/dl)				
								TC	HDL-C	LDL-C	VLDL-C	TG	TC	HDL-C	LDL-C	VLDL-C	TG
1	VADIVEL	50	MALE	30959	5yrs	4yrs	120	203	55	120	18	93	209	52	134	23	129
2	KANNAM	69	MALE	36926	10yrs	-	295	284	62	101	120	260	256	52	131	73	369
3	KUPPUSAMY	60	MALE	38876	10yrs	2yrs	315	317	77	182	28	144	188	52	107	28	198
4	VELLAIYAN	64	MALE	39108	5yrs	5yrs	162	167	31	42	24	120	182	28	130	50	180
5	NALLATHAMBI	55	MALE	32592	8yrs	-	253	261	51	166	43	218	265	40	180	50	270
6	JEYARAMAN	67	MALE	10893	20yrs	5yrs	172	191	30	129	32	160	137	30	74	33	165
7	ARUMUGAM	60	MALE	33780	6yrs	-	224	174	56	99	18	93	217	57	136	23	118
8	NATESAN	62	MALE	37612	10yrs	-	98	115	27	76	11	156	110	31	68	10	198
9	MARIYAPPAN	48	MALE	37566	5yrs	-	362	168	28	100	39	197	183	30	92	60	301
10	GOPAL	65	MALE	30484	15yrs	6yrs	160	129	33	77	18	92	150	44	75	30	180
11	MUTHUSAMY	57	MALE	32384	8yrs	-	360	170	28	106	35	106	125	31	70	24	126
12	USMAN	55	MALE	25742	8yrs	-	172	110	26	93	65	108	93	28	44	30	148
13	VAIYYAPURI	60	MALE	25886	9yrs	-	223	224	42	153	28	141	221	40	127	53	267
14	RAVIBALAN	60	MALE	26786	11yrs	4yrs	371	324	39	149	54	328	257	50	152	72	465
15	CHANDIRAN	48	MALE	27860	10yrs	9yrs	143	196	35	85	76	412	232	10	112	82	622
16	SANTHAN	60	MALE	31938	ND	-	220	142	31	87	23	116	119	23	72	15	186
17	JAYAVEL	57	MALE	32372	ND	-	95	168	52	90	28	126	178	40	108	30	150
18	BABUK	43	MALE	10963	4yrs	-	108	141	46	79	15	79	139	44	70	24	123
19	BOOPATHI	51	MALE	33844	2yrs	-	176	130	31	56	42	214	138	25	61	52	260
20	PERUMAL	65	MALE	37786	12yrs	6yrs	222	136	22	82	32	160	156	18	102	36	180

21	KANNUGOUNDAR	70	MALE	98924	10yrs	6yrs	185	152	27	84	41	207	150	22	78	50	249
22	KUMAR	49	MALE	98974	8yrs	-	211	140	25	78	36	182	146	21	83	42	212
23	NATESAN	61	MALE	10562	9yrs	9yrs	233	263	46	186	30	151	231	56	137	37	187
24	PERUMAL	61	MALE	37932	7yrs	-	107	184	36	119	28	143	198	30	134	34	170
25	DHARMAPPAN	65	MALE	98965	11yrs	8yrs	232	142	42	60	40	200	128	43	43	42	230
26	KANDASAMY	70	MALE	107204	8yrs	-	215	170	47	87	36	187	175	42	75	59	296
27	SUGUMAR	38	MALE	109044	3yrs	-	300	186	44	71	70	351	189	41	50	97	486
28	PATCHIYAPPAN	55	MALE	109218	9yrs	-	422	152	28	82	41	206	151	31	21	48	282
29	AYYAPERUMAL	63	MALE	3000	5yrs	-	345	135	34	85	16	89	143	39	81	22	168
30	GANESAN	46	MALE	10798	6yrs	-	388	204	33	92	78	294	210	25	105	80	396
31	KAMALA	65	FEMALE	42414	9yrs	6yrs	201	227	43	157	26	133	230	35	165	30	152
32	ANARGALI	38	FEMALE	42548	ND	-	177	248	34	176	38	190	245	24	139	80	402
33	LAKSHMI	37	FEMALE	21910	1yr	-	376	144	32	78	34	170	188	36	120	32	196
34	SAMPOORNAM	68	FEMALE	21930	6yrs	-	133	218	37	161	20	104	200	30	145	24	153
35	JAYA	50	FEMALE	28140	4yrs	-	253	150	24	95	30	151	148	23	82	41	208
36	MUNIYAMMAL	70	FEMALE	9773	8yrs	4yrs	188	193	26	138	28	140	206	28	149	28	181
37	RANGAMMAL	49	FEMALE	30168	6yrs	6yrs	256	197	50	120	25	128	182	44	109	27	186
38	PALANIYAMMAL	65	FEMALE	30188	9yrs	6yrs	467	147	31	78	38	189	153	33	73	47	237
39	KAMALA	55	FEMALE	34302	4yrs	2yrs	167	136	22	85	28	141	145	18	95	32	180
40	PAAPATHI	45	FEMALE	6326	ND	-	159	116	21	65	30	151	130	18	79	33	195
41	SULOCHANA	52	FEMALE	1529	6yrs	-	241	118	20	75	24	118	120	20	72	28	142
42	SAMPAGAVALLI	64	FEMALE	7868	8yrs	6yrs	190	197	42	119	35	175	181	41	109	30	198
43	NAGAMMAL	50	FEMALE	7978	4yrs	-	309	159	35	102	24	110	160	39	89	27	137
44	MADHAMMAL	68	FEMALE	8024	8yrs	6yrs	361	237	26	155	54	274	232	24	153	53	309
45	CHELLAMMA	60	FEMALE	2231	5yrs	-	99	102	30	54	20	80	110	26	64	20	156
46	VASANTHA	43	FEMALE	11106	3yrs	-	383	98	27	13	57	281	110	25	23	62	310
47	THAMARAISELVI	58	FEMALE	13130	8yrs	-	92	188	43	108	36	183	193	36	115	42	211
48	SOWRIYAMMAL	70	FEMALE	13196	10yrs	8yrs	289	130	20	42	70	311	144	22	46	74	376
49	CHINNAKKA	60	FEMALE	16498	12yrs	8yrs	172	161	20	105	42	213	145	20	80	44	260
50	RAMAYEE	65	FEMALE	16448	4yrs	-	100	174	43	116	14	71	167	40	110	16	126



## **KEY TO MASTER CHART**

DM : Diabetes mellitus

F : Female

HDL-C : High density lipoprotein - cholesterol

HTN : Hypertension

LDL-C : Low density lipoprotein - cholesterol

M : Male

ND : Newly detected

RBS : Random blood sugar

TC : Total cholesterol

TG : Triglycerides

VLDL-C : Very low density lipoprotein - cholesterol