"FACTORS AFFECTING LIPID PROFILE AMONG PATIENTS ATTENDING OPD AT KLES DR. PRABHAKAR KORE HOSPITAL & MRC, BELAGAVI-A ONE YEAR OBSERVATIONAL CROSS SECTIONAL STUDY"

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This is to certify that the dissertation entitled "**FACTORS AFFECTING LIPID PROFILE AMONG PATIENTS ATTENDING OPD AT KLES DR. PRABHAKAR KORE HOSPITAL & MRC, BELAGAVI - A ONE YEAR OBSERVATIONAL CROSS SECTIONAL STUDY**" is a bonafide research work done by **REG. NO. BG0116006.**

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ABBREVIATIONS

Glossary	Abbreviations
TC	Total Cholesterol
LDL	Low Density Lipoprotein
HDL	High Density Lipoprotein
TG	Triglycerides
HTN	Hypertension
DM	Diabetes Mellitus
CVD	Cardiovascular Disease
SFA	Saturated Fatty Acids
MUFA	Monounsaturated Fatty Acids
PUFA	Polyunsaturated Fatty Acids
PA	Physical Activity
CHD	Coronary Heart Disease
NCEP	National Cholesterol Education Program
HMG CoA	β-Hydroxy β-methylglutaryl-CoA
PCSK 9	Proprotein convertase subtilisin/kexin type 9

ABSTRACT

Objective: To study the changes in lipid profile in an individual at different time interval and factors responsible for the changes.

Methods: The present study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi on patients during the period of January 2017 to December 2017.Patients attending OPD at the Department of Medicine at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi and having minimum 2 lipid profiles minimum 3 months apart were recruited sequentially by Convenient sampling method till the sample size of 200 subjects was reached. The selected patients were briefed about the nature of the study and a written informed consent was obtained (Annexure–I). Demographic data like gender and age were collected along with relevant history and recorded on predesigned and pretested proforma (Annexure-II). A thorough clinical examination was conducted and the findings were also recorded. All patient relevant data were noted. History of preexisting diseases like Diabetes Mellitus, Hypertension, Stroke, Ischemic Heart Disease, and previous admission to hospital and present symptomatology was listed and detailed physical examination was done. Details of medical interventions were recorded. The data was analysed using EPI info (version 7.2). The qualitative variables were expressed in terms of percentages. The quantative variables were both categorised and expressed in terms of percentages or in terms of mean and standard deviations. Difference between two proportions was analysed using chi square or fisher exact test. Difference between the two means was tested using student t test. All tables were graphically represented. All analysis was 2 tailed and the significance level was set at 0.05.

RESULTS: The mean age of the study subjects was 51.24 ± 14.72 years. Most common age group was 50 to 60 years followed by 60 to 70 years and 40 to 50 years. In our study, 44.50% of them had past history of diabetes, 19% had hypertension, 5% had IHD, 9.50% had hypothyroidism and 25.50% had dyslipidemia. We found a significant difference between the proportions of hypothyroidism and dyslipidemia among the gender. The proportions of tobacco use, alcohol and smoking were significantly higher among the males when compared to females. Over all, the prevalence of tobacco use in our study was 23%, alcohol use was 32% and 19% of them were smokers. Majority of the study subjects were having low or sedentary physical activity levels in our study. In our study, 52.94% of the people having dyslipidemia used statins but the rest discontinued their statins (47.06%). About 30% of the subjects had lifestyle modification and 17.50% had knowledge about dyslipidemia. Among the diabetics, 27.66% had controlled their sugar levels in past 3 months and among the hypertensives, 42.11% had controlled their blood pressures in past 3 months. About 84.21% who had elevated TSH levels were started on treatment of hypothyroidism. About 27.50% underwent dietary changes. Between the 1^{st} and 2^{nd} lipid profile, the total cholesterol levels decreased significantly with lifestyle modification, knowledge about dyslipidemia, controlled sugars, controlled blood pressure and dietary changes. But, in case of discontinuation of statins, the total cholesterol level significantly increased. Use of statins did not affect the decrease in the total cholesterol levels. And treatment of hypothyroidism did not find any significant decrease in total cholesterol levels. The LDL levels significantly decreased in the patients with lifestyle modification, knowledge about dyslipidemia and dietary changes. Discontinuation of statins increased the levels significantly. But, use of

statins, controlled sugars, controlled blood pressure and treatment of hypothyroidism did not yield any significant results.

The HDL levels significantly increased with interventions like lifestyle modification, knowledge about dyslipidemia and use of statins and significantly decreased with discontinuation of statins. But there is no significant difference in the HDL levels from the 1st and 2nd lipid profile in case of controlled sugars, controlled blood pressures, treatment of hypothyroidism and dietary changes. The changes in triglyceride levels were significantly noted in controlled sugars and dietary changes. But in case of use of statins, discontinuation of statins, lifestyle modification, knowledge about dyslipidemia, treatment of hypothyroidism and controlled blood pressures, there was no significant difference. Upon detailed analysis, we found that there was significant decrease in the total cholesterol levels of 1st and 2nd reports who had received Rosuva 10mg, Atorva 40mg, Atorva 20mg and Rosuva 5mg but there was no significant difference in cases who had taken Atorva 10mg. When the LDL levels were assessed, there was significant decrease in LDL levels in patients who received Rosuva 10mg, Atorva 40mg, Atorva 10mg and Rosuva 5mg but there was no significant decrease in case of Atorva20mg. When the HDL levels and the drugs were assessed, there was significant increase the levels only in case of patients who used Atorva 20mg. Upon detailed analysis, the triglyceride levels were significantly decreased in the patients who used Rosuva 10mg, Atorva 40mg, Atorva 20mg, Rosuva 5mg and Atorva 10mg.

CONCLUSION:

- Subjects more than 40 years of age had raised LDL, triglyceride levels by 18.40 % and 12.44 % respectively and decreased HDL levels by 9.33 %as compared to those less than 40 years of age.

- Males had raised LDL, triglyceride levels by 15.11 % and 12.44 % respectively and decreased HDL levels by 3.42 %as compared to females.
- Diabetic individuals had raised LDL, triglyceride levels by 22.27 % and 33.52 % respectively and decreased HDL levels by 12.52 % as compared to the non diabetics.
- Subjects who had sedentary lifestyle had raised LDL, triglyceride levels by 23.20 % and 27.79 % respectively and decreased HDL levels by 9.33 % as compared to the individuals who had moderate to vigorous physical activity.
- Smokers had raised LDL, triglyceride levels by 27.81 % and 22.98 % respectively and decreased HDL levels by 9 % as compared to the non smokers.
- Subjects who didn't have knowledge about dyslipidemia had raised LDL, triglyceride levels by 18.17 % and 19.54 % respectively and decreased HDL levels by 9.46 % as compared to those who had knowledge about dyslipidemia.
- Subjects who had less than 2 visits to doctor had raised LDL, triglyceride levels by 16.76 % and 23.27 % respectively and decreased HDL levels by 6.92 % as compared to those who had more than 2 visits.
- Subjects with abnormal waist-hip ratio had raised LDL, triglyceride levels by 22.08 % and 27.33 % respectively and decreased HDL levels by 9% as compared to those who had a normal waist-hip ratio.
- Our study revealed that use of statins have a favourable effect on the LDL levels (18% decrease), HDL levels (8.08 % increase) and triglycerides

(22.42 % decrease). The change in triglycerides was mainly due to control of sugars.

- Atorva 20 mg followed by Rosuva 10 mg were the statins used by most of the subjects in our study. However, the percent reduction of LDL levels by the statins used by the subjects in our study were almost same.
- Discontinuation of statins (either because of statin intolerance or ignorance) increased the LDL levels (by 13%), triglyceride levels (by 19.72 %) and decreased the HDL levels (16.75 %). None of the subjects enrolled in our study were receiving Fibrates.
- Diabetic patients with controlled blood sugar levels had decreased LDL levels by 9.25 %, increased HDL levels by 13.04 % and decreased Triglyceride levels by 25.04 %.
- Lifestyle modification along with dietary modification had a favourable effect on LDL, HDL values. Particularly, moderate physical activity, cessation of smoking and tobacco use altered the values favourably. Dietary modification and lifestyle modification decreased the LDL levels by 23.88 % and 13.25 % respectively, increased the HDL levels by 8.08 % and 17.7 % respectively and decreased the triglyceride levels by 22.42% and 7.85 % respectively.

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INTRODUCTION

Dyslipidemia is defined as the derangements of one or more of the lipoproteins in blood, such as elevation in total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and/or triglycerides (TG), or low levels of high density lipoprotein cholesterol (HDL-C) alone.[1]

The results of other studies suggested that many persons with dyslipidemia were overtly under-diagnosed and it is estimated that prevalent cases of dyslipidemia in the nine major countries will increase at the rate of 1.76 % per year to surpass 500 million in 2022.[2]

The number of people with dyslipidemia is expected to reach 78 million in the major countries by 2022.[2] The prevalence of dyslipidemia is high and increases continuously in many developing countries as a result of the westernization of diet, obesity, aging of population, reduced physical activity, and other adverse lifestyle changes[3].

Dyslipidemia is one of the most important and modifiable risk factors for cardiovascular diseases, which is also a major cause of morbidity and leads to mortality worldwide.[4]

In 2000, in the age group of 35 to 64, India lost 9.2 million years of productive life (PYLLs), almost six times the figure for US. Further, in the absence of any national program for prevention and management of Cardiovascular diseases, it is expected to increase to 17.9 million PYLLs by 2030, more than nine times the corresponding figure for the US.[5]

Several clinical trials have indicated that the treatment of dyslipidemia is effective in both primary and secondary prevention of cardiovascular events.[6,7] Treatment of dyslipidemia can reduce the risk of heart disease by approximately 30 % over a 5-year period.[8]

Lipid profile variation is associated with various factors. It is poorly understood. Statins are the mainstay in dyslipidemia but, statin intolerance leads to dosage reduction or discontinuation in day to day practice. Concomitant medications of other diseases (e.g Diabetes mellitus or Hypertension) also have effect on dyslipidemia.

Lifestyle modifications (e.g.Diet, Exercise) are important factors which affect dyslipidemia.[9-10] Self education (Knowledge of the disease, medication compliance), control of comorbid conditions also are important in control of dyslipidemia. No study has been done which tell us which factor contributes how much to the outcome.

So, in view of all these factors, this study is to know the multiple factors involved in dyslipidemia.

OBJECTIVES

The objective is to study the changes in lipid profile in an individual at different time interval and factors responsible for the changes.

REVIEW OF LITERATURE

HISTORY AND REVIEW OF LITERATURE

Medicine first recognized the existence of abnormal fatty content of the circulating blood through the milky appearance observed during the days when blood letting was widely practiced. The term lipemia was formulated by Babington in the 18th century, when he showed that fats were responsible for giving this miky appearance to the serum. The presence of lactescent serum with diabetes was first noted by Mariet in 1799 and in 1958 by Thannhauser S.J. Owing to lack of research facilities no further advance was made till the beginning of the 20th century. The deficiency in knowledge was made evident in 1903 when Fischer reviewed the subject. He listed all the conditions where doctors had earlier observed milky appearance of blood. These included apoplexy, peritonitis, malaria, jaundice, leprosy, etc. He finally retained diabetes and alcoholic lipaemia as being genuine.

BRIEF ACCOUNT OF THE LIPID CHEMISTRY

(MAYES, P.M, and Chaterjee)

The lipidology has emerged as an important branch of research that the amount of knowledge has altered the diagnostic approach to patient with lipid disorders and promise to have major impact on therapy as well.

The lipids have four major biological functions:

1. In all cells, the major structural elements of membranes are composed of lipids.

2. Certain lipids such as triacylglycerol serve as efficient reserves for the storage of energy.
3. Many of the vitamins and hormones found in animals are lipids or derivatives of lipids.
4. The bile acid lipids helps to solubilise the other lipid classes during digestion.

The lipids are classified as given below:

a) **Simple lipids** (esters of fatty acid with alcohol)

1. Neutral fats
2. Waxes

b) **Complex lipids** (These are all esters of fatty acids containing some additional groups)

1. Phospholipids
2. Glycolipids
3. Lipoproteins.

c) **The derived lipids** and compounds associated with lipids in distribution Fatty acids, Steroids

Eg. Long chain alcohols, Retinol, Cholesterol

d) **Eicosanoids**: They are synthesized in our body from essential fatty acids

e) **Fat soluble vitamins** Vit A, D, E and K

FATTY ACIDS

They are present as such in minute concentrations in plasma cells. Fatty acid may be defined as organic acids that occur in neutral triglycerides and in monocarboxylic acid ranging in chain lengths from C4-C24 carbon atoms.

Lipid Chemistry

Fatty acids are of two types:

a) Saturated fatty acids - Those which contain no double bonds

b) Unsaturated fatty acids - Those which contain one or more double bonds

Saturated fatty acids having 10 or less carbon atoms are called "Lower fatty acids" e.g-Acetic acid, butyric acid

Saturated fatty acids having more than 10 carbon atoms are called "higher fattyacids". e.g. Palmitic acid, stearic acid.

Unsaturated fatty acids are classified according to degree of saturation

1. **Mono unsaturated fatty acids**. These are those fatty acids which contain one double bond.

   e.g Oleic acid

2. **Polyunsaturated fatty acids**. These are fatty acids which contain more than one double bond

3. **Poly unsaturated fatty acids of Biological importance**

   e.g. Linoleic acid series

   Linolenic acid series

   Arachidonic acid series

Essential fatty acids are those which cannot be synthesized in body and must be provided in the diet. Lack of these essential fatty acids in diet can produce growth retardation and other deficiency syndromes.

Free fatty acids are immediately available energy source and provide much of the energy requirements of body. Normal value ranges from 250 - 400 mg/dl.

CHOLESTEROL

Cholesterol is widely distributed in all cells of the body. It is the best known steroid because of its association with atherosclerosis. It occurs as a white or faintly yellow, almost odourless, pearly leaflets or granules. It is insoluble in water, sparingly soluble in alcohol and soluble in ether, chloroform, hot alcohol, ethyl acetate alcohol and vegetable oil. The structure of cholesterol is $C_{24}H_{45}OH$.

Cholesterol is found in largest amounts in normal human adult brain and nervous tissue of about 20%, in liver 0.3% , skin 0.3%, intestinal mucosa 0.2%.

Certain endocrine glands namely adrenal cortex contain about 10%. The normal level of serum total cholesterol in adults varies from 150-250 mg/dl. About 50-90 mg occurs as free cholesterol (about30% of total) and 110-120 mg as cholesterol esters (about 70% of total).

An elevation of total cholesterol in plasma is considered to be a prime risk factor for HD and MI.[11] The Framingham study has demonstrated a linear increase in coronary heart disease risk with increment of total cholesterol level from 180mg upward. The Lipid Research Clinics Coronary Primary Prevention Trial, has presented the firm proof of that, in human a lowering of plasma cholesterol level,

reduced the coronary thrombosis, myocardial infarction and mortality. *One conclusion was that a 1% fall in total cholesterol reduced the IHD risk by 2%*.

TRIGLYCERIDES (NEUTRAL FATS)

These molecules are used to provide energy. In the body, stored fat in adipose tissue is the storage form of energy.Important sites of adipose tissue are subcutaneous tissue around some internal organs and omentum. Fat under the skin prevent heat loss in winter and the intestinal organs get support from fataround them. The triglycerides constitute the body's main caloric reserve. Normal value ranges from 40-150 mg %.

PHOSPHOLIPIDS

Phospholipids are compound lipids. They contain in addition to fatty acids and glycerol one more alcohol or phosphoric acid residue nitrogen containing base and other substituents. They are classified into 3 groups.

1. Glycophopsholipid - Here glycerol is the alcohol group
   e.g. Lecithin, Cephalin
2. Phosphoinositides - Here inositol is the alcohol group
   e.g. Liposito
3. Phosphosphingolipids - Here sphingosines is the alcohol group
   e.g. Sphingomyelin

The lecithins are the most abundant phospholipids at the cell membrane and represent a large portion of body's store of choline. It is a very effective surface active agent preventing adherence due to surface tension of the inner surface of lungs. They become brown when exposed to acid due to autooxidation and is hygroscopic and

mixes well with water to form cloudy colloidal solution. Normal value range from 150-275 mg %.

LIPOPROTEIN OF PLASMA

In plasma, cholesterol and triglycerides forma integral component of macromolecule complex called lipoprotein which are conjugated proteins. Lipid part is the prosthetic group and lipid tree protein are designated as apolipoproteins or apo proteins. Protein separation including electrophoresis and ultracentrifugation shows progress in lipoprotein chemistry. Teselius et al in 1941 reported existence of two lipoprotein classes separated by moving boundary electrophoresis. In 1954 Gofmen et al separated lipoproteins by ultracentrifugation into five major density classes.

LIPOPORTEIN CLASSES

Five major classes are recognised and each subdivided into subclasses and even to spectrum of molecules. It follows that as proportion of lipid to proteins in lipoprotein increases the density increases. This property is used in separating the various lipoproteins in plasma by ultracentrifugation and the crude classification sufficient for many purposes including broad definition of metabolic functions and relationship to dense states.

The rate at which each lipoprotein floats through a solution of sodium chloride (sp. gravity - 1.063) may be expressed in Svedberg (SF) unit of floatation. One SF unit is equal to 10-13 m/s/dyne g at 26°C.

Relatively high content of triglycerides in chylomicron and VLDL is reflection of their principal roles in the transport of triglycerides from intestines to liver and

from liver to other tissues. There is also evidence indicating that LDL is formed from VLDL fraction by the removal of triglycerides.

LDL (about 20 nm) carry most (about 2/3rd) of the cholesterol in normal plasma. The LDL is about 50% by weight of cholesterol and 20% by weight of protein, HDL molecule (8nm) are about 50% of protein by mass and 50% lipid and hence they are high density.

The clinical laboratory usually analyse only for total cholesterol content and total triglycerides content of the plasma. Knowing the general composition of the lipoproteins one can draw useful inference about lipoprotein patterns.

Physical properties of major categories of Human Plasma Lipoproteins (Mayes P.A)

Class of lipoprotein	Density	Floatation Constant (SF)	Electrophoretic mobility (paper or agarose)	Diameter	Source
Chylomicrons	< 0.95	>400	Remain at origin	90-1000	intestine
Very low Density(VLDL)	0.96 – 1.006	20-400	PreB	30-90	Liver
Intermediate Density (IDL)	1.006-1.019	12-20	B to Pre B	25-30	VLDL
Low Density (LDL)	1.019-1.063	2-12	Beta	20-25	VLDL
High Density (HDL 1)	1.063 -1.125	Analyzed separately	Alpha	10-20	Liver intestine
(HDL 2)	1.125 – 1.210	Analyzed separately	Alpha	7.5-10	Chylomic ron
(HDL 3)					VLDL
Lipoprotein (a)	1.085		Pre B	25	
(Harper's Biochemistry RM 60)					

Typical Lipid And Protein Composition Of Lipoprotein

Class	Percent present as lipid						% of Protein	% total Lipid
	Triglycerides	Phospholipids	Cholesterol Esters	Free Cholesterol	NEFA	Apo Protein		
Chylomicrons	88	8	3	1	-	A-1-111 B C1-11-C111	2	98-99
VLDL	56	20	15	8	1	BCI, CII, CIII	7-10	90-98
IDL	29	26	34	9	1	CII	89	
LDL	13	28	48	10	<1	B	21	79
HDL 1	16	43	31	10	-	AI AIII	33	67
HDL 3	13	46	29	6	1	-	57	43

CHYLOMICRONS

Chylomicrons are the largest of the lipoproteins. Their primary function is to transport the dietary or exogenous triglycerides and cholesterol from the intestinal lumen to sites of metabolism or storage.

In the lumen of the Gl Tract, dietary fat is degraded into free fatty acids and monoglycerides. These substances enter the intestinal villi where they are reconstructed into a triglyceride particles.The triglyceride and cholesterol esters are then combined with apos - beta 48, AI and AIV within the intestinal wall to form chylomicron particles.

The nascent chylomicrons enter the systemic circulation by way of the lymphatics. Apos E and C are then added to the particles. Normally the chylomicrons

are cleared rapidly from the blood and are virtually absent in the fasting state. The cleaning of the chylomicrons is modulated by the enzyme lipoprotein lipase (LPL).

The chylomicron remnants are cleared rapidly from the circulation by receptors present on the surface of liver cells. These receptors recognise the apo and component of the remnant particle

Chylomicron remnants are thought to be atherogenic and an abnormal delay in their clearance is therefore undesirable. The delay in clearance may be secondary to a genetically inherited deficiency of LPL as its activator, apo CII. Clearance of the remnant particles may damage the vascular endothelium and then predispose to atherosclerosis.

Hyperchylomicronaemia also may be secondary to other acquired hyper triglyceridemic states, such as those seen with exogenous estrogen use, uncontrolled diabetes and excessive alcohol intake. The presence of chylomicrons in the serum is necessary for the diagnosis of type I or V hyperlipoproteinemia in the Fredrickson and Lees classification system.

VERY LOW DENSITY LIPOPROTEINS

VLDLS are intermediate in size between chylomicrons and IDLs. They are relatively large particles with diameters from 500-800. VLDLs are produced in the liver.[12]They are the primary lipid component in triglyceride, but cholesterol, cholesterol esters and phospholipids are also present. Their surface components are apo B-100, C and E and phospholipid. The function of VLDL is to transport endogenously synthesized triglycerides and cholesterol into the peripheral tissues where the lipids fatty acids can be utilised for energy or stored as triglycerides. When

VLDL particles enter the systemic circulation their triglyceride core is hydrolysed by LPL.

The remaining VLDL remnant is called IDL. Unlike the chylomicron reminant IDL contains Apo B 100 rather than Apo B 48. Some of the larger particles appear to be directly removed from the circulation. The rest of the particles enter the cascade in which they are converted to IDL and eventually to LDL.

INTERMEDIATE DENSITY LIPOPROTEIN.

IDLs which carry both cholesterol and triglycerides are the product of the enzymatic (LPL-mediated) breakdown of VLDL. After their formation, IDLs may be removed by the liver by means of the binding of apo E to LDL or *BIE* receptor. The remaining are converted to LDL, a process thought to be mediated by hepatic triglyceride lipase. Elevation of IDLs are thought to predispose to premature CAD andperipheral artery disease.

LOW DENSITY LIPOPROTEIN

LDL is the major carrier of cholesterol to the nerve tissue, cell membranes and other cells that require the cholesterol for metabolic functions, including the synthesis of steroid hormones. LDL usually is formed from VLDL breakdown. Direct synthesis has not been completely excluded. Increased LDL synthesis may occur by means of enhanced conversion of VLDL remnants or direct hepatic production of apo Bcontaining lipoproteins. Apo B 100 is the only protein found in LDL. LDL particles are heterogenous, differing in their hydrated density and cholesterol ester content.Patients with greater concentration of small dense LDL have been reported to have three times greater risk for acute myocardial infarction (MI).

Small dense LDL molecules are commonly associated with male gender, diabetes, depressed HDL levels and familial combined hyperlipoproteinemia. Bound LDL particles are then internalized into the cells. About 75 percent of the LDLs in the blood stream are removed by this specific receptor mediated binding.

The remaining LDL particles are cleared by scavenger or macrophage receptors or by non-receptormediated mechanisms. The number of LDL receptors is not fixed and can be modified by genetic defects, saturated fat and cholesterol intake or certain pharamacological agents. About 80% of the patients with an elevated LDL value do not have only one gene defect, the dyslipidemia is secondary to polygenic factors. Hence elevation of LDL due to primary defects are relatively uncommon.

HIGH DENSITY LIPOPROTEIN

HDL are produced by the liver and the GI tract and by the peripheral catabolism of chylomicrons and VLDLS. HDL particles carry cholesterol ester as their major lipid and apos AI and AII as their major proteins. Much of the apoprotein component of HDL is transferred in the systemic circulation to VLDLS ofchylomicrons. Apo CII, an obligatory activator of LPL in one of the apoprotein transferred by HDL.

HDL particles exist in several subtypes. For clinical purposes, HDL and HDL 2 which migrate with alpha mortality in the subfraction must closely be associated with statistical protection against premature atherosclerosis.

Alcohol consumption increases both HDL sub fraction with a greater impact on HDL 3. Lower levels of both subtractions are associated with male gender, hypertriglyceridemia, diabetes mellitus, obesity, uraemia, use of androgens,

progestins, tobacco products and diets rich in polyunsaturated fat, but low in total fat content.

Several epidemiological studies have addressed whether there is a varying clinical impact on CAD depending on the relative levels of HDL 2 and HDL 3.In males with CAD who have an associated low level of circulating HDL, both fractions of HDL are depressed with more of decline in HDL 3. HDL particles are thought to participate in the reverse transport of free cholesterol from peripheral tissues by way of a putative HDL receptor. Oram and coworkers report that apos AI and AII interact with this receptor. This receptor mediated reverse transport could explain why patients with elevated HDL concentrations are less prone to HDL is increased on a genetic basis and has been described as being associated CAD. Just as low levels of HDL are statistically associated with atherosclerosis, HDL is increased on a genetic basis and has been described as being associated with longevity.

LIPOPROTEIN (a)

Lipoprotein (a) or LP (a) has been established as an independent CAD risk factor. The structure is similar to that of an LDL molecule linked by a disulphide bridge to apoprotein (a) LP(a) levels range from 1 mg/dl to 100 mg/dl with the largest number of values below 20 mg/dl.

Although LP(a) is structurally similar to LDL, the former appears to be regulated independently and carries an independent relation to overall coronary risk. If serum levels of both LDL and LP (a) are elevated the risk of CAD is markedly increased.

The mechanism by which high levels of LP (a) are related to coronary atherosclerosis is unclear. It has been suggested that became of the structural similarities of LP(a) to plasminogen, high levels of LP(a) may inhibit the thrombolytic activity of naturally occuring tissue plasminogen activity. An alternative explanation for the association between elevated LP (a) levels and atherosclerosis in that LP(a) may some how alter the LDL mediated delivery of cholesterol to the atherosclerotic plaque.

APO PROTEINS

Apoproteins are key lipoprotein components that serve both as enzymatic co-factors and as recognition elements that bind to specific receptors on peripheral tissues, including the vascular endothelial cells. It is the apo component of the chylomicron remnant that is recognised by receptors on the hepatocyte. This apoproteins are distinguished alphabetically and numerically as apo Al through apo E. A great deal of research has been conducted in the use of apoproteins as CAD markers. Some investigations have found that the concentration of apo Al and apo B 100 are better predictors of CAD then are measurements of total plasma lipids or lipoprotein.

Apoprotein-A

Apo A I, the prototype of apo A, is a major protein in HDL and also is seen in chylomicrons. Apo AII is a minor constituent of HDL and does not appeal to be present in all species. Human apo AII is of hepatic origin. Apo AII maybe an activator of hepatic triglyceride lipase which hydrolyses triglyceride and phospholipid while utilizing HDL2 as its preferred substrate. Apo A Nis synthesized in the gut and is

present in HDL, chylomicrons and as a free protein. It may also be an activator of arm of chromosome Il Combined Al Cill deficiency is associated with severe LCAT. The genetic codes for apos Al. A IV and CIII are close together on the long arm of chromosome II.Combined AI CIII deficiency is associated with premature atherosclerosis.

Apoprotein-B

Apo Boccurs in two forms namely Apo B 100 and B28. Apo B 100 is found in VLDL, IDL and LDL Apo B 100 is the primary apoprotein of LDL and accounts for 25% of its weight. It is also the recognition site for the LDL, or apo B/E receptor on cell surfaces. The gene for apo B 100 has been localised to chromosome 2. The structure in the amino acid sequence of human apo B 100 and the corresponding CDNA messenger CID has recently been determined. A unique editing mechanism introduces a stop codon into the mRNA for apo B by means of single base change. This allows the biosynthesis of two proteins from a single gene and mRNA with either apo B-100 or apo B 48 being synthesized. Apo B 48 is synthesised by small intestine and apo B 100 is secreted by the liver.

Apoprotein - E

Apo E accounts for about 15 percent of the protein content of VLDL.7 percent of chylomicron remnants and 2 percent of protein content of HDL. It can be recognised by the LDL or apo *BIE* receptor and by specific apo E receptors in the liver whose function appears to be the removal of chylomicron remnants Apo is polymorphic and contains three major alleles, apo E2, E3 and E4. The various combinations results in homozygotes for apo E2/2 EG/4. Also apos E2/3, E2/4 and

E3/4 exists in the heterozygous state. The polymorphism of apo E has been determined on a molecular basis and results from the substitution of an amino acid at residues 112 and 158 in the protein.

Apo E isoform may account for as much as 15 percent of variability of cholesterol and LDL levels in the population. Recent Finnish studies suggest that E4 may be associated with increased cholesterol absorptionin the GI tract. In the Prospective Cardiovascular Muenster (PROCAM) study E2 was associated with lower cholesterol levels and E3 or E4 with higher levels of total cholesterol and LDL in population with and without CAD.CID focussed on LDL, but oxidation of VLDL and LP (a) has been shown to increase their atherogenicity

New Lipoprotein phenotypes:

Raised plasma cholesterol, LDL C and reduced HDL C are major risk factors for CAD which had been accepted. However some persons develop premature CAD with apparently normal cholesterol and LDLCh. A wide range of commonly occuring abnormal lipoprotein phenotypes has been seen in patients with CAD. There is thus a need to identify these new lipid and lipopotein factors to determine their relationship with CAD more clearly.

HYPERLIPIDEMIA AND HYPERLIPOPROTEINEMIA

Hyperlipoproteinemias are disturbances of lipid transport that result from accelerated synthesis or retardation of lipoprotein that transport cholesterol and triglycerides through plasma. Elevated plasma lipoprotein levels are important clinically because they cause two life threatening diseases such as myocardial infarction and pancreatitis. Despite refinements in lipoprotein electrophoresis and

improved resolution of lipoprotein classes, there are reasons for dissatisfaction with the phenotyping methodology. Recently attempts have been made to base diagnostic and therapeutic strategies solely on fasting cholesterol and triglyceride values among with inspection of the plasma or serum (an important step that is often ignored).This permits the distinction between three general types of hyperlipidemias that roughly correspond to certain types of hyperlipoprotenemias.

Hyperlipidemia caused by concentration of plasma lipoprotein by one or more causes of lipoprotein may accumulate in the blood stream as the result of either their increased production or secretion into circulation or their decreased clearance or removal from the circulation and in some cases both of these co-exist.

Alterations resulting from genetic defects are classified as "primary disorder of lipid metabolism and alternatively other factors that alter lipoprotein metabolism such as diabetes mellitus, hypothyroidism, etc leading to increased plasma lipoproteins are classified as "secondary disorder of lipid metabolism. In dyslipidemia circulatory levels of lipid or lipoprotein fraction are abnormal that alter production, catabolism or clearance of CID lipoprotein from the circulation. Dyslipidemia may be classified according to which lipoprotein levels are abnormal as in Fredrickson classification system. This classification is not diagnostic and does not consider HDL or LP(a). So this classification has lost utility because it has been recognised that certain disorders can manifest different phenotypes at different times in the same person and that different phenotype may occur in different family members with the same disease.

Fredrickson classification of hyperlipidemia[13]

Phenotype	Lipoprotein	Plasma Cholesterol Level	Plasma Triglyceride Level	Atherogenicity	Relative Frequency
I	Chylomicrons	Nor ↑	↑↑↑↑	Nor↑	<1%
II a	LDL	↑↑	N	++++	10%
II b	LDL, VLDL	↑↑	↑↑	+++	40%
III	LDL	↑↑	↑↑↑	+++	<1%
IV	VLDL	Nor ↑	↑↑	+	45%
V	VLDL Chylomicrons	↑ or ↑↑	↑↑↑↑	+	5%

Major Plasma Lipid Abnormality

Type of Disorder	Increased Cholesterol	Increased Ch+ Triglycerides	Increased Triglycerides
Primary	Familial Hypercholesterolemia Familial defective Apo B-100 Polygenic Hypercholesterolemia	Familial Combined Hyperlipidemia Type II Hyperlipidemia	Familial Hyper-triglyceridemia LPL deficiency Apo-C-II deficiency Sporadic Hyper Triglyceridemia
Secondary	Hypothyroidism Nephrotic Syndrome	Hypothyroidism Nephrotic Syndrome Diabetes Mellitus	D.M Alcoholic Hyperlipidemia Estrogen Therapy

Treatment:

LIPIDS AND ATHEROSCLEROSIS

Several evidences have contributed to our current understanding of the relationship between increase in plasma cholesterol and development of CHD. Premature atherosclerosis results from high cholesterol levels,[14]even in the absence of other cardiovascular risk factors. Large population surveys have shown that plasma cholesterol level is predictive of CHD. In the Framingham study, for individuals below 50 years, cholesterol level was directly related to cardiovascular mortality. The Framingham study highlights the profound effects of lipoprotein abnormalities on incidence of coronary artery disease in diabetics compared to nondiabetics.[15] Although microvascular disease is the specific lesion associated with diabetes, atherosclerosis accounts for majority of deaths in diabetic patients. Atherosclerosis proceeds more rapidly and is more extensive in diabetic than non diabetic individuals.[16] The onset of atherosclerosis occurs early in life with diffuse regular thickening of the arterial intima in childhood. The smooth appearance of the arterial tree is usually lost during the teenage years with formation of nodular aggregates or cushions of fibro-elastic tissue, termed fatty streaks.[17]

Fatty streaks are collections of lipid mainly cholesterol esters in macrophages and smooth muscle cells deposited in the intima of the artery. These fatty streaks are the precursors of the hallmark of atherosclerosis, the fibrous atheromatous plaque. The fibrous plaques are white lesions that usually protrude into the vessel lumen and consists of a core of cholesterol, cholesterol ester, phospholipid and necrotic cells covered by a fibrous cap of elastin and collagen. There is also proliferation of the

smooth muscle cells into the media Another important component is the foam cells, which contain a large quantity of lipid.[18]

In a large prospective study, the Multiple Risk Factor Intervention Trial over 350,000 men aged 35 to 57 years were followed for 6 years. A curvilinear relationship between plasma cholesterol and coronary death rate was observed. If risk ratio of 1 is assigned for a cholesterol level of 200 mg/dl, then at 250 mg/dl the risk is doubled. This relation between cholesterol and CHD is not lost in the presence of other risk factors such as diabetes. In the Framingham study, the presence of diabetes further increased the risk of a given cholesterol level. Because most cholesterol in plasma is transported in LDL, it is believed that it is responsible for the correlation between plasma cholesterol and CHD. Another important predictor of cardiovascular risk is HDL level. The cholesterol content of HDL is relatively smal fractiofl of plasma cholesterol (20-25%). This fraction is inversely related to cardiovascular risks HDL decreases the risk of CHD increases and vice-versa. In the Framingham study average HDL level in middle aged men was 45 mg/dl and 55 mg/dl in the female counterparts.

The relationship between high triglyceride and CHD remams controversial. Some patients with hypertriglyceridemia are at increased cardiovascular risk others are not. However epidemiological studies suggest that the increased risk Seen be due to lither risk factors such as obesity. low HDL and hypercholesterolemia Hypertriglyceridemia also maybe a marker of an individual with a genetic defect of lipoprotein metabolism, such as accumulation of VLDL remnants which are associated with prematureathel osclerosis.

An important factor for the development of atheromatous plaques is oxidized LDL, which causes increased chemotaxis of monocytes, and increased uptake of oxidized LDL by macrophages.[19]

EFFECTS OF DIABETES ON LIPOPROTEIN METABOLISM

The most common lipid anomaly in diabetes is hypertriglyceridemia, caused by increase in plasma VLDL triglyceride, but sometimes chylomicrons may accumulate. Changes in plasma HDL and LDL metabolism can also occur.[20]

Postheparin lipoprotein lipase (LPL) is the key enzyme for the catabolism of chylomicrons and VLDL.[21] Since LPL is an insulin dependent enzyme, a decrease in insulin action, seen in poorly controled type-l and type 2 diabetics will lead to increased VLDL levels.

The impaired VLDL clearance can lead to increased remnant concentrations which are thought to be atherogenic.[22] Diminshed hepatic triglyceride lipase activity which is also insulin-sensitive, may also contribute to impaired remnant clearance. Another abnormality that occurs is nonenzymatic glycosylation of apoprotein B, thus trapping LDL, and potentially accelerating lipid accumulation in damaged vascular endothelium. Also in diabetes, there is relative increase in oxidation of LDL, which is a potential atherogenic agent.[23]

TYPE 2 DIABETES

The most common anomaly in type 2 diabetes is hypertriglyceridemia caused by increase in VLDL. The effect of type 2 diabetes on TG is moderate and increases in plasma TG>500 mg/dl is caused by the coexistence of a genetic form of hypertriglyceridmeia aggravated by the hyperglycemia. Type 2 diabetes causes both

overproductionand impaired clearance of VLDL triglyceride.[24] The mechanism of overproduction of VLDL TG most likely is because of increased flow of glucose and free fatty acids to the liver. The removal defect is caused by impaired lipoprotein lipase activity, but is minimal except in poorly controlled type 2 diabetes. VLDL overproduction and lipoprotein lipase levels can be controlled with normalization of glucose levels. There is also increased production of VLDL apoprotein-B which may be related to obesity. Plasma LDLc in type 2 diabetes is increased because of decreased clearance of LDL, the mechanism of which is the same as in type 2 diabetes. In some individuals with type 2 diabetes, LDL production is low because of impaired conversion of VLDL to LDL. These patients have normal LDL levels but increased levels of VLDL. HDLc in type 2 diabetes is consistently low, especially HDL2. Studies have shown that an inverse relation between HDLC and arterial disease is present.[25] They increase with diabetic treatment, but often remain low. The mechanism appears to be both increased catabolism and reduced production, the former being related to increased hepatic lipase activity. Insulin is more effective than sulphonylureas in raising HDLc levels.

HYPERLIPIDEMIC SYNDROMES ASSOCIATED WITH DIABETES

CHYLOMICRONEMIA SYNDROME IN DIABETES

Diabetic lipemia is a rare but well recognized manifestation of uncontrolled diabetes. It is characterized by the development of gross lipemia caused by accumulation of chylomicrons and VLDL in patients with chronic hyperglycemia. Usually patients develop eruptive xanthomas, lipemia retinalis, chronic abdominal pain or pancreatitis. The lipemia corrects with insulin treatment and is thought to be caused by decreased lipoprotein lipase activity secondary to insulin deficiency. In

many individuals with type 2 diabetes, insulin treatment ameliorates the severe hypertriglyceridemia but does not retum plasma lipid values to normal; these individuals often have hypertriglyceridemic relatives, suggesting the coexistence of a familial form of hypertriglyceridemia. For this group of patients the term "chylomicronemia syndrome[26]describes development of massive issused which hypertriglyceridemia resulting from the interaction of genetic and secondary forms of hyperlipidemia.

Studies of triglyceride metabolism in patients with type 2 diabetes and hypertriglyceridemia show both overproduction and impaired clearance of VLDL triglyceride. Both improve with treatment, but do not necessarily return to normal. These patients appear to have abnormality of lipoprotein metabolism, which is aggravated by poorly controlled diabetes. They require lipid-lowering therapy along with treatment for diabetes.

PRIMARY DIABETES AND SECONDARY HYPERLIPIDEMIA

This is frequently seen during poor diabetic control and is characterized by mild to moderate hyperlipidemia. Most of these patients rarely develop increases in TG > 500 mg/dL and often only mild to moderate hypercholesterolemia, both of which return to normal levels after treatment with insulin or oral hypoglycemic drugs. Occasionally patients develop secondary hypercholesterolemia alone even with good diabetic control because of carbohydrate restricted and high fat diet which was prescribed earlier change in diet to more prudent fat or low cholesterol approach often controls this secondary hypercholesterolemia (American Diabetes Association).[27] This group of patients represents a primary from of diabetes and secondary form of

hyperlipidemia due to either poor diabetic control primarily affecting the triglycerides or high fat diet.

PRIMARY HYPERLIPIDEMIA AND SECONDARY GLUCOSE INTOLERANCE

An increased incidence of abnormal glucose tolerance has been reported in individuals with various primary forms of hyperlipidemia (Glueck, C.J1969). One reason for this may be that obesity is common in patients with primary form of hyperlipidemia and this may also result in glucose intolerance (Blerman, E.L1968). A second reason maybe related to the fact that insulin resistance is oftenobserved in patients with endogenous onset of hypertriglyceridemia (Steiner.G 1981, Olefsky. J.M 1974) and this may increase the likelihood of developing glucose intolerance and/or overt diabetes. The clinical significance of this association is that treatment of hyperlipidemia frequently results in amelioration of glucose intolerance".[28] Thus primary emphasis in the treatment of this group of patients should be directed towards treatment of hyperlipidemia and they do not require specific treatment for diabetes.

PRIMARY DIABETES MELLITUS AND PRIMARY HYPERLIPIDEMIA

The association of primary forms of diabetes mellitus and hyperlipidemia is greater than would be expected by chance alone. Brunzell et al (1975) studied the frequency of diabetes in adults, first degree relatives of patients with familial forms of hypertriglyceridemia. In the families with both familial hypertriglyceridemia and diabetes, diabetes occurred with equal frequency in normolipemic and hyperlipemic relatives. Similar findings were found in families of individuals with only hypertriglyceridemia, but in them the overall frequency of diabetes in the relatives were much lower. These finding suggested diabetes frequently with that IS associated

hypertriglyceridemia, genetic hypertriglyceridemia does not carry an increased risk of diabetes. Thus diabetes and genetic forms of hypertriglyceridemia appear to be independent entities which may happen to coexist by chance in the same individual.

These investigators further evaluated diabetic patients with either familial forms or sporadic forms of hypertriglyceridemia with regard to their response to diabetic treatment.[29] They observed that the triglyceride levels before treatment were much higher in patients with a coexistent familial form of hypertriglyceridemia compared to those with sporadic forms. However after diabetic triglyceride levels in patients with sporadic treatment, hypertriglyceridemia often returned to normal while those from patients with familial forms of hypertriglyceridemia remained elevated. This finding suggest that patients who show persistent hyperlipidemia following appropriate diabetic control may also suffer from a primary form of hyperlipidemia. While treatment of diabetes should be the first step in the management of such patients, persistent hyperlipidemia following appropriate diabetic control deserves additional therapy.

CLINICAL FEATURES

The most common hyperlipidemia in diabetes is hypertriglyceridemia is characterized by increased VLDL-TG. Fasting plasma triglyceride is in the range of 200-800 mg/dl and the plasma is opalescent on inspection if TG concentration is more than 300 mg%. At times there is associated fasting chylomicronemia, usually increasing fasting plasma TG to more than 1000mg%. The plasma becomes more opalescent with a layer of chylomicrons floating to the top of the plasma.

The clinical signs and symptoms of hypertriglyceridemia are as follows:

Signs:

- Eruptive xanthomas
- Hepatosplenomegaly
- Hyperuricemia
- Sjogren-like syndrome

Symptoms:

- Abdominal pain (pancreatitis)
- Arthralgia
- Peripheral neuropathy

Although these manifestations are said to occur with increased VLDL alone, they are ordinarily seen with chylomicronemia. The characteristic skin lesions are eruptive xanthomas which are small, firm, non-tender papules[30]with yellow tip on an erythematous base, erupting over a period of several weeks. When hypertriglyceridemia is severe and diabetes is in poor control, they are usually seen on the buttocks and extensor surface of the extremities. They rarely involve the face and resolve in months hypertriglyceridemia is controlled. Xanthelasma is a distinctive type of xanthoma that occurs on eyelids. They begin as small yellow macules that thicken to form oval foamy plaques.[31] Lipemia retinalis is a blanching of retinal arteries and veins. Hepatosplenomegaly is due to lipid accumulation.

The most common disease associated with chylomicronemia is acute pancreatitis, the pathophysiology of this is unclear, but two hypotheses have been proposed, Kalatskin and Gordon (1952) suggested that there is obstruction of pancreatic capillaries due to microscopic fat emboli. Havel, R.G suggested that pancreatic lipase produces locally toxic free fatty acids, which initiate the inflammatory process, neither being proved. Pancreatitis of any cause compromises insulin secretion, so it maybe expected that endogenous insulin reserve will be impaired and diabetes worsened by pancreatitis. A vicious cycle is thus established with poorly controlled diabetes causing chylomicronemia, which in turn causes pancreatitis, which exacerbates diabetes. This cycle maybe broken by adequate insulinization. Peripheral symmetric polyneuropathy has been reported in severe hypertriglyceridemia (Goldman, LA 1972) even without diabetes. In the setting of diabetes, it is impossible to distinguish this syndrome from the classical diabetic polyneuropathy. Nevertheless, when symptomatic peripheral neuropathy is present in a diabetic subject with chylomicronemia correction ofthe latter is indicated.

Joint stiffness polyarthitis associated with have been hypertriglyceridemia and occasionally with Sjogren-like syndrome. Athough chylomicrons will cause these clinical syndromes, it is worth noting that chylomicronemia, as such will not add to the risk of cardiovascular disease associated with high VLDL- TG or low HDL. The correction of chylomicronemia may thus be indicated for avoidance of pancreatitis, amelioration of neuropathy or of eruptive xanthomas. But there is no proof that one therefore lessens the risk of cardiovascular disease.

TREATMENT OF HYPERLIPIDEMIA IN THE DIABETIC PATIENT

BENEFITS OF TREATMENT OF HYPERLIPIDEMIA

Since1984, a number of studies have been published that shows that it is possible to prevent coronary artery disease by reducing cardiovascular risk factors particularly elevated plasma cholesterol. Probably the most important research study was the Lipid Research Clinics-Coronary Primary Prevention Study."This was a multicenter, randomized placebo controlled, double-blind trial testing the efficacy of cholesterol lowering with bile acid resin cholestyramine in reducing CHD in otherwise healthy middle aged men with hypercholesterolemia. The treatment group had 8.5% reduction in total cholesterol and 12.6% reduction in LDL compared with the placebo group.After 7 years this difference in cholesterol levels resulted in a decrease in CHD deaths and myocardial infarction. Also they had 25% reduction in total cholesterol and 49% decrease in incidence of CHD compared with control subjects.

The DCCT Research Group (Diabetes Control and Complications Trial)[32] had done extensive work on the effect of intensive treatment of diabetes on the delayed development and progression of long-term complications in type-1 diabetes. Another important trial done was the UKPDS[33] (United Kingdom Prospective Diabetes Study), which compared conventional treatment with intensive blood glucose control in type 2 diabetes, and found that vigorous treatment can reduce the risk of complications in diabetes.

Three other major clinical trials have also shown significant reduction in CHD with treatment of hypercholesterolemia. The Helsinki Heart Study,[34] another primary

prevention study compared gemfibrozil to placebo in middle aged hypercholesterolemic men. After 5 years, there was a 34% reduction in myocardial infarction and cardiac death in the gemfibrozil group compared with the placebo group. This was associated with significant reduction in total and LDL cholesterol and triglycerides and increase in HDL. The Coronary drug Project examined the long-term effects of lipid lowering in men with previous myocardial infarction. In the niacin treatment group, there was significant reduction in cardiovascular and total mortality after 15 years of follow up. In the Veterans Affairs High Density Lipoprotein Cholesterol intervention Trial (V A-HIT), Secondary trial significant reduction in events occurred with improved HDL and triglycerides and no change in LDL cholesterol.

Several other recent investigations have used coronary angiograms to study the effect of lipid lowering on progression of coronary atherosclerosis. The most impressive results were noticed by the Cholesterol Lowering Atherosclerosis Study (CLAS). They tested the effect of hyperlipidemic treatment with combined colestipol and niacin in middle aged men who had undergone successful coronary bypass surgery. Non smoking, normotensive men, 40-50 years ago, with cholesterol between 185-350 mg/dl were randomized into drug versus placebo group and underwent coronary angiograms at baseline and after 2 years. In the drug treatment group, there was 26% reduction in total cholesterol 43% reduction in LDL and 37% increase in HDL.

This resulted in a significant reduction in the appearance of new lesions and the progression of pre existing lesions in both the native vessels and bypass grafts, compared with the placebo group. Furthermore, 16.2% of the colestipol-niacin treated

group showed improvement in their coronary angiograms after 2 years compared with only 2.4% of the placebo treated group. The CARE Study[35] has clarified that lowering cholesterol to 5 mmol/l or LDL<3.2 mmol/l did not confer any additional benefit. The statin treatment trials have clearly demonstrated that reducing total and LDLC significantly reduces the risk of CHD.

The DALI Study[36]has shown that aggressive versus standard lipid lowering therapy provides similar reductions of triglyceride levels in patients with type 2 diabetes. Thus, these studies clearly indicate the benefit of lowering cholesterol levels in high-risk patients. Several major trials using different drugs with different mechanism of action have proven the benefits of treatment beyond reasonable doubt. There is also evidence that aggressive treatment of even moderate elevations of plasma cholesterol may slow the progression of pre existing coronary atherosclerosis and in some cause regression of the disease.

NATIONAL CHOLESTEROL EDUCATION PROGRAM GUDELINES

In 1984, National Institute of Health convened a Consensus Development Conference on lowering blood cholesterol. After reviewing the evidence relating cholesterol levels to coronary heart disease, the panel unanimously concluded that elevated blood cholesterol levels is a major cause of CHD and that lowering blood cholesterol levels will reduce the risk of atherosclerosis. They recommended treating moderate risk adults with a low cholesterol diet and that high-risk adults be considered for drug therapy if not responsive to low cholesterol diet

In 1985, The National Cholesterol Education Program was initiated by the National Heart Lung and Blood institute to reduce the prevalence of "elevated blood cholesterol levels. The NCEP ATP III recommended that all adults over the age of 20 years and children of families with premature atherosclerosis should be tested for their serum cholesterol level. This initial blood sample for serum cholesterol screening can be obtained at any time of the day and does not require fasting. Acute illness, myocardial infarction or surgery can lower cholesterol levels, so such patients should have their serum lipids measured again after 8-12 weeks later, Current recommendations by NCEP are as follows:

Cholesterol levels:

Desirable: 200 mg/dl

Borderline high: 200-239 mg/dl

High: >240 mg/dl

If serum cholesterol is less than 200 mg/dl, no further evaluation is required and patient asked to repeat the test in 5 years. Patients with borderline high cholesterol levels should be advised to follow a cholesterol lowering diet and repeat the test in 1 year. Patients with cholesterol levels 200 mg/dl and CHD other cardiovascular risk factors, or with cholesterol 240 mg/dl should have complete assessment of their lipid status. This requires a fasting sample of blood and measurement of total cholesterol, triglycerides, HDL and LDL (calculated as total cholesterol-HDL-TG/5). The NCEP recommends that decisions about treatment of patients with hypercholesterolemia be based on LDL levels as follows:

- Optimal: < 100 mg/dL
- Near or above optimal: 100-129 mg/dL
- Borderline high: 130-150 mg/dL
- High: 160-189 mg/dL
- Very High: ≥ 190 mg/dL

High-risk patients should begin a program of intensive dietary therapy. High risk patients are described by the NCEP as given above. Patients are considered to have a high risk status if they have definite CHD or two or more other cardiovascular risk factors: male sex, family history of prior CHD, smoking, hypertension, low HDL diabetes, obesity.[37] Drug therapy should be reserved for patients who after an adequate trial of dietary therapy have the following, alsothe goal of the therapy is as follows:

Risk Category	10 year risk for CHD	LDL Cholesterol	
		Level at which to consider drug therapy	Primary Goal Of Therapy
Multiple (2+) Risk Factors	>20%	>100 mg/dL	<100 mg/dL
	10-20%	≥130 mg/dL	<130 mg/dL
	<10%	≥160 mg/dL	<130 mg/dL
0-1 Risk Factor	<10%	≥190 mg/dL	<160 mg/dL

The application of these guidelines to patients with diabetes requires some special considerations. First any male patient with diabetes already is in high risk because of presence of two cardiovascular risk factors. Women with diabetes lose their protective advantage in terms of cardiovascular risk. It is reasonable to consider being female in terms of cardiovascular risk. Second it is important to allow diabetic control combined with low cholesterol, low saturated fat diet an adequate trial prior to making a decision to start drug therapy. It often takes 2-3 months of diabetic treatment to see the full effect on lipoprotein profiles and to restore tissue lipoprotein levels to normal. The optimal level diabetic control necessary to lower plasma lipid levels is unknown but some studies have suggested that patients with glycosylated haemoglobin <11% do not have significant elevations in their plasma lipid levels. Also in patients with type 2 diabetes intensive insulin therapy may result in further lowering plasma LDL levels. Third, it is important to realize that there is considerable disagreement about the exact level of plasma total and/or LDL cholesterol at which to begin treatment. The results of the CLAS study suggest that patients with coronary artery disease maybe benefitted by greater reductions in LDL than recommended by NCEP.

Treatment of hypertriglyceridemia also remains controversial. The National Institute of Health Consensus Conference on Treatment of Hypertriglyceridemia recommended that fasting triglyceride level not be considered elevated unless>200 mg%. Hypertriglyceridemia always should be treated with better diabetic control, weight loss, alcohol restriction and fat restricted diet. Drug therapy is advised when TG levels are more than 200mg. Although the level of HDL is inversely related to risk of CHD there is no evidence that raising isolated HDL levels with drugs in patients

with otherwise normal plasma lipid levels reduces cardiovascular risk. When dealing with patients with low HDL levels, it is useful to remember the following:

1. There is a strong statistical association between elevated TG and low HDL and treatment of hypertriglyceridemia often increases HDL cholesterol.
2. In type-2 diabetes patients, changing diabetic treatment from sulfonylureas to insulin may raise HDL levels.

Reduction of high risk of CHD and peripheral arterial disease should be an essential part of diabetic management. Diet and glycemic control can improve serum lipid levels dramatically. Although these manoeuvres can increase HDL, it is unknown whether they actually decrease cardiovascular risk.

DIET THERAPY

Diet is the first step in the management of any patient with hyperlipidemia. Even when drugs are required, dietary therapy is important to achieve maximum benefits from drug treatment. In addition, some patients are unusually responsive to dietary changes and maybe able to achieve their therapeutic goal with diet alone. The diet currently recommended by the American Heart Association and NCEP limits cholesterol intake to less than 300 mg/day, total fat calories to less than 30% of daily intake and saturated fat to less than 10%. This is "Step I Diet . If after 3months, the desired response is not obtained, the diet should be advanced to "Step II Diet", which consists of cholesterol less than 200 mg/day and saturated fat less than 7% calories for another 3 months before considering drug therapy.

These dietary recommendations are compatible with current recommendations from the American Diabetes Association. In fact the increase in complex carbohydrates in type 2 diabetes compared with traditional diabetic diets actually may improve diabetic control in patients with type 2 diabetes, there is no evidence that the increase in carbohydrates causes deterioration of diabetic control.

DIETARY THERAPY OF HIGH BLOOD CHOLESTEROL

	Step – 1	Step – 2
Total Fat	< 30 %	< 30 %
Saturated	< 10 %	< 7 %
Polyunsaturated	< 10 %	< 10 %
Monounsaturated	10 – 15 %	10 – 15 %
Carbohydrates	50 – 60 %	50 – 60 %
Protein	10 – 20 %	10 – 20 %
Cholesterol	< 300 mg	< 200 mg

Three dietary habits typically contribute to elevated lipid levels

1. High intake of cholesterol, which suppresses the synthesis of hepatic LDL receptors.
2. High intake of saturated fats, which reduces the activity of LDL receptors.
3. Excess caloric intake accompanied by obesity, which causes an overproduction Of VLDL by the liver and increased conversion of VLDL to LDL.

Recent studies suggest that except in patients with very severe hyperlipidemia very low fat diets are not needed for an adequate cholesterol lowering response. There is the tendency to allow increased amounts of monounsaturated fats in the cholesterol lowering diets. This appears to be effective in lowering LDL levels too. Diets high in monounsaturated fats[38]do not raise TG levels or decrease HDL levels.

Increases in monounsaturated fat intake are often recommended in patients with hypertriglyceridemia or low HDL levels. It may also be helpful in patients with type 1 diabetes who have trouble with diabetic control on very high carbohydrate diets. Fish oil supplementation has received considerable attention.[39]It contains omega-3 fatty acids. They decrease elevated TG levels but do not lower LDL levels any more than other unsaturated fats. It also causes reduced platelet aggregation. The patients should also be advised to take high fiber diet and complex carbohydrates, avoid alcohol and to give up smoking.

DRUG THERAPY

In patients who do not respond adequately to dietary therapy, drug therapy should be used. There are several effective and safe drugs available for treatment of hyperlipidemia. However selection of the most appropriate hypolipidemic agent for an individual patient requires recognizing which lipoprotein is responsible for the hyperlipidemia. The different agents can be categorized as those used primarily to lower elevated LDL levels and those used to lower VLDL levels.[40] If the major problem is elevated cholesterol levels, then an agent that affects LDL metabolism is used. If TG levels are raised then drugs that affect VLDL metabolism are appropriate.

AVAILABLE DRUG THERAPIES

The major classes of drugs of consideration are

A. Bile acid Sequestrants:
    a. Cholestyramine
    b. Cholestipol
B. Nicotinic acid.
C. HMG COA reductase inhibitors:
    a. Lovastatin
    b. Simvastatin
    c. Pravastatin
    d. Fluvastatin
    e. Pitavastatin
    f. Atorvastatin
    g. Rosuvastatin
D. Fibric Acid Derivatives:
    a. Probucol
    b. Clofibrate
    c. Gemfibrozil
E. PCSK 9 Inhibitors:
    a. Alirocumab
    b. Evolocumab.
F. Hormones that may be considered are estrogen replacements.

A. BILE ACID SEQUESTRANTS

Cholestyramine, Colestipol

- LDL cholesterol decreased by 15-30%[41]
- HDL cholesterol increased by 3-5%
- Triglycerides no effect

Major use:

1. To lower LDL cholesterol
2. Reduce CAD and MI risk

Contraindications:

Absolute Familial dysbetalipoproteinemia

Triglycerides > 500mg/dl

Relative Triglycerides > 200 mg/dl

Major side adverse effect:

Upper and lower gastrointestinal complaints

Decreased absorption of other drugs.

	Usual daily dose	MAX. DAILY DOSE
Cholestyramine	4-16 gm	24gm
Colestipol	5-20 gm	30 gm

B. NICOTINIC ACID

Crystalline nicotinic acid

Sustained release Nicotinic acid

- LDL Ch decreased by 10-25%
- HDL Ch increased by 15-35%
- Triglycerides decreased by 20-25%

Major use:

- Useful in most lipid and lipoprotein abnormalities
- Reduces CAD risk.

Contraindications:

Absolute: Chronic liver disease

Relative: Type Il diabetes mellitus

Gout (severe)

Hyperuricemia.

Major side / Adverse effects:

Flushing

Hepatotoxicity Hyperglycemia

Hyperuricaemia or gout

Upper gastrointestinal complaints

	Usual daily dose	MAX. DAILY DOSE
Crystalline nicotinic acid	1.5 – 3 gm	6 gm
Sustained release nicotinic add	1 – 2 gm	2 gm

C. HMG COA REDUCTASE INHIBITORS

Lovastatin, Pravastatin, Simvastastin, Atorvostatin, Rosuvastatin

- LDL Ch: decreased by 20-40%
- HDL Ch: increased by 5-15% Triglycerides decreased by 10-20%
- Decrease Apo B by 25%

Major use[42]:

To reduce LDL Cholesterol

To reduce CAD risk

Contraindication:

Absolute: Active or chronic liver disease

Relative: Concomitant use of Cyclosporine, Gemfibrozil or Niacin.

	Usual daily dose	MAX. DAILY DOSE
Lovastatin	10 – 40 mg	80 mg
Pravastatin	10 – 40 mg	40 mg
Simvastatin	5 – 20 mg	40 mg
Atorvastatin	10 – 20 mg	40 mg

D. FIBRIC ACID DERIVATIVES

Gemfibrozil, Clofibrate, Fenofibrate

- Primarily increase lipoprotein lipase activity.
- Triglyceride level decreased by20-50%[43]
- HDL Ch increased by 10-15% LDL-Ch decreased by 10-15%

Major use:

To lower triglyceride levels in combined hyperlipidemia

Contraindications:

Gall stones

Major side/ adverse effects:

Gastrointestinal complaints.

	Usual daily dose	MAX. DAILY DOSE
Gemfibrozil	600 mg	1200 mg
Clofibrate	2 gm	3 gm
Fenofibrate	200 mg	400 mg

E. PCSK 9 INHIBITORS

Alirocumab and Evolocumab are first of the agents that have been used as the monoclonal antibody treatment targeting PCSK9 , have received regulatory approval in Europe and USA in 2015. Both these agents are now licensed for use in management of adult patients with hypercholesterolemia or mixed dyslipidemia. Evolocumab is licensed for the treatment of adults and adolescents aged 12 years and over with homozygous familial hypercholesterolemia also. Administration of a PCSK9 inhibitor can at least halve the level of LDL cholesterol even when added to statin - based lipid-modifying therapy. Moreover, these agents appear from short-term clinical trials, at least, to be sufficiently well tolerated to support long-term administration to patients with hypercholesterolaemia. The initial data on cardiovascular outcomes presented recently provide an intriguing hint of a possible improvement in long-term cardiovascular prognosis with these agents. Any patient who is at an elevated risk of an adverse cardiovascular outcome due to elevated LDL cholesterol could benefit from treatment with a PCSK9 inhibitor, particularly people with the severe hypercholesterolaemia phenotype associated with familial hypercholesterolaemia.

F. ANTIOXIDANTS

Vitamin E: Sternberg and other investigators have established the ability of alpha tocopherol or Vit. E, to inhibit oxidation of LDL cholesterol. However there are several other mechanisms by which antioxidants may act to inhibit the development of atherosclerosis.[44]For example recently published data suggests that B carotene may prevent endothelial damage by preventing uptake of oxidised LPL. B carotene however does not appear to inhibit oxidation of LDL. In plasma, each of the

antioxidant Vit B Carotene, Vit E, Vit C achieves its effects via a different mechanism.

G. TREATMENT TO RAISE HDL CHOLESTEROL

At present there is no highly effective therapy to raise HDL cholesterol levels. Estrogen can be given to post menopausal women and exercise in sustained amount may moderately increase HDL cholesterol levels.[45]Alcohol when consumed in modest quantities can also increase HDL cholesterol level.

Niacin result in the largest increase in HDL cholesterol levels (15 - 25%) Gemfibrozil and HMG COA reductase inhibitors incease HDL cholesterol by about 10%.[46]

The order of priorities for treatment of diabetic dyslipidemia in adults is as follows:

a) LDLc lowering:

1. First choice-HMG CoA reductase inhibitors.
2. Second choice – Bile-acid binding resin.

b) HDLcincrement:

1. Behavorial changes such as weight loss, increased physical activity and smoking cessation.
2. Nicotinic acid or fibrates.

c) Triglyceride lowering:

1. Glycemic control first priority.
2. Fibric acid derivatives (gemfibrozil, fenofibrate).
3. Statins.

COMBINED HYPERLIPIDEMIA

FIRST CHOICE - Improved glycemic control plus high dose statins.

SECOND CHOICE - Improved glycemic control plus statins, fibric acid derivative.

THIRD CHOICE –

Improved glycemic control plus statins, nicotinic acid.

Improved glycemic control plus resin plus fibric acid derivative.

Estrogens should be the first line of therapy in postmenopausal women with high cholesterol levels.

Estrogens decrease LDLc levels and raise HDLc levels, but also increase triglyceride levels.

DIABETES AND DYSLIPIDEMIA

In the years that followed data accumulated about hyperlipemia accompanying diabetes. Man and Peters (1935) found that triglyceride was the primary lipid to be elevated. Harries et al (1952) found elevations of serum lipid levels in diabetic acidosis. More recently. Chaturvedi et al (2001) found elevation in triglyceride rich VLDL to be a common abnomality. In a study of Lowy A.D et al (1957) found a significant increase in the incidence of hyperlipidemia in association with poor diabetic control.

In a study of the significance of blood lipid alterations in diabetes mellitus, Mazzone T et al (2000) measured plasma triglyceride and cholesterol levels in large series of diabetic and non-diabetic subjects of all ages. Their results showed that

plasma triglycerides increase with age in diabetics but not in nondiabetics, while cholesterol levels increase with age in both groups.

Albrink et al (1963) studied 139 diabetics over a period of 30 years with regard to the serum lipid concentration and the vascular complications of diabetes mellitus and found a trend towards increasing serum triglyceride concentrations and increasing incidence of atherosclerosis in coronary and other arteries.

Dewind et al. (1952) carried out studies in patients with advanced diabetic atherosclerosis and found no obvious correlation between any of the lipid tractions although the mean serum cholesterol values were significantly higher in diabetics than in non-diabetic elderly controls.

Aldersberg et al. (1956) found that in patients with uncomplicated diabetes, the concentration of the lipids were within normal limits. Diabetics with retinopathy. without renal involvement showed increase of total serum lipids and neutral fats whereas serum cholesterol and phospholipidis remained within normal limits.

Sait et.al (1960) showed that the concentrations of serum triglyceride B lipoproteins. esterified fatty acids and phospholipids were all elevated in treated diabetic children and that these values returned towards normal within 24 to 48 hours after starting therapy with insulin.

Stirred Wet al (1963) showed that in well-controlled diabetics, serum levels of cholesterol and phospholipids were normal whereas those of NEFA and TG were raised. Some of the well-controlled elderly diabetics had increase in all lipid fractions. But where the control was poor, as in diabetic coma, all the lipid fractions were elevated both in young and elderly diabetics.

Strisower E H et al (1958) found significant increase in serum cholesterol, LDL and VLDL values in poorly controlled insulin treated diabetics, which returned to normal on achieving rigid control.

Mathur et al (1961) did not observe a definite relationship of any of the blood lipids to the severity of diabetes, but found a uniform elevation in all lipids in ketotic patients.

Ahuja and Gossain (1966) found higher values of cholesterol and triglycerides in patients having a fasting blood sugar greater than 130 mg%.

Bagdade et al. (1967) studied five patients with chronic symptomatic diabetes and minimal ketoacidosis who had marked hyperlipidemia and concluded that diabetic lipemia can be considered to be a reversible form of dietary fat induced lipemia secondary to chronic insulin deficiency.

Chance et al. (1960) studied serum lipids and lipoproteins in 135 diabetic children prior to treatment and found elevated serum total lipids in 64% of the patients and elevated cholesterol in 43%. Abnormal lipoprotein patterns were found in 77%, the commonest anomaly being increase in pre P-lipoprotein.

Sharma D et al. (1970) studied serum lipid profile in type Il diabetic patients below 40 years of age and found significant elevations in the level of serum cholesterol, phospholipids, esterified fatty acids and triglyceride as compared to control group.

Nikkila EA and Homila P (1978), concluded that the average serum lipid and lipoprotein pattern of insulin treated chronic diabetic patients was not more atherogenic than non-diabetic subjects of similar age and sex. On the contrary the

increase in HDLC levels which they found, should make them less able to develop coronary heart disease. Thus they felt that the increased incidence of cardiovascular disease in type Il diabetes must be accounted for by some other factors.

In a study of HDLC in diabetics by P.K.Bijlani et al. (1983), it was found that the HDLC values in diabetics and subjects with impaired glucose tolerance were significantly lower than normal controls, Females in all groups had higher HDLC than males. Higher HDLC values were also observed in diabetics on insulin therapy and with better glycemic control.

V.J. Retnam et al (1983) reported hyperlipoproteinemia in a study of 152 adult diabetics on treatment. They found that 20 out of 70 controlled patients and 48 of 82 uncontrolled patients had hyperlipoproteinemia.

Over the past years there has been increasing awareness on the part of the physicians and general population of the potential benefits of detecting and treating hypercholesterolemia. This is particularly important in diabetics for two reasons:

1) There already is an increased risk of premature coronary heart disease inpatients with diabetes independent of raised plasma cholesterol levels.
2) Alterations in plasma lipoprotein metabolism are common in diabetes and tends to exaggerate any pre-existing tendencies towards elevated lipid levels.

Intensive dietary therapy in 57 newly diagnosed type 2 diabetic patients led to an increase in HDL and HDL: cholesterol ratio after 3 months. The increase in HDLC was related to the degree of weight loss achieved in 28 patients whose weight reduced by 10% or more average body weight during months, HDLC rose from 122 to 1.36 (p less than 0.001) whereas patients who lost less weight showed no significant increase

in HDLC The increase in mean serum HDLc levels in female patients was associated with a mean weight reduction of 121 average body weight. Patients who were obese at diagnosis lost more weight during the study than non-obese patients, and showed a significant increase in serum HDLC levels. So intensive dietary therapy may lead to a less atherogenic lipid profile in type 2 diabetics, especially in those who achieved a major weight reduction (Kennedy et al 1982).

Zurro - Hernadez et al (1991) correlated the higher prevalence of peripheral arterial disease in diabetics compared to normal glucose tolerance subjects with increased mean level of triglyceride and systolic blood pressure.

The use of biguanidine derivative in the treatment of patients with type 2 diabetes mellitus concurrent with insulin leads to correction of most unfavourable changes in biochemical and immunological parameters. The presence of abdominal obesity (BMI) is a factor that favors the appearance of high levels of serum triglycerides and low levels of HDLC in type 2 diabetes mellitus. On the other hand. DM is a factor that increases the levels of triglycerides with low levels of HDLc which already exist in abdominal obesity.

Zurro-Hernandez etal 1991, Hokanson JE, et al (1996) stated that plasma triglyceride is an independent risk factor for the development of cardiovascular disease.

Thus it is seen that extensive work has been carried out over the decades regarding the hyperlipidemia in diabetics. Inspite of this much remains to be leamed and further research is needed to elucidate the coexisting interrelationship between diabetes and hyperlipidemia.

LIPIDS AND LIFESTYLE MODIFICATION

Lifestyle changes remain the cornerstone of management of lipid and lipoprotein disorders and obesity, and are warranted in primary as well as secondary prevention settings. Lifestyle changes recommended for those with high cholesterol levels include adopting a diet low in saturated and *trans* fatty acids, incorporating functional foods rich in bioactive substances such as fiber, antioxidants, plant sterols and stanols, exercising regularly, and maintaining a healthy weight. Based on a large body of evidence, current dietary guidelines uniformly recommend reducing intakes of saturated and *trans* fatty acids with replacement by increasing intake of mono- and polyunsaturated fatty acids.

Seven Countries Study findings:15- year death rates were related positively to average percentage of dietary energy from saturated fatty acids (SFA), negatively to dietary energy percentage from monounsaturated fatty acids (MUFA), and were unrelated to dietary energy percentage from polyunsaturated fatty acids (PUFA), proteins, carbohydrates, and alcohol in the diet[47]. Keys was the first to associate the traditional Mediterranean diet (olive oil as the main fat, high in cereal products, legumes, fruit and vegetables, moderate in fish and low in dairy and meat products, moderate wine consumption) with a low risk of CHD.

Dietary guidelines have universally recommended reducing the intake of saturated fat to lower low-density lipoprotein cholesterol (LDL-C) levels and reduce CHD risk.Current dietary recommendations, however, are to reduce saturated fat intake and increase intakes of dietary MUFA and PUFA, resulting in a moderate fat diet.

2013 American Heart Association (AHA)/American College of Cardiology Guideline on Lifestyle Management to Reduce Cardiovascular Risk[48] recommends reducing saturated fat intake to 5 to 6% of total calories and reducing the percentage of calories from *trans* fats.

Unique properties of individual SFA in altering blood lipid profile: Individual SFA have diverse biological and cholesterol-raising effects. The chain length of SFA plays an important role in defining biological functions, such as susceptibility to oxidation and solubility in water, as well as effects on blood lipids and lipoproteins. The most commonly consumed SFA are palmitic acid (16:0; major source: vegetable oil, dairy, and meat), stearic acid (18:0; meat and dairy), myristic acid (14:0; dairy and tropical oil) and lauric acid (12:0; dairy and tropical oil).These SFA, excluding stearic acid, have been associated with increases in TC, LDL-C, and HDL-C levels.[49-51]

"Physical Activity" refers to any bodily movement produced by skeletal muscles that results in an expenditure of energy, which includes a broad range of occupational, leisure and daily activities; whereas "exercise" refers to planned or structured PA, performed for a reason, and can include aerobic exercise, resistance training or combined aerobic and resistance training

A 1999 report of the Nurses' Health Study examined the association between total PA and CHD events in >72,000 nurses (age range; 40 and 65 years). It demonstrated that women who walked vigorously for greater than 150 min/wk had a 35% reduction in CHD events compared with those who walked infrequently.[52]

Aerobic exercise training (AET) includes cardiorespiratory endurance exercises such as jogging, running, and cycling.[53] A 6-month AET intervention,

which progressed from 50 to 85% of maximum aerobic power for 20–60 min 3 times/wk resulted in significant decreases in TC and the TC/HDL-C ratio.[54]

Pickering and Sandersen 1945 found no evidence to suggest that smoking produced coronary vasoconstriction in for smoking before or after exercise did not produce exercise tolerance in a subject with angina pectoris. They felt that smoking was a factor in producing pain by virtue of increasing the work of heart to raising the pulse rate and blood pressure.It is indeed possible that the smoking habit and ischemic heart disease related indirectly in that both may be related to a third common factor [BMJ 1955].

In the Finnish survey higher serum cholesterol values were found in heavy smokers.Smoking of tobacco by people started centuries ago but the health andenvironmental hazards, posed by it was recognized only in the 20h century.

Atherogenesis, which is important risk factor for ischemic heart disease (IHD) and cerebrovascular accident, is thought to be accelerated by smoking. The exactatherogenie mechanism of smoking is still unclear. It has been observed, by workersthat smoking lead to dyslipidemia which is a major factor for atherosclerosis.

The Framingham heart study was initiated in 1948 by the United StatesPublic Health Service to study the relationship of number of risk factor (eg serum cholesterol, blood pressure, weight smoking) to the subsequent development ofcardiovascular disease. The town of Framingham (Massachusetts) had a population of28,000 in 1948. The study was planned for 20 years in view of the slow development of heart disease.[55]

The lower and upper limits of the study population, was set at 30 and 59 yearsof age. Out of 10,000 people, in this age group a sample of 6507 person of both sexeswere invited to participate in the study, out of which 5209 participated. The initialexamination revealed that 82 subject had clinically evident CHD. They were excludedfrom the sample leaving a total of 5127.4469 (69%) of the 6507 in the initial sample actually underwent the firstexamination. After the first examination, the study population was examined every 2 year period Information was obtained with regard to serum cholesterol, bloodpressure, weight and cigarette smoking. Although biennial examinations were thatmain source of follow up information, other means were also adopted to detect CHD(eg. Death Certificate Record) Among other things, the study showed increasing risk of coronary heartdisease (CHD) with increasing serum cholesterol level in the 45-54 age group. Thestudy also showed that the association between smoking and CHD varied with manifestations of disease. Thus, smoking was more strongly associated with sudden death from CHD than with less fatal forms of the disease. Risk factor have been foundto include male sex, advancing age, high serum lipids concentration, high bloodpressure, cigarette smoking, diabetes mellitus, obesity, low vital capacity and certainECG abnormalities. The predictive value of serum lipids, blood pressure and cigarettesmoking had been repeatedly demonstrated. The Framingham heart study became prototype of similar studies in US and other countries.

The relation between smoking and blood lipids and apolipoproteins (AI,B100)were studied in a group of 1024 12- to 18-year-old school children in the Comunidadde Madrid. The percentage of smokers was 19% (17% for girls and 21% for boys).The average consumption of cigarettes per day was 7.83 +/- 5.06 in boys and 6,04 +) 3.49 in girls (p less than 0.05). As compared with male nonsmokers, male

smokersshowed a higher mean level of low-density lipoprotein (LDL) cholesterol (112 versus100 mg/dl.,p less than 0.05), a higher LDL cholesterol to HDL-cholesterol ratio (2.27versus 1.94, p less than 0.001), a higher mean level of apolipoprotein B100 (59 versus53 mg/dL, p less than 0.05), and a higher apolipoprotein B100 to apolipoprotein Alratio (0.45 versus 0.40, p less than 0.01). Female smokers tended to show the same results, although significant differences were only found for LDL cholesterol to HDLcholesterol ratio and apolipoprotein B100 to apolipoprotein Al ratio (1.8 versus 1.59and 0.41 versus 0,38 respectively, both p less than 0.05). This work provides new dataabout the effects of smoking on apolipoproteins in adolescents and emphasizes on theneed for preventive programs.[56]

Development of coronary artery disease (Athersclerosis) begins in childhooditself (FELIC study). It is therefore important to identify potential risk factor earlywhen prophylactic care must be cost effective. E.g. cigarette smoking.[57]

The serum anti-atherogenic HDL-C level is significantly low in chronic smokers irrespective of the number of cigarettes smoked. The serum level of totalcholesterol, LDL-C and VLDL-C and TG are significantly increased in persons smoking 11-20 cigarettes or beedis per day as compared to those smoking 1-10 cigarettes or beedis per day and therefore raising the cardiovascular disease risk.[58]

W Y Craig, G E Palomaki, and J. E Haddow demonstrated Overall, smokers had significantly higher serum concentrations of cholesterol (30%), triglycerides (9.1%), very low density Lipoprotein cholesterol (10.4%), and lowdensity lipoprotein cholesterol (1.7%) and lower serum concentrations of high density Lipoprotein cholesterol (-5.7%) and apolipoprotein Al (-4.2%) compared with non smokers

Among non-smokers and light, Moderate, and heavy smokers a significant dose response effect was present for cholesterol (0, 1.8, 43, and 45% respectively,Triglycerides (0, 10.7, 115, and 18.0%), very low density lipoprotein cholesterol (0.72, 44.4, and 39.0%), low density lipoprotein cholesterol (0.-1.1, 1.4, and 11.0%), high density lipoprotein cholesterol (0, -4.6.-6.3, and -89%), and apolipoprotein Al(0.-3.7 and -5.7% in non-smokers and light and heavy smokers).These dose response effects may provide new evidence for a causal relation between exposure to cigarette smoke and changes in serum lipid and lipoprotein concentrations whether as a direct result of physiological changes or of dietary changes induced by smoking. Adequate prospective data to estimate the excess risk of coronary artery disease existed only for cholesterol concentration. When that information was combined with data from the present study, and given that smokers as a group face an average overall excess risk of coronary artery disease of 70%, it was estimated that the observed increased serum cholesterol concentration in smokers may account for at least 9% of that excess risk. Furthermore, the dose response effect of smoking on serum cholesterol concentration suggests a gradient of increased absolute risk of coronary artery disease between light and heavy smokers.[59]

The association between extent and duration of smoking habit and severity of coronary atheroma was examined in 387 patients undergoing routine coronary ateriography before valve replacement surgery. Total number of cigarettes smoked in life correlated significantly with severity of coronary artery disease ($p < 0.001$) and number of coronary arteries with stenoses of 50% or more ($p < 0.001$). Severity of coronary artery disease in current smokers was similar to that in former smokers. Multiple regression analysis showed diastolic blood pressure, cigarette consumption,

age, ratio of total cholesterol to high density lipoprotein cholesterol, and history of angina to be the important predictors of severity of coronary artery disease.

An estimate of the number of cigarettes smoked in life can be useful in identifying patients with coronary artery disease if used in conjunction with data on other important risk factors.[60]

Smoking is the leading preventable cause of illness and premature death in Germany, claiming over 110,000 lives a year because it directly increases the risk of dying from heart disease, stroke, emphysema and a variety of cancers. The overwhelming majority of smokers begin tobacco use before they reach adulthood.

Among those young people who smoke, the average age is now 13-14. In Germany,about 39% of male and 31% of female adults (age 18-60 years) continue to smoke,despite information about the unequivocally negative health consequences of smoking.

The exact mechanisms of smoking-related vascular disease are not yet known. Smoking causes acute hemodynamic alterations such as increase in heart rate, systematic and coronary vascular resistance, myocardial contractility, and myocardial oxygen demand. These short-term effects could lower the ischemic threshold in smokers with coronary artery disease and contribute to the increased risk for acute cardiovascular events. Endothelial damage is thought to be an initiating event in atherosclerosis and early studies have demonstrated that long-term smoking has direct toxic effects with structural changes of human endothelial cells. Recent research has shown the importance of the functional role of the endothelium in regulating vascular

tone, platelet-endothelial interactions, leukocyte adhesion and smooth muscle cell proliferation via synthesis and release of a variety of substances such as nitric oxide.

There is strong evidence that smoking leads to endothelial dysfunction mainly by increased inactivation of nitric oxide by oxygen-derived free radicals. Smoking also increases oxidative modification of LDL and is associated with lower HDL plasma levels. Smoking induces a systemic inflammatory response with increased leukocyte count and elevation of the C-reactive protein level. Importantly, the prothrombotic effects of smoking have been repeatedly demonstrated to cause alterations in platelet function, imbalance of antithrombotic vs prothrombotic factors,and decrease of fibrinolytic activity.[61]When compared with non-smokers, boy and girl smokers showed significantly higher serum levels of total cholesterol, LDL-cholesterol, triglycerides and apolipoprotein B100, and significantly lower serum levels of HDL-cholesterol

Adolescent smokers tended to show a two-fold higher risk of altered lipid-lipoprotein levels than non-smokers.[62]

Alcohol consumption was positively and linearly associated with high density lipoprotein cholesterol (HDL-C) levels and negatively associated with both low density lipoprotein cholesterol (LDL-C) levels and the ratio of total cholesterol(TC)/HDL-C ($P<0.05$ $P<0.001$) among Japanese American males and Japanese American females and Native Japanese males. Current smoking habit was observed to be negatively associated with HDL-C levels and positively with TCHDL-C ratio and log TG levels (logarithmic transformation of triglyceride values) ($P<0.05$ to $P =0.001$) among all three groups Body mass index (BMI) was negatively associated with HDL-C levels and positively associated with log TG and TC/HDL-C

ratio among all three groups (P<0.05 to P<0.001). Moderate alcohol consumption was negatively associated with log TG levels among Japanese American males and females (P <0.05), whereas heavy alcohol consumption was positively associated with log TG levels in Native japanese males (P<0.001). Smoking was positively associated with TC and LDL-C levels (P <0.05) among Japanese American males, whereas a negative association (P<0.05) was observed in Native Japanese males.[63]

Thomas Heitzer and his associates demonstrate that cigarette smoking and hypercholesterolemia synergistically impair endothelial function and that their combined presence is associated with increased plasma levels of autoantibodies against oxidized LDL These observations raise the possibility that long-term smoking potentiates endothelial dysfunction in hypercholesterolemic patients by enhancing the oxidation of LDL.[64]Mean HDL cholesterol levels are lower in dyslipidemic children from households with smokers than in those without household smoke exposure. Passive smoking may worsen the risk profile for later atherosclerosis among high-risk youngpersons.[65]

The prevalence of smoking among males and females was 33.2% (N=150) and28.4% (N-108), respectively (mean cigarette consumption 13/day). As many as 349 males (77.2%) and 220 females (58,0%) reported consuming alcohol on a regular basis. The prevalence of low HDL-cholesterol (0.9 mmol/l) was 14.5% in males and 5.1% in females, and of high LDL-cholesterol levels (~4.1 mmol/l) in 11.1% of male and 5.5% of female participants. Smoking was related to higher triglyceride (-0.032), and lower HDL-cholesterol (p=0,037) serum levels. Total cholesterol, LDL-cholesterol, and the TC/HDL-cholesterol ratio were strongly related with the level of smoking (p 0.006,-0.008, and p-0.006 respectively).[66]

Craig W.Y and his collaborators from the foundation of blood research, scarborough analyzed 54 of published studies on cigarette smoking and lipid profile. In their study they found that over all smokers had a significant higher concentration of total cholesterol (3%) triglycerides (9.1%), VLDL cholesterol (10.4%) and LDL cholesterol (1.7%) and lower serum concentration of HDL cholesterol (-5.7%) compared with non smokers. They also found that a significant dose response effect was present in smokers. Non smokers, light smokers, moderate smokers, heavy smokers variations was, for total cholesterol (0,18,43 and 4.5% respectively), triglycerides (0,10,7,115 and 18% respectively), VLDL cholesterol (0,7.3,4.4 and 39% respectively), LDL cholesterol (0.-L1.1.4 and 11% respectively) HDL cholesterol (0,4.6.-6.3 and -8.9% respectively).

Smokers in general and female smokers in particular had decreased alpha tocopherol levels when compared with non smokers. Smokers had low HDL cholesterol but this difference was statistically significant in females. Regardless of sex in smokers there was positive correlation between alpha tocopherol and triglyceride levels.[67]

Kharb S, Singh GP studied changes in lipid peroxidation, vitamin E status and lipid profile due to smoking in healthy subjects, patients with acute myocardial infarction (MI), and in stabilized patients surviving MI A significant increase inmalondialdehyde (MDA) concentrations was observed in Ml patients, more than in smokers ($P<0.05$), as compared to control. The plasma vitamin E as well as the ratio of vitamin E lipids were significantly lower in Ml patients as compared to stable ischemic heart disease (IHD) patients and controls. Our data show that smoking is associated with lowered antioxidant status in MI.[68]

Tilwani R K and associates who studies total cholesterol, triglycerides, LDL,BLDL and HDL found that TG, LDL, VLDL and TC were significantly high, in smokers when compared to non smokers. Increasing progressively from light to heavy smokers, showed a direct relationship and an inverse dose relationship was found in HDL in smokers.[69]

A study of Khurana M and associates on lipid profile in cigarette smokers and tobacco chewers showed HDL cholesterol to be lower in smokers ($p<0.001$) as well as in tobacco chewers ($p<0,001$) than the controls. Both smokers and tobacco chewers had higher value of total cholesterol, low density lipoproteins cholesterol, very low density lipoproteins cholesterol and triglycerides as compared to non smokers, non tobacco chewers group. It was also noted smoking and tobacco chewing people have an equal and comparable adverse effect on lipid profile and therefore raising cardiovascular risk.[70]

Though different mode of addictions, smoking and tobacco chewing have an equal and comparable adverse effects on lipid profile and therefore raising cardiovascular risk in same proportion.

In a survey of a healthy population (n = 197). LDL cholesterol, plasma triglycerides and VLDL triglycerides were found to be substantially increased and plasma HDL cholesterol decreased in smokers. The lipid-associated atherogenic risk in smokers as assessed by the LDL/HDL ratio was significantly higher 2.89 (SD1.18, n-63)) than in non-smokers (2.38 (SD 0.98, n=86)$P<0.01$). The lower HDL level found in smokers was explained by a lower HDL-2 subfraction as determined by analytical ultracentrifugation HDL 26, 2a and 3a, measured by gradient gel electrophoresis, were all lower in the smokers but this was only significant for HDL

2a. Smoking had no effect on Lp(a) levels. HDL cholesterol and HDL-2 were strongly negatively correlated whereas LDL cholesterol and LDL/HDL ratio were strongly positively correlated with the plasma triglyceride concentration. There was a small but significant reduction in plasma CETP activity non-smokers 49% microliter (SD 17.n90), smokers 43% microliter (SD 17, n-66) P<0.05) but CETP activity was not correlated with any measure of HDL in this population. Smoking was found to bean important independent contributor to the variation in plasma triglyceride, HDL,HDL-2 and LDL/HDL ratio. After correcting for sex, age, BMI, alcohol consumption, oral contraceptive use and plasma triglycerides smoking was still found to be significantly associated with HDL and the LDL/HDL ratio Upon adjustment for covariant factors the mean differences between smokers and non-smokers for HDL cholesterol, HDL-2 and LDL/HDL were 0.15 mM 16 mg dl-1 and 0.39 respectively. There appeared to be important sex differences in the influence of smoking on plasma lipoproteins. In women the main impact of smoking was on triglyceride levels and they in turn affected LDL and HDL. In contrast, in men, smoking had little impact on triglycerides and affected HDL more directly. We conclude that smoking cigarettes has an important effect on plasma lipoprotein metabolism through multiplemechanisms.[71]

Tiwari AK and his associates studied the effect of cigarette smoking on serum total cholesterol and HDL cholesterol in normal subjects and coronary heart patients51 normal volunteers and 34 clinically established coronary heart disease patients were studied. 21 out of 51 normal and 16 out of 34 coronary heart disease were cigarette smokers. The cases were divided into two groups aged 20-40 years the younger age group and 41-6l years the older age group. TC and HDL cholesterol ofall causes where determined. The ratio of total cholesterol to HDL cholesterol was significantly higher in all normal and coronary heart diseases smokers. Hence, the

higher level of total cholesterol to high density lipoprotein cholesterol ratio approved toxic, one of the important parameter helps to ascertain the development of coronary heart diseases in cigarette smokers.[72]

Sinha AK and associates in view of controversies existing regarding the atherogenic potential of smoking conducted studies in 40 healthy group male cigarettes mokers and 40 age and weight matched male non smokers to find out the difference in serum lipid profile of both the groups. Subjected in both the groups were in the age range of 25-35 years having no history of alcohol abuse or disease like diabetes mellitus or obesity. The mean serum cholesterol (177.3432.5mg/dL.), LDL cholesterol (100.24310 mg/dL.) were significantly higher in smokers ($p<0.05$). whereas mean HDL cholesterol (43.245.8mg/dL.) was significantly lower ($p<0.05$) mean triglycerides (170.8.59.7mg/dL) was significantly higher in smokers than nonsmokers ($p<0.01$) in the fed state the total cholesterol level and triglyceride levels was increased by 10 4mg/dL and 51. Img/dl. respectivly in smokers where as the increase was 4.8mg/dl. and 24.3mg/dl. respectively in non smokers. There was less rise of HDL cholesterol (19mg/dl.) in smokers as compared to non smokers 3.4mg/dl in feed states.[73]

Concentrations of plasma lipoproteins in 10 men who were habitual smokers were monitored for six weeks after they stopped smoking and related to changes in diet and body weight. The energy intake increased by 10% (p less than 0.05) owing to higher consumption of carbohydrates and fat, and body weight increased by 2% (p less than 0.01). Plasma triglyceride, cholesterol, and low-density lipoprotein cholesterol concentrations did not change significantly. The most prominent finding was a rapid and pronounced increased in high-density lipoprotein concentrations.

From comparatively low values (mean 0.82 mmol/l) they rose by 29% (p less than0.01) within two weeks and remained at this value throughout the observation period. In three subjects who resumed smoking after the end of the study they again fell to initial values six weeks later. The initial increase in concentration could be accounted for mainly by an increase in the esterified fraction and only to a lesser extent in the free cholesterol fraction. The changes in concentrations were accompanied by similar but less pronounced rises in high-density lipoprotein phospholipid and in apolipoprotein Al concentrations (p less than 0.01), whereas high-density lipoprotein phospholipid and in apolipoprotein Al concentration (p less than 0.01), whereas high density lipoprotein triglyceride concentrations did not change significantly. These findings confirm and extend those of earlier cross-sectional studies which showed low concentrations of high-density lipoproteins in cigarette smokers, A significant correlation between the rise in high-density lipoprotein cholesterol concentrations and the increase in fat consumption after stopping smoking indicate that the changes in high-density lipoprotein concentrations may be partly due to nutritional factors.[74]

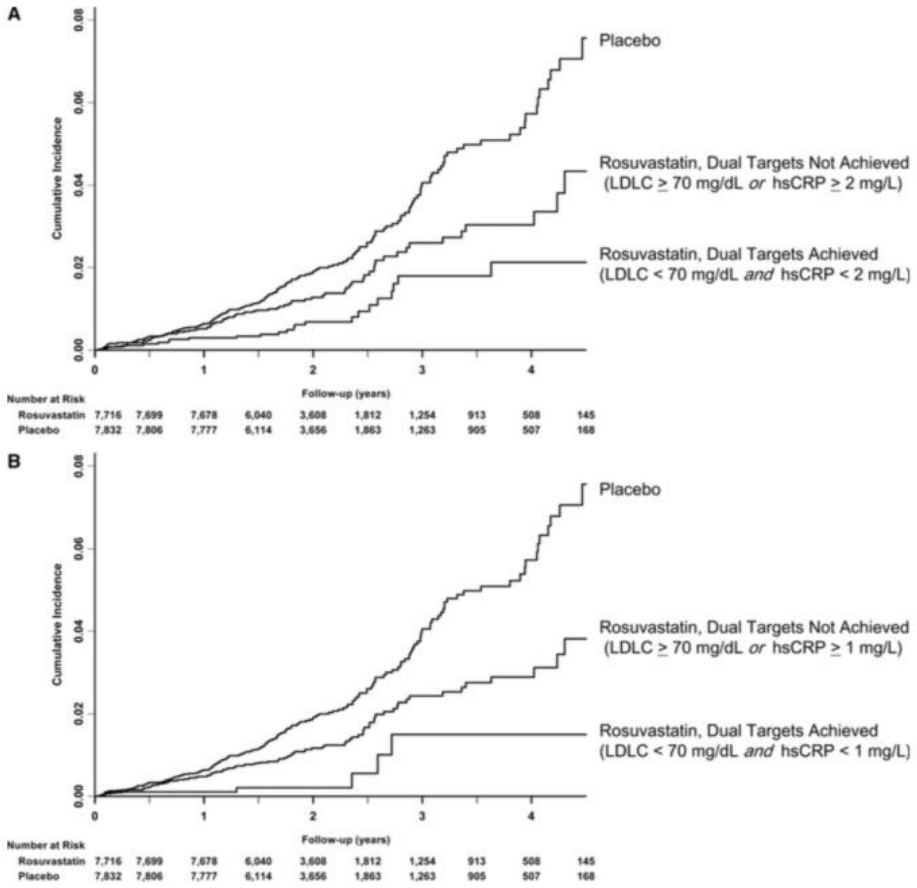
Siekmeier R, Walfroth P. Wieland H. Gross W. März W: Analyzed the susceptibility of low-density lipoproteins (LDL) to oxidation in 17 healthy smokers(43.3 +/- 16.8 pack-years) and 19 healthy nonsmokers, matched for age (smokers: 52+/- 7 years, nonsmokers: 53 +- 7 years), gender, and relative body mass.

Cholesterol, triglycerides, LDL cholesterol, HDL cholesterol, and apolipoprotein (apo) B were not different between smokers and nonsmokers, apo A-1was slightly lower in smokers (one-tailed P=0.066). To study whether LDL from smokers were prone to in vitro oxidation than LDL from nonsmokers, we measured

the time kinetics of diene formation and the production of malondialdehyde during oxidation of LDL in vitro.

In smokers and nonsmokers, respectively, the mean (+/-SD) lag times of diene formation were 111 +/- 26 and 100 +/- 27 min, the peak rates of diene formation(Vmax) were 5.99 +/- 2.34 and 6.34 +/- 2.30 mmol x min-1 x g.1, and the amounts of dienes produced during the propagation phase (dmax) were 250 +/- 264 and 248 +/56 mmol x g-1. Neither the malondialdehyde content of LDL (measured as thiobarbituric acid-reactive substances) before oxidation nor the amount of malondialdehyde generated during oxidation (smokers: 57.0 +/- 14 2 micromol x g.1.nonsmokers: 63.2 +/- 15.2 micromol x g-1 indicated any statistically significant effectof smoking. When nonsmokers and smokers were considered together, the amount of malondialdehyde generated during oxidation correlated with age (nonparametricts0.405), body mass index (2-0.573), and concentrations of apo B (ts 0.480) cholesterol (rs -0.448), triglycerides (rs = 0.436), and LDL cholesterol (rs 0.398).Our data show that smoking is not associated with increased oxidizability of LDL in healthy men and women at ages 42-63 years.[75]

The JUPITER trial demonstrated 44% reduction in the trial primary end point of all vascular events (P<0.00001), a 54% reduction in myocardial infarction (P<0.0002), a 48% reduction in stroke (P<0.002), a 46% reduction in need for arterial revascularization (P<0.001), and a 20% reduction in all cause mortality in patients treated with Rosuvastatin.



Cumulative incidence of cardiovascular events in JUPITER in the placebo and rosuvastatin groups according to whether or not reductions in both LDLC and hsCRP were achieved.

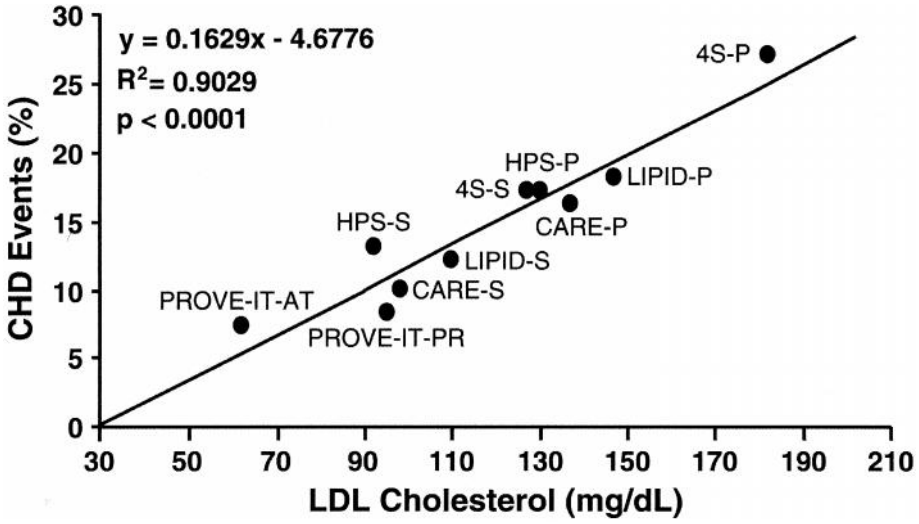
In the CARE trial, Pravastatin therapy lowered the mean LDL cholesterol level of 139 mg per deciliter by 32 percent and maintained mean levels of 97 to 98 mg per deciliter throughout the five-year follow-up. During follow-up, the LDL cholesterol level was 28 percent lower in the pravastatin group than in the placebo group, the total cholesterol level was 20 percent lower, the HDL cholesterol level was 5 percent higher, and the triglyceride level was 14 percent lower. Patients treated with pravastatin had a 24 percent lower incidence of the primary end point, fatal coronary heart disease or confirmed myocardial infarction, than patients in the placebo group.

Stroke, a specified end point in the CARE trial,was reduced significantly (by 31 percent) in the pravastatin group.

In the PROVE IT – TIMI Trial, among patients who have recently had an acute coronary syndrome, an intensive lipid- lowering statin regimen provides greater protection against death or major cardiovascular events than does a standard regimen. These findings indicate that such patients benefit from early and continued lowering of LDL cholesterol to levels substantially below current target levels.

In the REVERSAL Trial, baseline low-density lipoprotein cholesterol level (mean, 150.2 mg/dL in both treatment groups) was reduced to 110 mg/dL in the pravastatin group and to 79 mg/dL (in the atorvastatin group (P<.001). The primary end point (percentage change in atheroma volume) showed a significantly lower progression rate in the atorvastatin (intensive) group.

In the 4S Trial, over the 5.4 years median follow up period, simvastatin produced mean changes in TC, LDL & HDLcholesterol of -25%, -35%, and +8%, respectively. This 4S study shows that long term treatment with simvastatin is safe and improves survival in CHD patients.



A meta-analysis of all the major trials conducted so far shows that reducing the LDL-c levels below 70 mg/dL reduces the CHD events significantly.

Thus, while existing data offers some insights into fruitful interventions, there is a need to undertake well-designed, controlled, adequately powered, large- scale studies to bring more insights into the role of individual components of lifestyle changes in modifying cardiovascular risk factors and mortality.

All the studies done so far include a certain group of patients on whom interventions are done and/or studied. This study has been undertaken to study the changes in lipid profile in the patients attending OPD without any disease related exclusions. This study will allow us to understand the lipid changes in routine life i.e real time lipid changes.

METHODOLOGY

The present study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi on patients during the period of January 2017 to December 2017.

Study design:

This is a hospital based observational cross sectional study.

Study period and duration:

The present one year study was conducted during the period of January 2017 to December 2017.

Source of Data:

Patients attending OPD at the Department of Medicine at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi and having minimum 2 lipid profiles minimum 3 months apart.

Sample size and Sampling method:

200 SUBJECTS

Sample size was calculated by the following formula:

$n = 4 \times p \times q / d^2$

Where p= Prevalence of Hypercholesterolemia (50 %)

q= 100 - p d= absolute error (i.e 7)

Convenient sampling method.

All patients fulfilling the inclusion criteria were included in the study.

Inclusion Criteria:

All patients above the age of 18 years of either gender.

Exclusion Criteria:

Patients not giving consent for the study.

Procedure:

The study was approved by the Institutional Ethics Committee of Jawaharlal Nehru Medical College, Belagavi. Patients attending OPD at the Department of Medicineat KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi and having minimum 2 lipid profiles minimum 3 months apartwere evaluated. The selected patients were briefed about the nature of the study and a written informed consent was obtained (Annexure–I).

Demographic data like gender and age were collected along with relevant history and recorded on predesigned and pretested proforma (Annexure-II). A thorough clinical examination was conducted and the findings were also recorded.

All patient relevant data were noted. History of preexisting diseases like Diabetes Mellitus, Hypertension, Stroke, Ischemic Heart Disease, and previous admission to hospital and present symptomatology was listed and detailed physical examination was done. Details of medical interventions were recorded.

Definitions:

- Knowledge about Dyslipidemia: During the past 1 year,has any health professional told you that you have dyslipidemia.
- Light physical activity: Causing no sweating or shortness of breath.
- Moderate to vigorous intensity physical activity: Causing some sweating or shortness of breath.
- Dietary modification: Reduction of calorie intake and fatty foods.
- Habitual Drinker: >1 drink per day.
- Non Habitual Drinker: 6 drinks /week to 1 drink /month.
- Lifestyle Modifications: Physical Activity, cessation of smoking, alcohol.

Statistical analysis:

The data obtained was tabulated on Excel spread sheet (Annexure IV).The data wasanalysed using EPI info (version 7.2). The qualitative variables were expressed in terms of percentages. The quantative variables were both categorised and expressed in terms of percentages or in terms of mean and standard deviations. Difference between two proportions was analysed using chi square or fisher exact test. Difference between the two means was tested using student t test. All tables were graphically represented. All analysis was 2 tailed and the significance level was set at 0.05.

RESULTS

We included 200 study subjects in our study.

Table 1: Distribution of study subjects based on the age group

Age group	Frequency	Percentage
18 to 20	4	2
20 to 30	20	10
30 to 40	16	8
40 to 50	37	18.50
50 to 60	57	28.50
60 to 70	51	25.50
70 to 80	14	7
80 to 90	1	0.50
Total	200	100
Mean	51.24	
SD	14.72	

The mean age of the study subjects was 51.24 ± 14.72 years. Most common age group was 50 to 60 years followed by 60 to 70 years and 40 to 50 years.

Table 1: Distribution of study subjects based on the age group

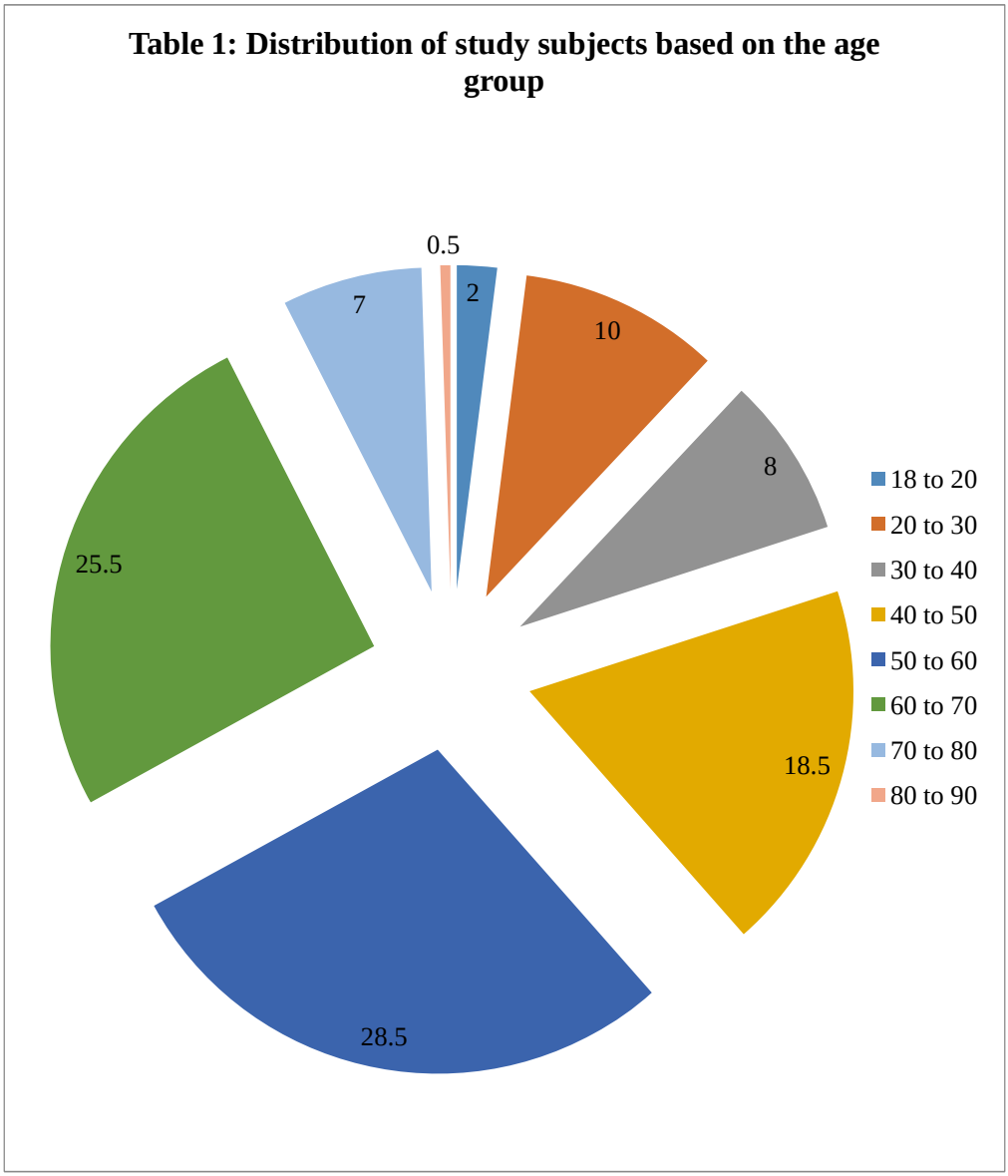


Table 2: Distribution of study subjects based on the gender

Gender	Frequency	Percentage
Female	84	42.00
Male	116	58.00
Total	200	100

Majority of the study subjects were males (58%).

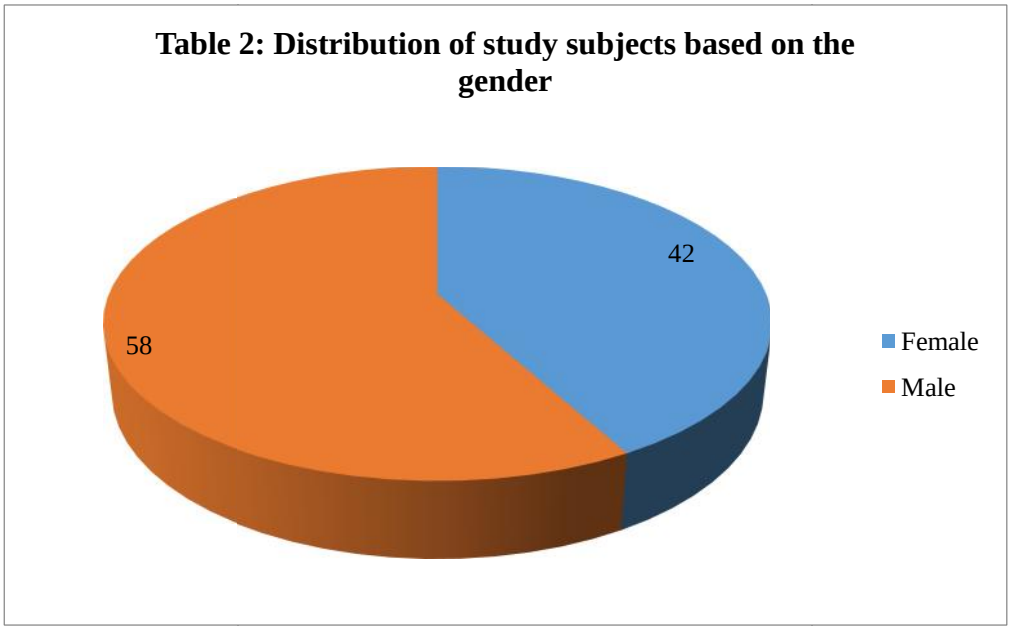


Table 3: Distribution of study subjects based on the past history

Past history	Males (n=116)		Females (n=84)		Total (n=200)		P value
	No[r]	%	No[r]	%	No[r]	%	
Diabetes	52	44.83	37	44.05	89	44.50	0.9127
Hypertension	22	18.97	16	19.05	38	19.00	0.9883
IHD	27	23.27	11	13.09	38	19.00	0.0710
Hypothyroidism	7	6.03	12	14.29	19	9.50	0.0495
Dyslipidemia	23	19.83	28	33.33	51	25.50	0.0350
Family history of dyslipidemia	12	10.34	8	9.52	20	10.00	0.3412

In our study, 44.50% of them had past history of diabetes, 19% had hypertension, 5% had IHD, 9.50% had hypothyroidism and 25.50% had dyslipidemia. We found a significant difference between the proportions of hypothyroidism and dyslipidemia among the gender.

Chart 3: Distribution of study subjects based on the past history

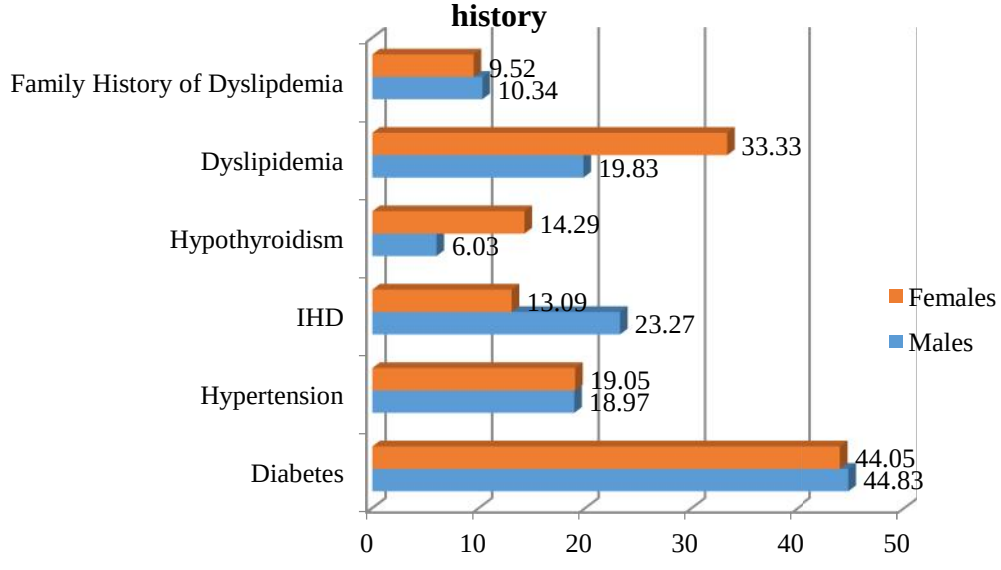


Table 4: Distribution of study subjects based on the personal history

Personal history	Males (n=116)		Females (n=84)		Total (n=200)		P value
	No[r]	%	No[r]	%	No[r]	%	
Tobacco use	42	36.21	4	4.76	46	23.00	<0.001
Alcohol	59	50.86	5	5.95	64	32.00	<0.001
Smoker	41	35.34	7	8.33	48	19.00	<0.001
Physical activity level							
Low	80	68.96	38	45.23	118	59	0.0032
Moderate	24	20.68	30	35.71	54	27	
High	12	10.36	16	19.06	28	14	

The proportions of tobacco use, alcohol and smoking were significantly higher among the males when compared to females. Over all, the prevalence of tobacco use in our study was 23%, alcohol use was 32% and 19% of them were smokers. Majority of the study subjects were having low or sedentary physical activity levels in our study.

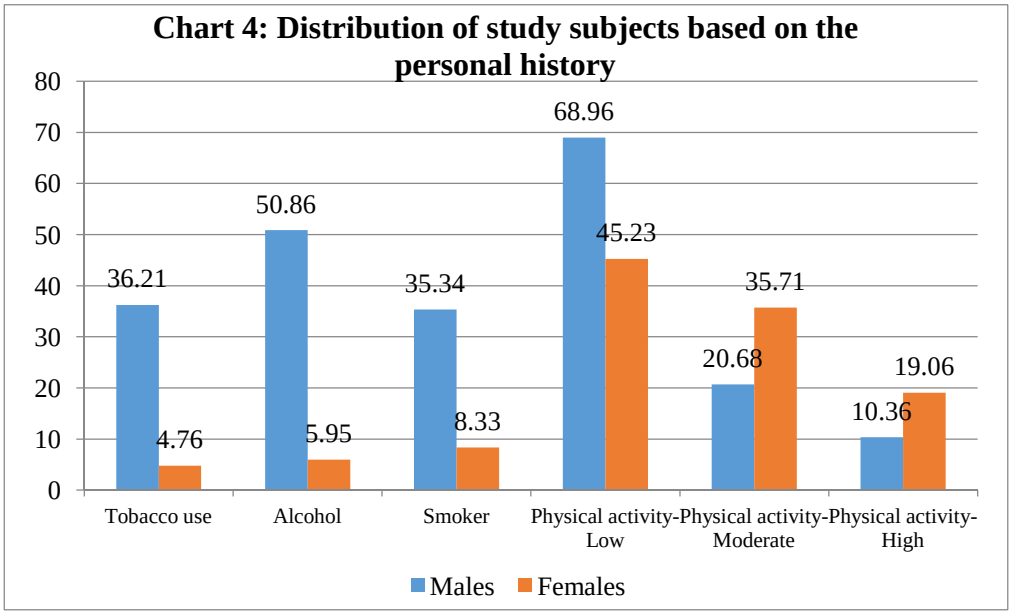


Table 5: Distribution of study subjects based on the body mass index

Body mass index	Frequency	Percentage
<18.5	44	22.00
18.5 to 25.00	102	51.00
25.00 to 30.00	45	22.50
>30.00	9	4.50
Total	200	100
Mean	21.94	
SD	4.40	

About 22% of our study subjects were underweight, 51% were normal, 22.50% were overweight and 4.50% were obese in our study.

Chart 5: Distribution of study subjects based on the body mass index

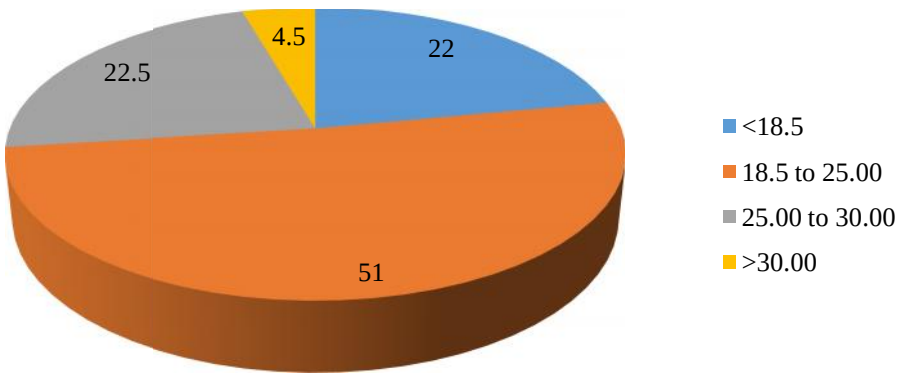


Table 6: Distribution of study subjects based on the waist hip ratio

Waist to hip ratio	Frequency	Percentage
Normal	108	54.00
Abnormal	92	46.00
Total	200	100
Mean	0.92	
SD	0.10	

Based on the waist hip ratio, 46% were having abnormal waist: hip ratio i.e. 46% were having central obesity.

Chart 6: Distribution of study subjects based on the waist hip ratio

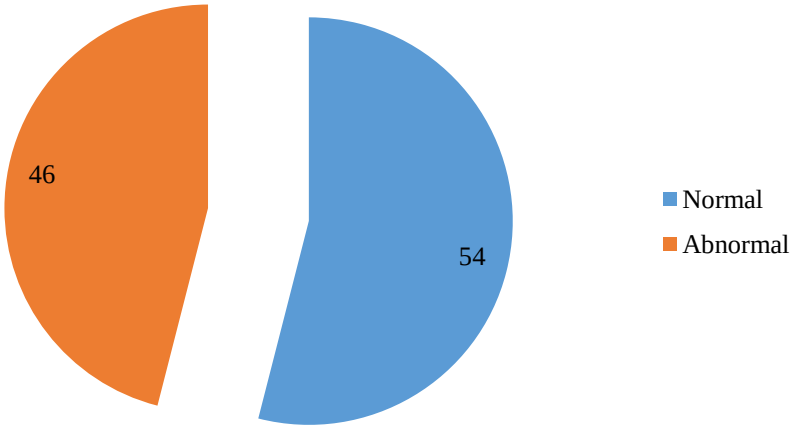


Table 7a: Distribution of study subjects based on intervention in the period between first and second lipid profile

Intervention seeked	Frequency	Percentage
Use of statins	106	52.94
Discontinuation of statins	94	47.06
Lifestyle modification	60	30.00
Knowledge about dyslipidemia	35	17.50
Controlled sugars	26	27.66
Controlled blood pressure	16	42.11
Treatment of hypothyroidism	16	84.21
Diet change	55	27.50

In our study, 52.94% of the people having dyslipidemia used statins but the rest discontinued their statins (47.06%). About 30% of the subjects had lifestyle modification and 17.50% had knowledge about dyslipidemia. Among the diabetics, 27.66% had controlled their sugar levels in past 3 months and among the hypertensives, 42.11% had controlled their blood pressures in past 3 months. About 84.21% who had elevated TSH levels were started on treatment of hypothyroidism. About 27.50% underwent dietary changes.

Chart 7a: Distribution of study subjects based on intervention in the period between first and second lipid profile

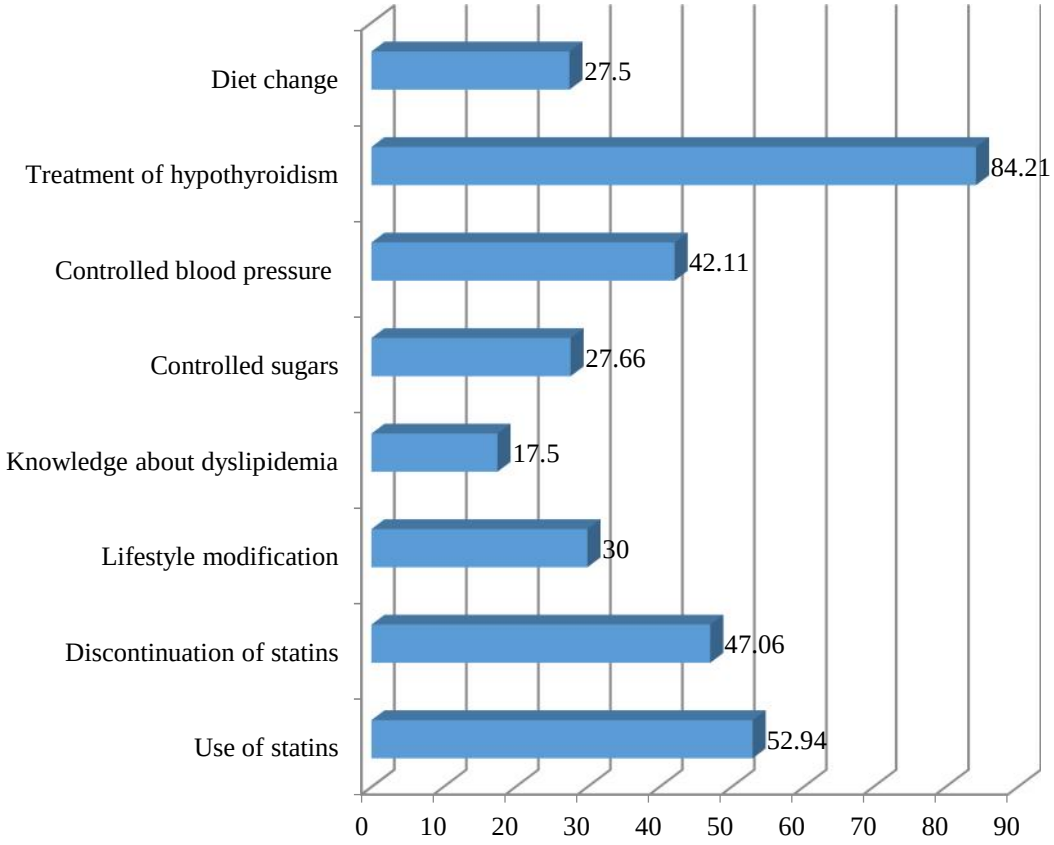


Table 7b: Distribution of study subjects based on the reason for discontinuation of statins

Intervention seeked	Frequency	Percentage
Discontinuation of statins	94	
Intolerance	69	73.91
Ignorance	25	26.08

Among the cases that discontinued the statins, the main reason was intolerance to statins (73.91%) followed by ignorance (26.08%).

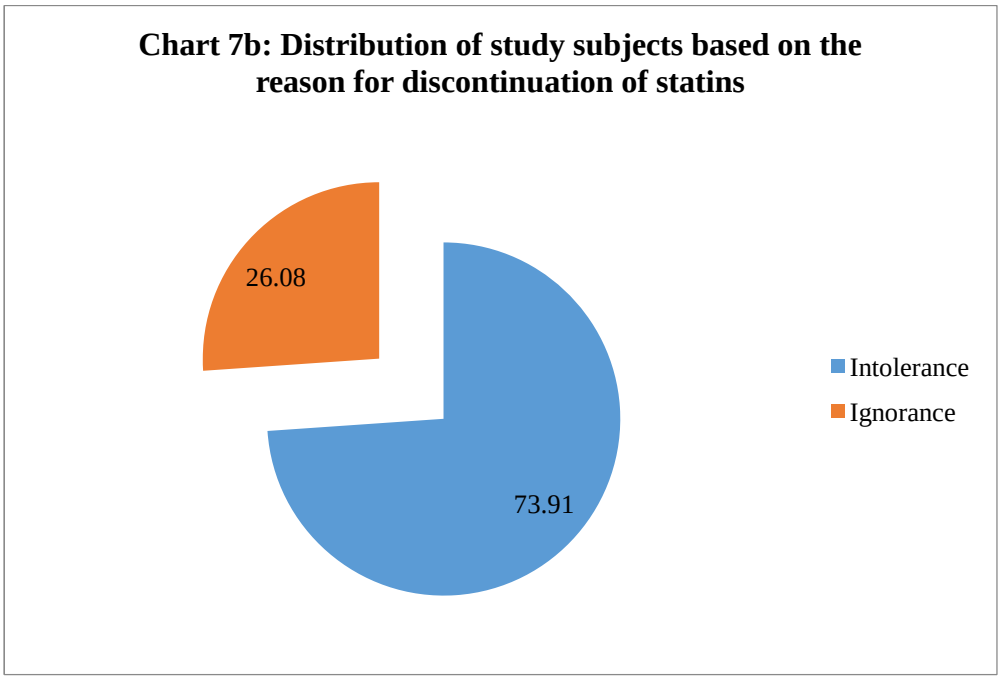


Table 8: Change in total cholesterol levels in the different interventions studied.

Intervention seeked	1st lipid profile		2nd lipid profile		P value
	Mean	SD	Mean	SD	
Use of statins	190.12	43.12	165.11	46.05	0.0442
Discontinuation of statins	190.25	45.12	214.12	42.13	0.0497
Lifestyle modification	194.68	48.08	175.52	49.66	0.0338
Knowledge about dyslipidemia	194.13	43.23	172.13	34.12	0.0428
Controlled sugars	182.54	45.41	155.04	47.80	0.0392
Controlled blood pressure	193.88	61.98	152.13	42.72	0.0342
Treatment of hypothyroidism	195.38	51.99	170.19	27.12	0.0962
Diet change	203.45	32.14	165.10	22.13	<0.001

Between the 1st and 2nd lipid profile, the total cholesterol levels decreased significantly with lifestyle modification, knowledge about dyslipidemia, controlled sugars, controlled blood pressure and dietary changes. But, in case of discontinuation of statins, the total cholesterol level significantly increased. Use of statins did not affect the decrease in the total cholesterol levels. And treatment of hypothyroidism did not find any significant decrease in total cholesterol levels.

Chart 8: Change in total cholesterol levels in the different interventions studied

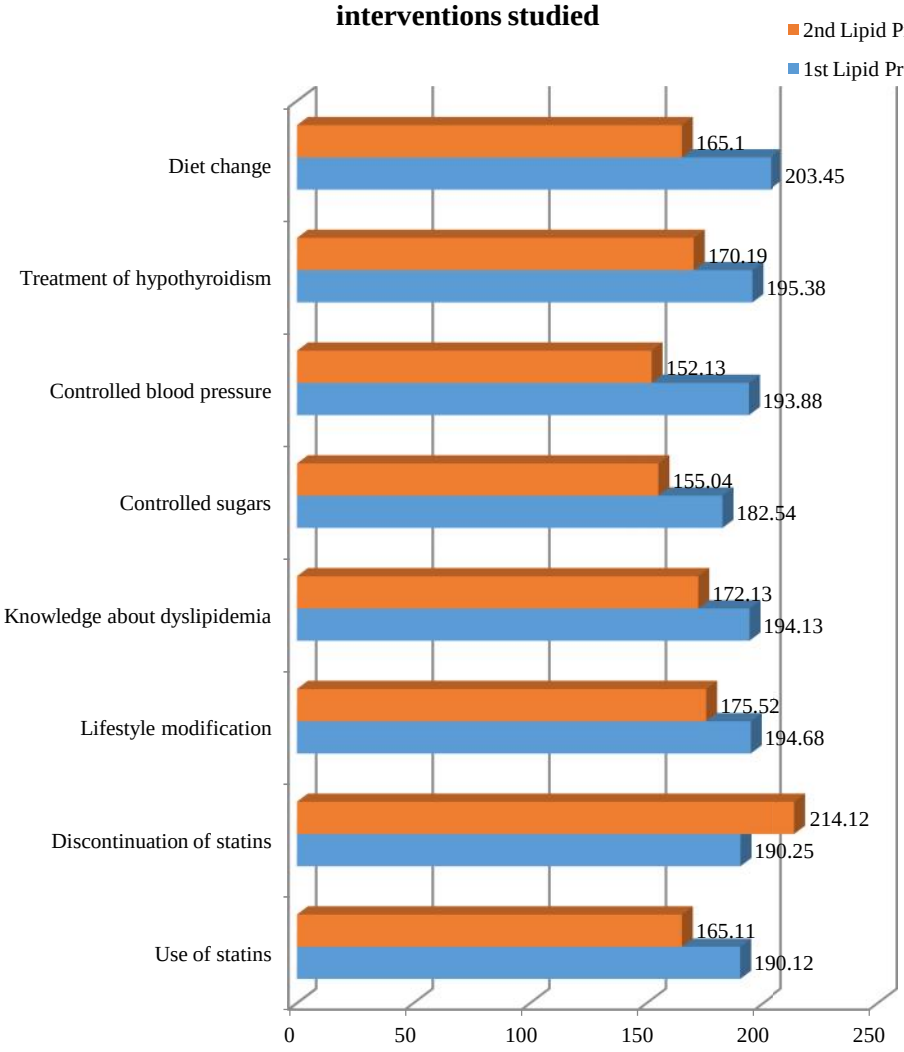


Table 9: Change in LDL levels in the different interventions studied

Intervention seeked	1st lipid profile		2nd lipid profile		P value
	Mean	SD	Mean	SD	
Use of statins	123.45	46.23	100.93	32.12	0.0425
Discontinuation of statins	116.79	31.16	134.12	32.14	0.0478
Lifestyle modification	119.12	41.88	103.33	42.33	0.0421
Knowledge about dyslipidemia	119.23	33.15	101.19	32.16	0.0475
Controlled sugars	116.22	41.69	105.46	41.69	0.3545
Controlled blood pressure	124.31	50.12	103.45	43.76	0.2195
Treatment of hypothyroidism	117.18	47.70	101.13	30.49	0.2658
Diet change	134.45	34.51	102.34	48.71	0.0212

The LDL levels significantly decreased in the patients with lifestyle modification, knowledge about dyslipidemia and dietary changes. Discontinuation of statins increased the levels significantly. But, use of statins, controlled sugars, controlled blood pressure and treatment of hypothyroidism did not yield any significant results.

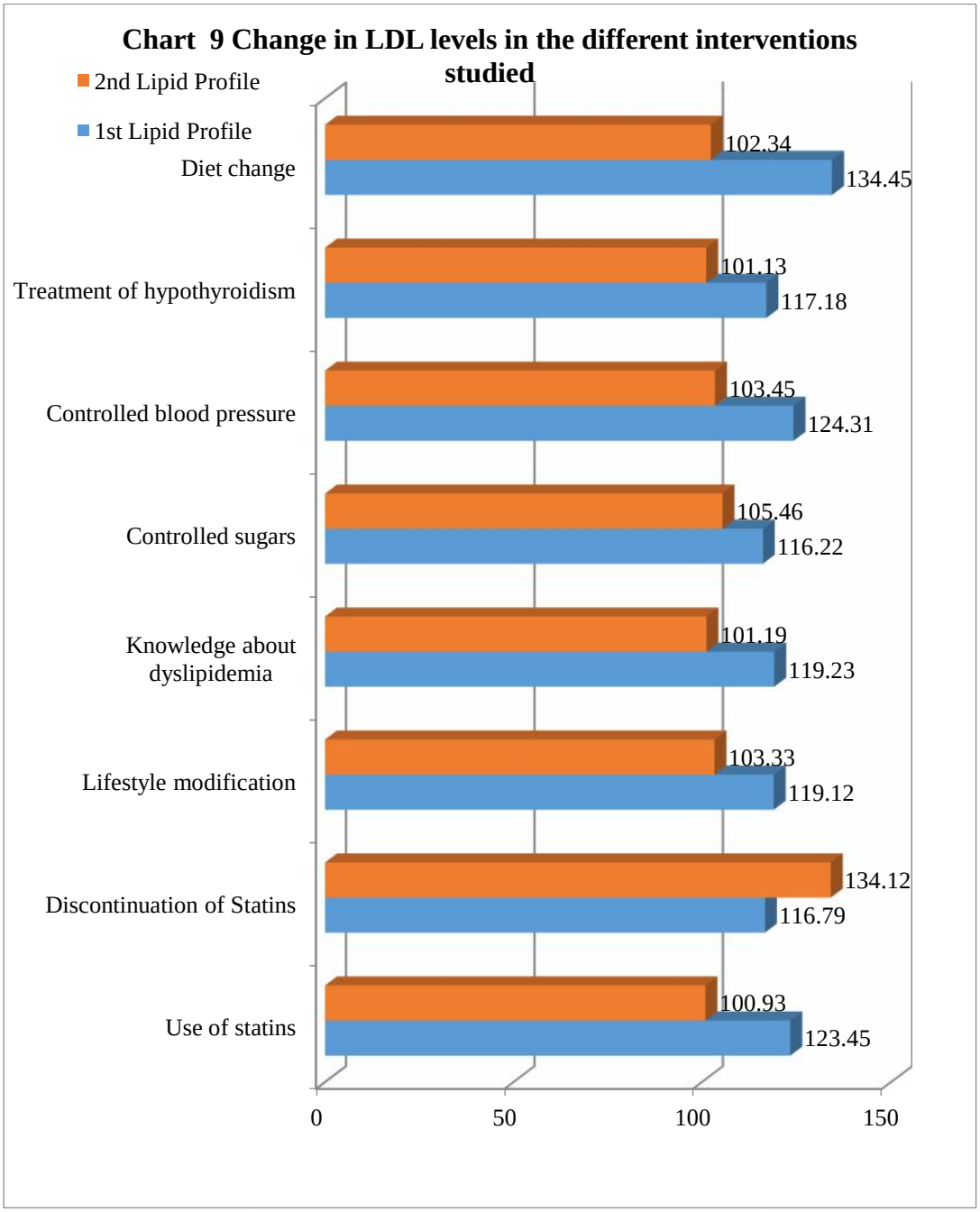


Chart 9 Change in LDL levels in the different interventions studied
2nd Lipid Profile
1st Lipid Profile
Diet change
102.34
134.45
Treatment of hypothyroidism
101.13
117.18
Controlled blood pressure
103.45
124.31
Controlled sugars
105.46
116.22
Knowledge about dyslipidemia
101.19
119.23
Lifestyle modification
103.33
119.12
Discontinuation of Statins
134.12
116.79
Use of statins
100.93
123.45
0
50
100
150

Table 10: Change in HDL levels in the different interventions studied

Intervention seeked	1st lipid profile		2nd lipid profile		P value
	Mean	SD	Mean	SD	
Use of statins	33.96	10.38	40.23	11.52	0.0450
Discontinuation of statins	33.78	10.12	28.12	9.28	0.0369
Lifestyle modification	32.45	11.16	39.43	11.40	0.0271
Knowledge about dyslipidemia	31.23	12.34	37.19	11.56	0.0125
Controlled sugars	33.73	13.49	38.27	16.15	0.3950
Controlled blood pressure	32.45	9.67	39.10	9.72	0.0618
Treatment of hypothyroidism	34.75	11.74	37.13	10.07	0.5429
Diet change	34.12	10.78	37.12	13.78	0.4479

The HDL levels significantly increased with interventions like lifestyle modification and knowledge about dyslipidemia and use of statins and significantly increased with discontinuation of statins. But there is no significant difference in the HDL levels from the 1st and 2nd lipid profile in case of use of statins, controlled sugars, controlled blood pressures, treatment of hypothyroidism and dietary changes.

Chart 10: Change in HDL levels in the different interventions studied

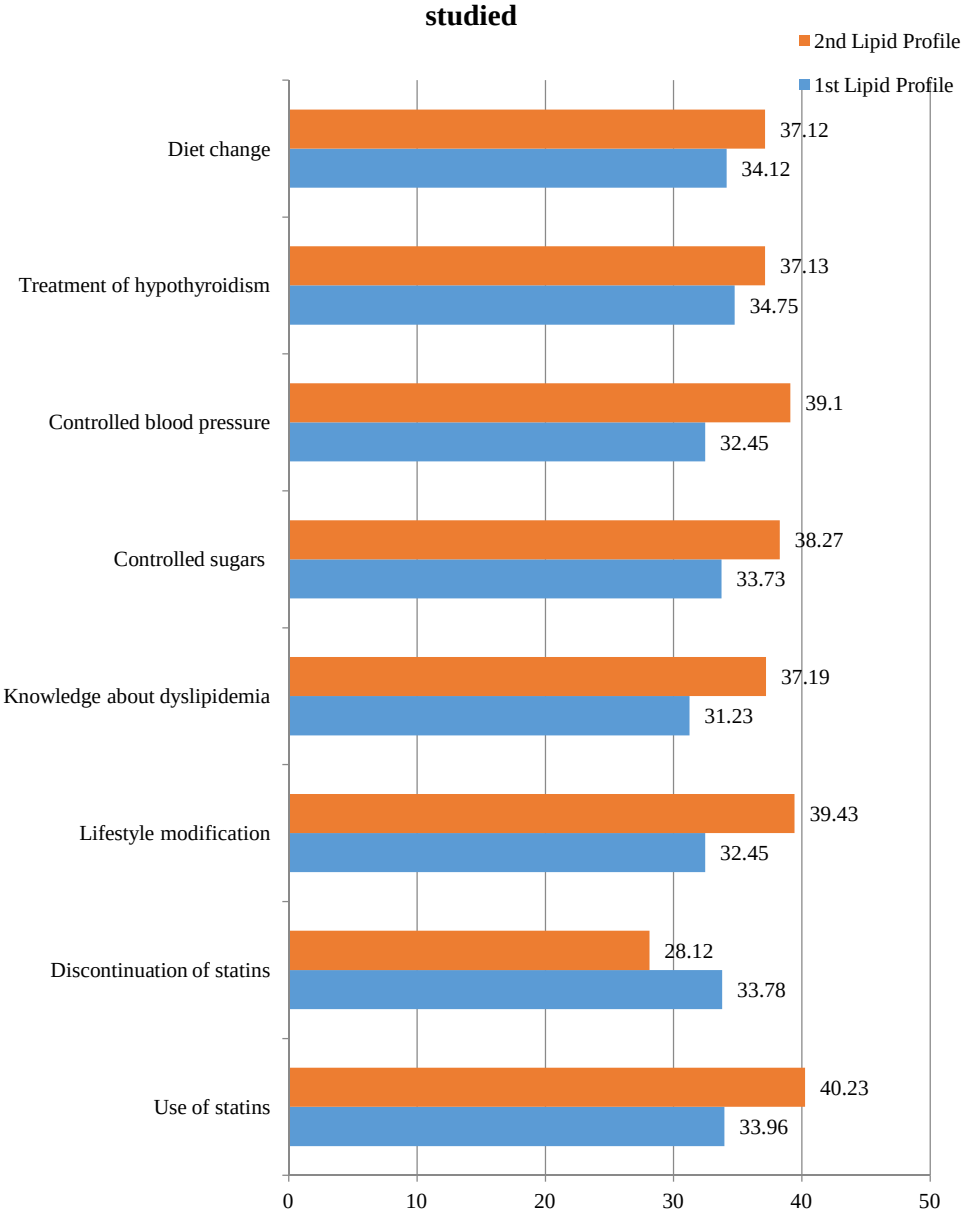


Table 11: Change in TG's levels in the different interventions studied

Intervention seeked	1st lipid profile		2nd lipid profile		P value
	Mean	SD	Mean	SD	
Use of statins	218.89	102.34	163.12	98.12	0.0460
Discontinuation of statins	192.13	109.23	239.34	112.34	0.1237
Lifestyle modification	191.12	132.96	176.11	101.93	0.7226
Knowledge about dyslipidemia	201.25	102.34	178.34	117.23	0.3357
Controlled sugars	220.27	155.04	165.12	110.12	0.0437
Controlled blood pressure	223.12	132.14	167.12	109.34	0.2027
Treatment of hypothyroidism	236.38	155.79	166.19	134.60	0.1821
Diet change	205.12	117.12	159.12	108.12	0.0440

The changes in triglyceride levels were significantly noted in controlled sugars and dietary changes. But in case of use of statins, discontinuation of statins, lifestyle modification, knowledge about dyslipidemia, treatment of hypothyroidism and controlled blood pressures there was no significant difference.

Chart 11: Change in TG's levels in the different interventions studied

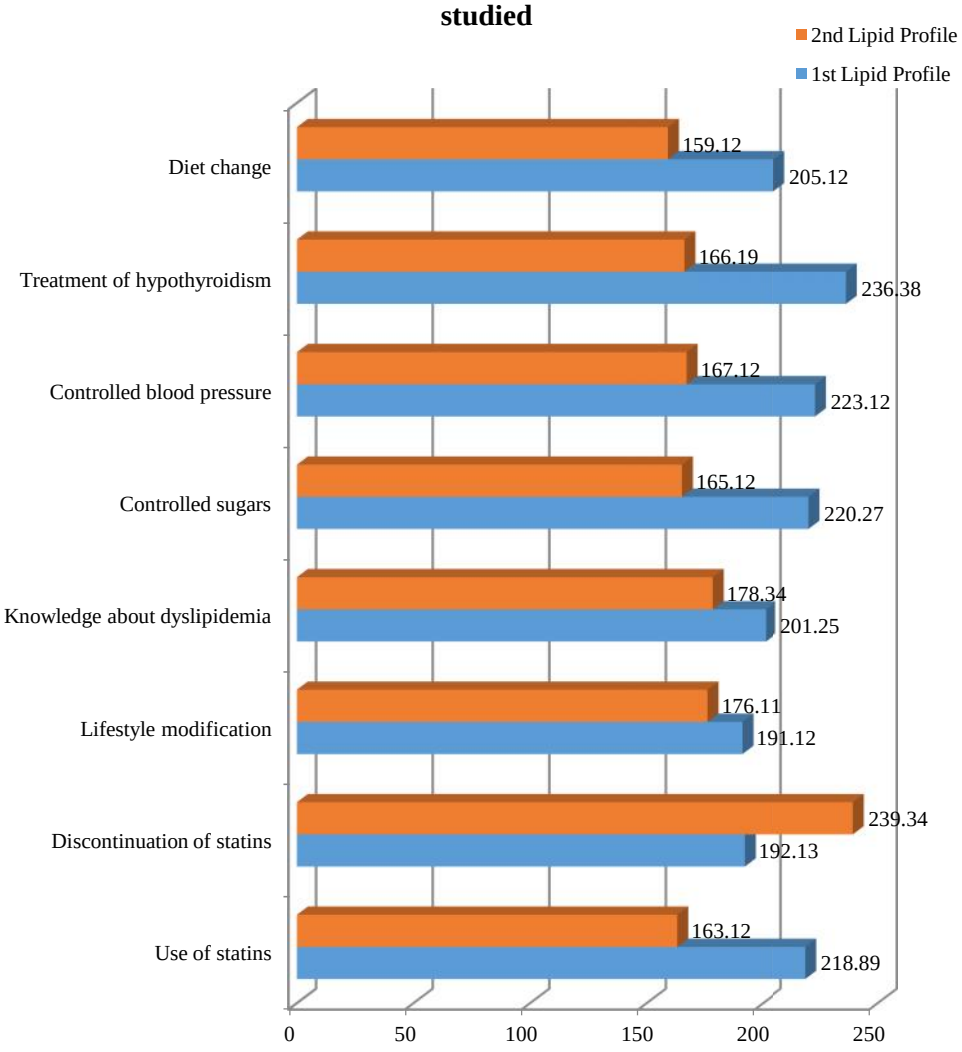


Table 12: Change in Total cholesterol levels in the different drugs used for dyslipidemia

Intervention seeked	1st lipid profile		2nd lipid profile		P value
	Mean	SD	Mean	SD	
Rosuvastatin 10mg	181.45	12.37	167.37	11.56	<0.001
Atorva 40mg	181.56	11.67	168.12	12.89	<0.001
Atorva 20mg	182.67	13.23	170.56	11.45	0.0007
Rosuva 5mg	181.38	11.28	172.33	14.23	0.0124
Atorva 10mg	182.32	12.32	178.12	13.34	0.2334

Upon detailed analysis, we found that there was significant decrease in the total cholesterol levels of 1st and 2nd reports who had received Rosuva 10mg, Atorva 40mg, Atorva 20mg and Rosuva 5mg but there was no significant difference in cases who had taken Atorva 10mg.

Chart 12: Change in Total cholesterol levels in the different drugs used for dyslipidemia

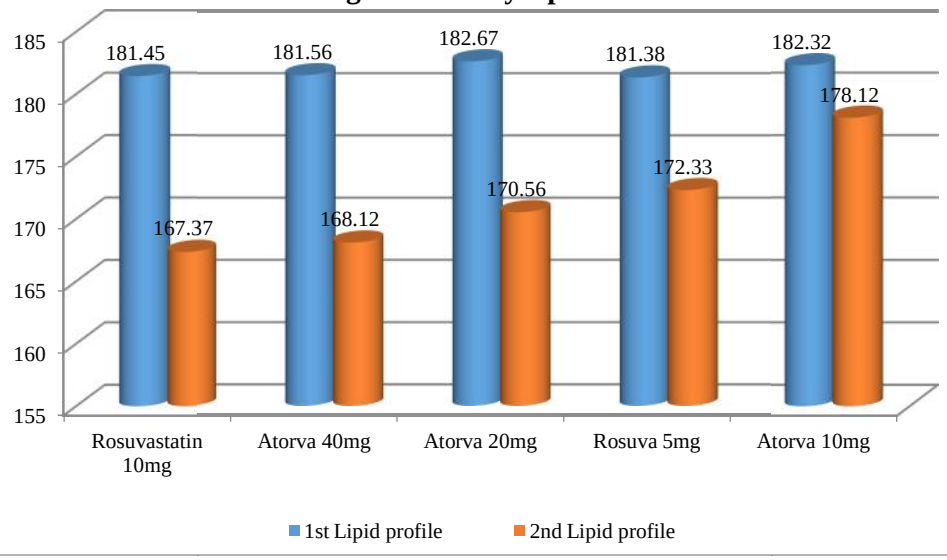


Table 13: Change in LDL levels in the different drugs used for dyslipidemia

Intervention seeked	1st lipid profile		2nd lipid profile		P value	% Change
	Mean	SD	Mean	SD		
Rosuvastatin 10mg	146.78	9.06	111.78	8.87	0.0455	23.84
Atorva 40mg	147.56	9.82	110.97	9.02	0.0131	24.79
Atorva 20mg	147.12	8.12	113.78	8.34	0.1420	22.66
Rosuva 5mg	145.78	8.76	110.45	8.89	0.0387	24.23
Atorva 10mg	146.67	8.92	111.32	9.01	0.0328	24.10

When the LDL levels were assessed, there was significant decrease in LDL levels in patients who received Rosuva 10mg, Atorva 40 mg, Atorva 10 mg and Rosuva 5mg but there was no significant decrease in case of Atorva 20 mg.

Chart 13: Change in LDL levels in the different drugs used for dyslipidemia

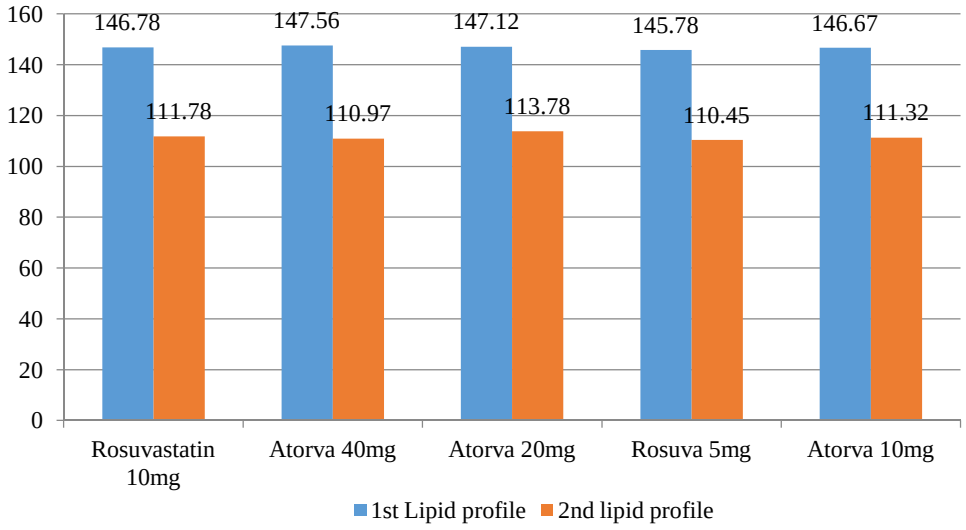


Table 14: Change in HDL levels in the different drugs used for dyslipidemia

Intervention seeked	1st lipid profile		2nd lipid profile		P value
	Mean	SD	Mean	SD	
Rosuvastatin 10mg	33.23	2.34	34.67	3.78	0.0964
Atorva 40mg	34.10	3.47	35.69	4.55	0.1530
Atorva 20mg	33.45	3.12	35.89	4.34	0.0214
Rosuva 5mg	34.23	2.69	35.45	4.23	0.2215
Atorva 10mg	34.78	3.42	35.23	4.76	0.6919

When the HDL levels and the drugs were assessed, there was significant increase the levels only in case of patients who used Atorva 20mg.

Chart 14: Change in HDL levels in the different drugs used for dyslipidemia

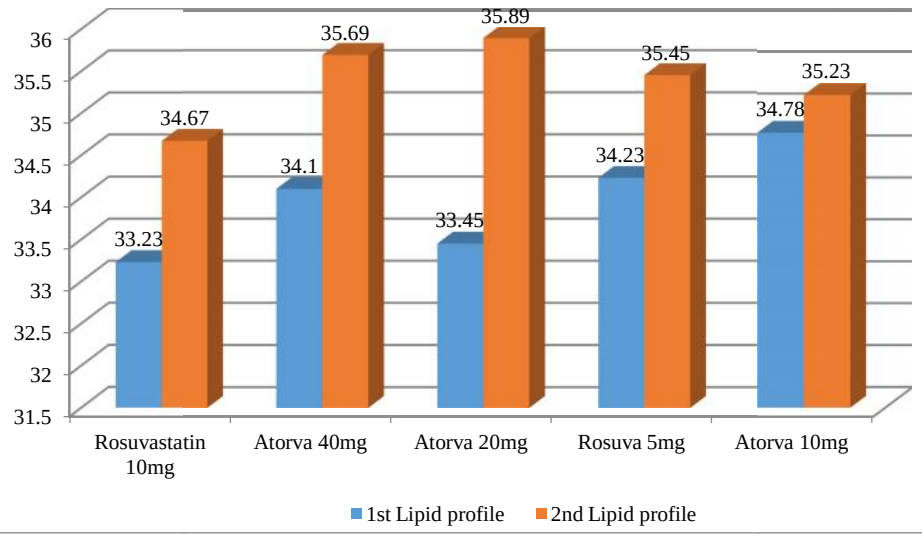


Table 15: Change in TG's levels in the different drugs used for dyslipidemia

Intervention seeked	1st lipid profile		2nd lipid profile		P value
	Mean	SD	Mean	SD	
Rosuvastatin 10mg	204.67	11.78	178.60	10.77	<0.001
Atorva 40mg	203.86	12.77	181.79	11.98	<0.001
Atorva 20mg	205.67	13.98	184.97	13.98	<0.001
Rosuva 5mg	204.56	12.89	186.96	12.67	<0.001
Atorva 10mg	205.78	11.98	191.69	12.97	<0.001

Upon detailed analysis, the triglyceride levels were significantly decreased in the patients who used Rosuva 10mg, Atorva 40mg, Atorva 20mg, Rosuva 5mg and Atorva 10mg.

Chart 15: Change in TG's levels in the different drugs used for dyslipidemia

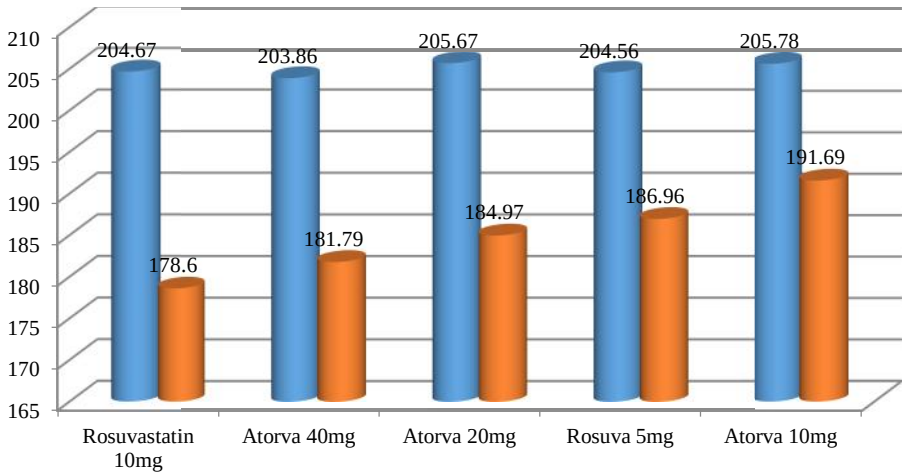


Table 16: Initial Lipid profile in patients with family history of dyslipidemia, abnormal waist hip ratio and ischemic heart disease

Lipid parameters	Family history of dyslipidemia		Abnormal waist hip ratio		Ischemic heart disease	
	Mean	SD	Mean	SD	Mean	SD
Total cholesterol	221.52	49.66	231.52	34.56	255.57	35.12
LDL cholesterol	153.67	45.17	133.78	36.78	171.34	32.45
HDL cholesterol	30.56	3.32	31.45	3.45	28.32	4.56
Triglycerides	274.92	89.78	251.38	85.34	256.34	82.34

The total cholesterol levels, LDL cholesterol, HDL cholesterol and triglycerides were 221.52 ± 49.66, 153.67 ± 45.17, 30.56 ± 3.32 and 274.92 ± 89.78 in patients with family history of dyslipidemia. The total cholesterol levels, LDL cholesterol, HDL cholesterol and triglycerides were 231.52 ± 34.56, 133.78 ± 36.78, 31.45 ± 3.45 and 251.38 ± 85.34 in patients with abnormal waist hip ratio. The total cholesterol levels, LDL cholesterol, HDL cholesterol and triglycerides were 255.57 ± 35.12, 171.34 ± 32.45, 28.32 ± 4.56 and 256.34 ± 82.34 in patients with ischemic heart disease.

Chart 16: Lipid profile in patients with family history of dyslipidemia, abnormal waist hip ratio and ischemic heart disease

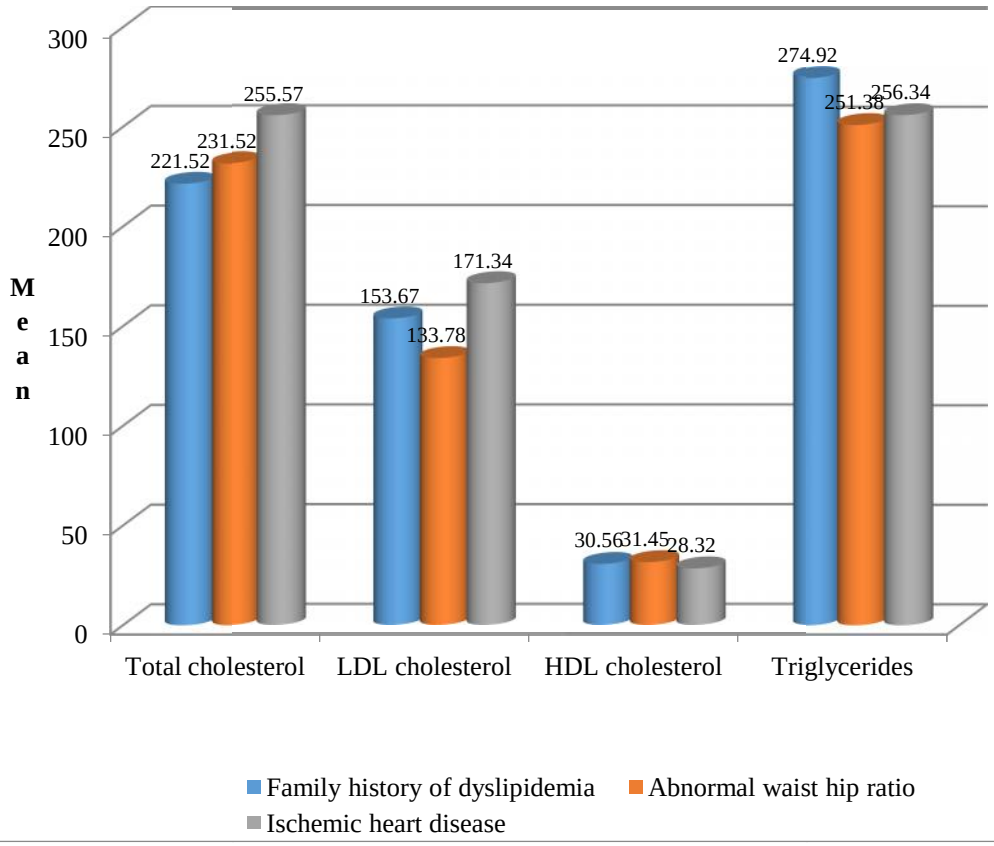


Table 17: Lipid profile in diabetics and non diabetics

Lipid profile	Diabetics (n=89)		Non diabetics (n=111)		P value	% Change
	Mean	SD	Mean	SD		
Total cholesterol	192.72	43.21	164.89	41.43	0.0449	
LDL cholesterol	130.67	42.34	101.56	43.76	0.0390	22.27
HDL cholesterol	34.82	12.76	36.56	10.34	0.6384	4.75
Triglycerides	234.87	140.34	156.12	102.34	0.0465	33.52

We found the total cholesterol levels, LDL cholesterol and triglycerides to be significantly higher in diabetics when compared to non diabetics. ($p<0.05$) But, the HDL cholesterol levels were not associated significantly with the diabetic status of the patients. ($p>0.05$)

Chart 17: Lipid profile in diabetics and non diabetics

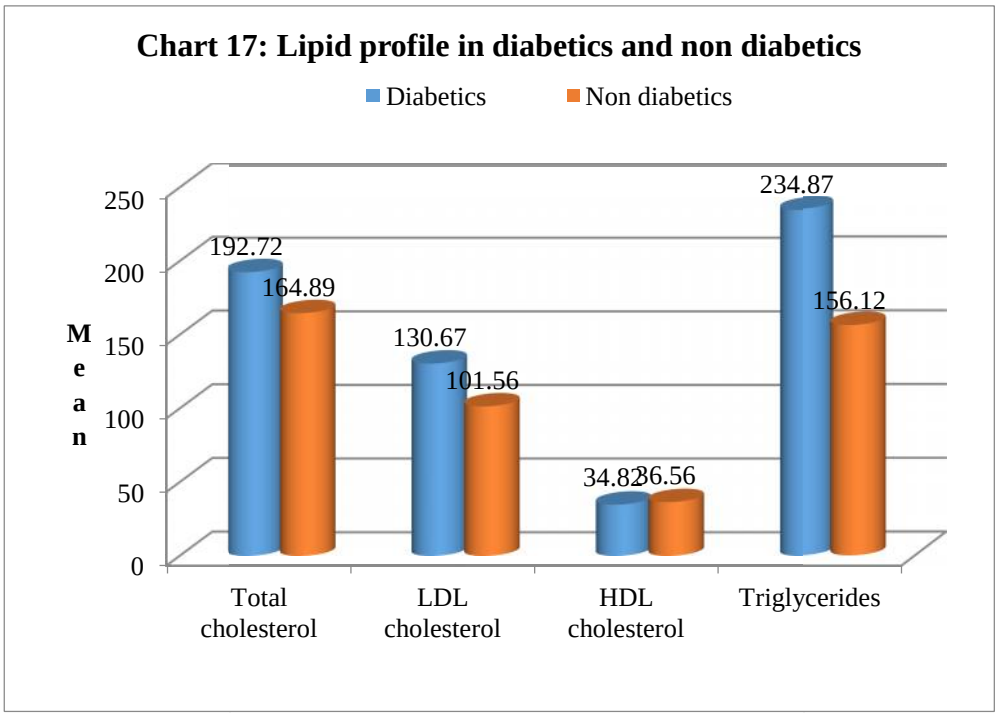


Table 18: Lipid profile based on physical activity

Lipid profile	Moderate to vigorous (n=186)		Sedentary (n=14)		P value	% Change
	Mean	SD	Mean	SD		
Total cholesterol	162.56	39.12	195.16	38.56	0.0115	
LDL cholesterol	103.33	34.56	134.56	36.45	0.0087	23.20
HDL cholesterol	37.45	12.32	32.76	10.67	0.2059	12.52
Triglycerides	167.12	98.76	231.45	101.23	0.0485	27.79

We found the total cholesterol levels, LDL cholesterol and triglycerides to be significantly higher in sedentary patients when compared to moderate to vigorous physical activity patients. ($p<0.05$) But, the HDL cholesterol levels were not associated significantly with the physical activity status of the patients. ($p>0.05$)

Chart 18: Lipid profile based on physical activity

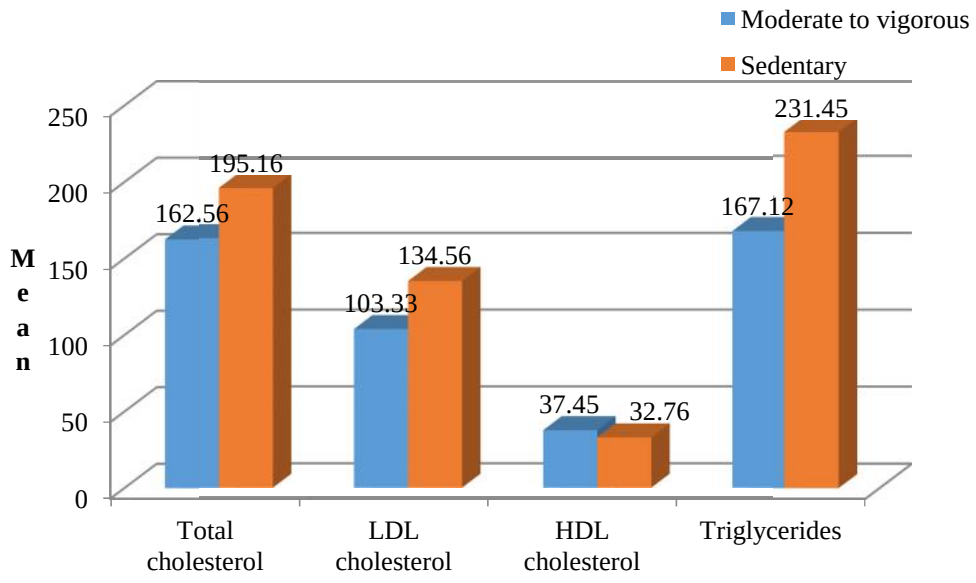


Table 19: Lipid profile based on smoking status

Lipid profile	Smoker (n=48)		Non smoker (n=152)		P value	% Change
	Mean	SD	Mean	SD		
Total cholesterol	241.45	95.45	178.23	94.56	0.0420	
LDL cholesterol	145.16	34.52	104.78	32.45	0.0004	27.81
HDL cholesterol	33.78	8.92	37.12	9.31	0.2539	9
Triglycerides	222.34	99.02	171.23	101.23	0.1148	22.98

We found the total cholesterol levels and LDL cholesterol to be significantly higher in smokers when compared to non smoker patients. ($p<0.05$) But, the HDL cholesterol and triglycerides levels were not associated significantly with the smoking status of the patients. ($p>0.05$)

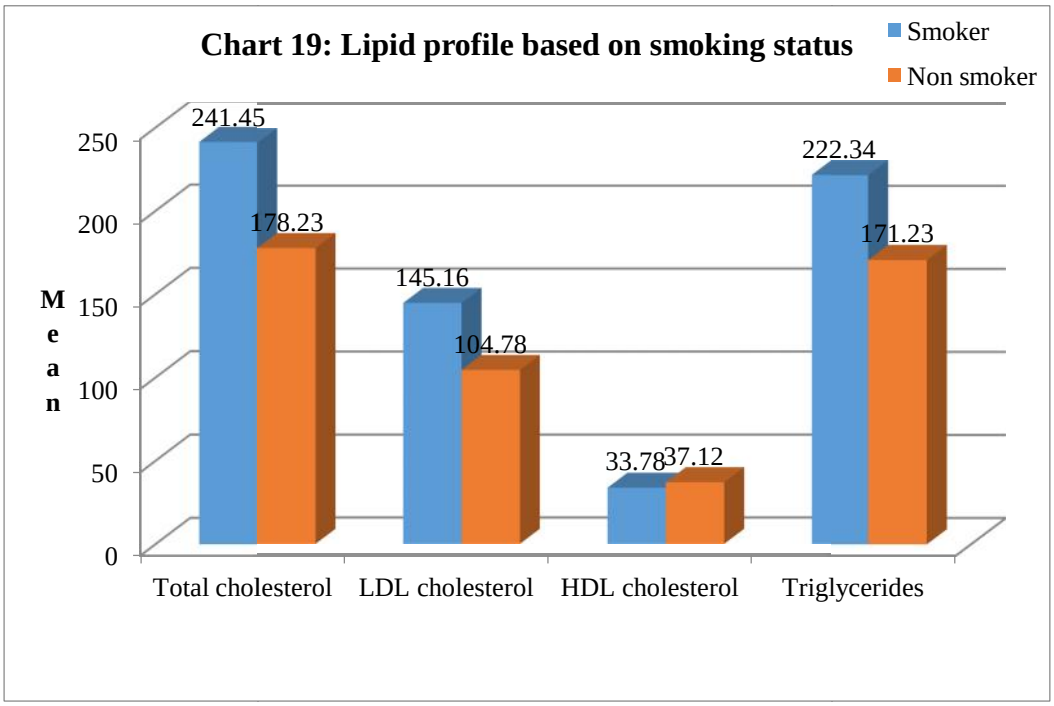


Table 20: Lipid profile based on dietary changes

Lipid profile	Present (n=55)		Absent (n=145)		P value	% Change
	Mean	SD	Mean	SD		
Total cholesterol	165.10	22.13	203.45	32.14	<0.001	
LDL cholesterol	102.34	48.71	134.45	34.51	0.0212	23.88
HDL cholesterol	37.12	13.78	34.12	10.78	0.4479	8.08
Triglycerides	159.12	108.12	205.12	117.12	0.0440	22.42

We found the total cholesterol levels and LDL cholesterol to be significantly higher in patients with no dietary modification when compared to patients with dietary modification done. ($p<0.05$) But, the HDL cholesterol and triglycerides levels were not associated significantly with the dietary changes of the patients. ($p>0.05$)

Chart 20: Lipid profile based on dietary changes

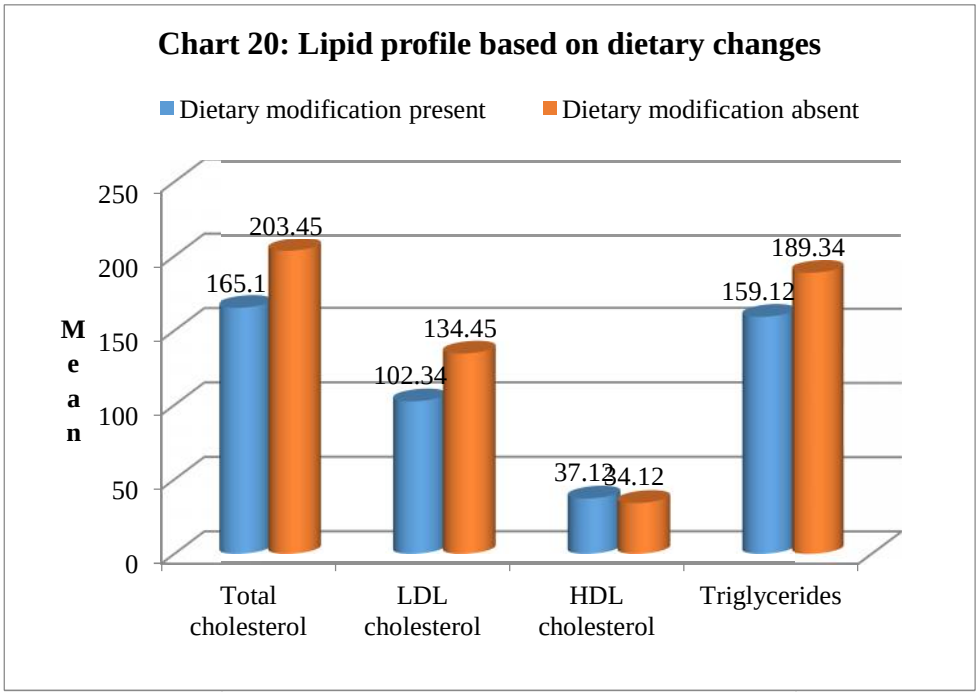


Table 21: Lipid profile based on gender

Lipid profile	Females (n=116)		Males (n=84)		P value	% Change
	Mean	SD	Mean	SD		
Total cholesterol	189.34	34.15	167.12	35.12	0.0495	
LDL cholesterol	132.34	32.42	112.34	29.04	0.0456	15.11
HDL cholesterol	39.12	11.32	37.78	10.78	0.7036	3.42
Triglycerides	189.23	98.45	171.12	101.23	0.5697	9.57

We found the total cholesterol levels and LDL cholesterol to be significantly higher in males when compared to females ($p<0.05$) But, the HDL cholesterol and triglycerides levels were not associated significantly with gender. ($p>0.05$)

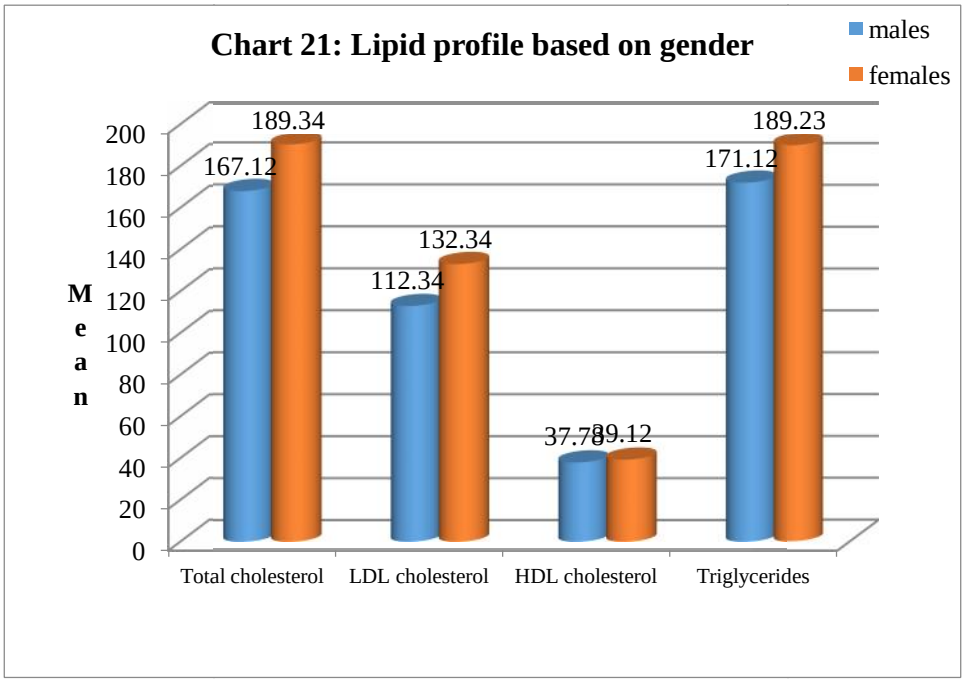


Table 22: Lipid profile based on Knowledge about dyslipidemia

Lipid profile	Knowledge-Present (n=35)		Knowledge-Absent (n=165)		P value	% Change
	Mean	SD	Mean	SD		
Total cholesterol	172.13	34.12	192.34	32.13	0.0612	
LDL cholesterol	101.19	32.16	123.66	31.23	0.0309	18.17
HDL cholesterol	37.19	11.56	33.67	10.43	0.3184	9.46
Triglycerides	178.34	117.23	221.67	101.34	0.2910	19.54

We found the LDL cholesterol to be significantly higher in patients with no knowledge about dyslipidemia when compared to those who had knowledge ($p<0.05$) But, the HDL cholesterol, total cholesterol and triglycerides levels were not associated significantly with gender. ($p>0.05$)

Chart 22: Lipid profile based on Knowledge about dyslipidemia

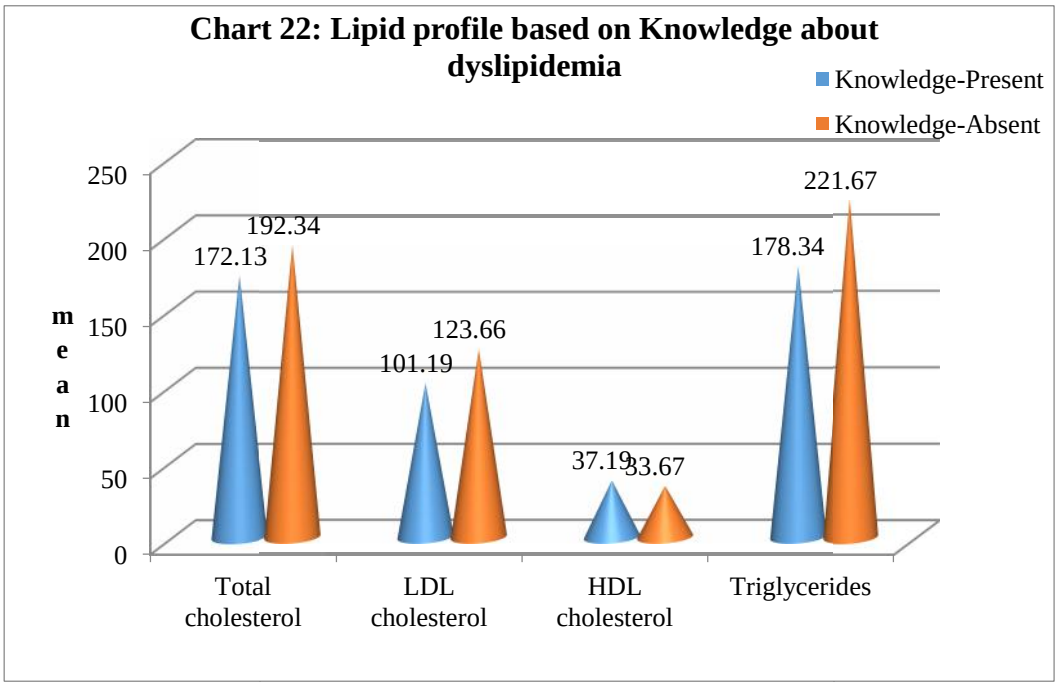


Table 23: Lipid profile based on number of doctor visits

Lipid profile	<2 visits (n=45)		>2 visits (n=155)		P value	% Change
	Mean	SD	Mean	SD		
Total cholesterol	223.67	101.98	178.12	99.03	0.1600	
LDL cholesterol	121.88	31.22	101.45	34.22	0.0559	16.76
HDL cholesterol	37.34	10.98	40.12	9.78	0.4031	6.92
Triglycerides	223.45	107.78	171.45	102.34	0.1260	23.27

We did not find any significant change in LDL cholesterol, HDL cholesterol; total cholesterol and triglycerides levels with the number visits the patient visited the doctor. (p>0.05)

Chart 23: Lipid profile based on number of doctor visits

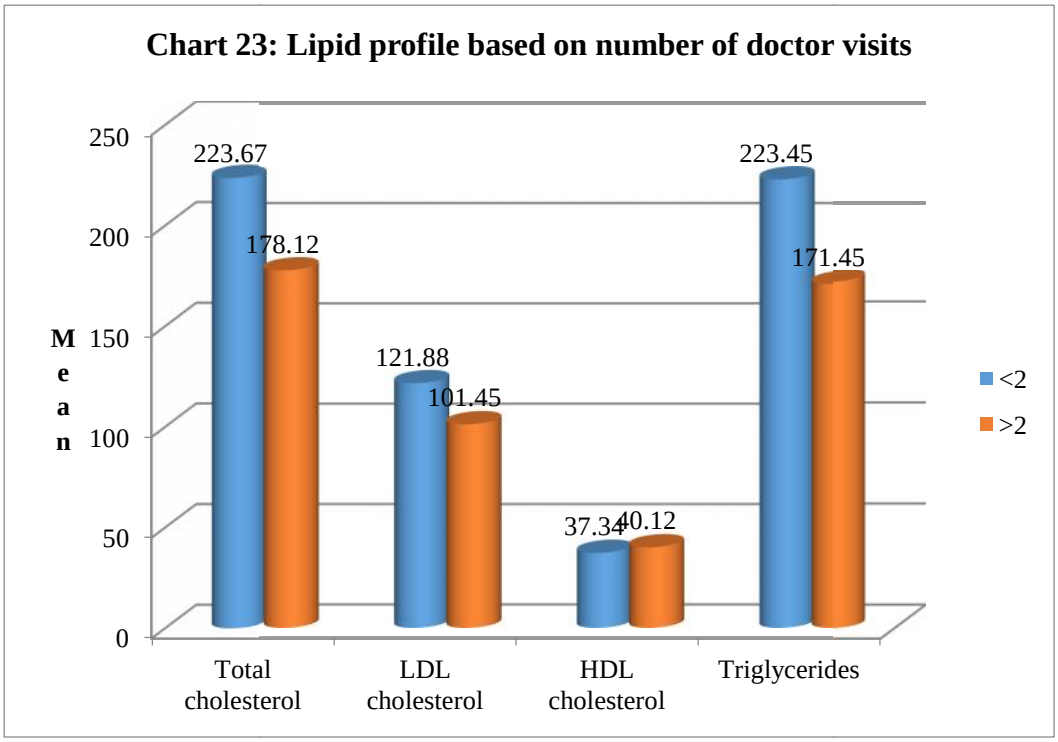


Table 24: Lipid profile based on waist hip ratio

Lipid profile	Normal (n=108)		Abnormal (n=92)		P value	% Change
	Mean	SD	Mean	SD		
Total cholesterol	171.67	45.12	231.52	34.56	<0.001	
LDL cholesterol	104.23	29.03	133.78	36.78	0.0072	22.08
HDL cholesterol	34.56	10.34	31.45	3.45	0.2097	9
Triglycerides	182.67	98.23	251.38	85.34	0.0234	27.33

We found the total, LDL cholesterol, HDL cholesterol and triglycerides to be significantly higher in patients with abnormal waist hip ratio when compared to those having normal waist hip ratio.

Chart 24: Lipid profile based on waist hip ratio

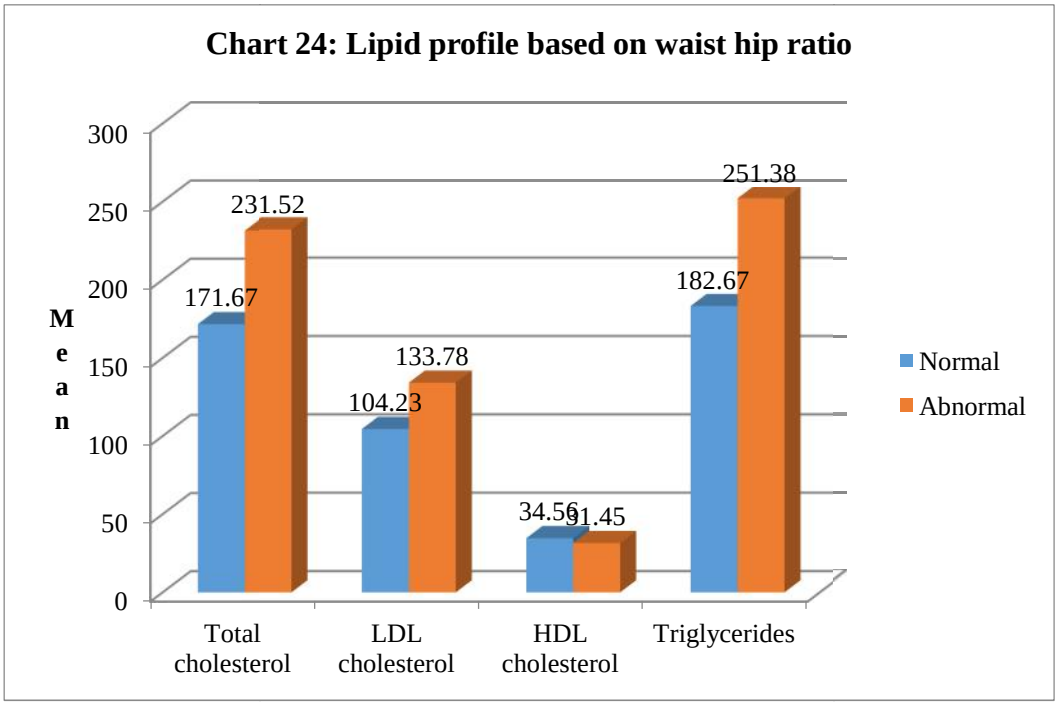
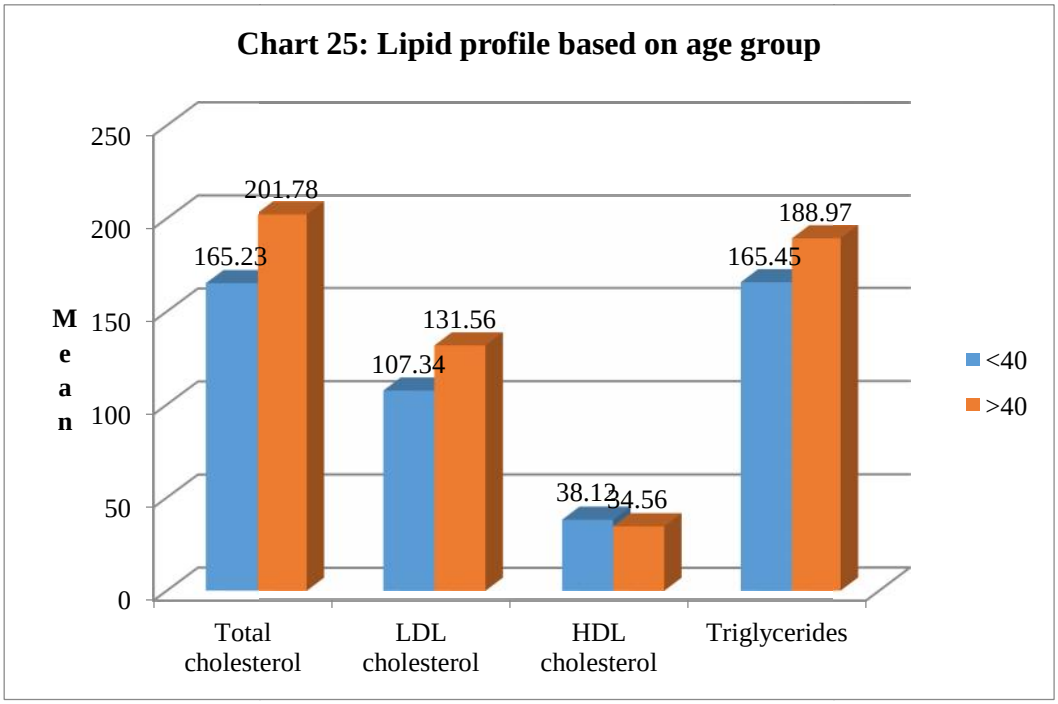


Table 25: Lipid profile based on age group

Lipid profile	<40 (n=40)		>40 (n=160)		P value	% Change
	Mean	SD	Mean	SD		
Total cholesterol	165.23	51.23	201.78	43.23	0.0195	
LDL cholesterol	107.34	32.01	131.56	30.12	0.0183	18.40
HDL cholesterol	38.12	11.23	34.56	10.37	0.3042	9.33
Triglycerides	165.45	78.23	188.97	89.56	0.3810	12.44

We found the total and LDL cholesterol to be significantly higher in patients with age more than 40 years when compared to those less than 20 years ($p<0.05$) But, the HDL cholesterol, and triglycerides levels were not associated significantly with age group. ($p>0.05$)

Chart 25: Lipid profile based on age group



DISCUSSION

Dyslipidemia is a well recognised risk factor for cardiovascular diseases which are currently the leading cause of mortality and morbidity across the world. The fact that this risk factor is modifiable, interests us to study the different interventions that affect the lipid profile of patients attending our outpatient department. So we conducted a cross sectional study and noted two consecutive lipid profiles of 200 subjects and retrospectively analysed the factors responsible for change in the lipid profile during this duration between 2 lipid profiles.

Demographic distribution:

Majority of the study subjects were in the range of 50 to 60 years followed by 60 to 70 years and 40 to 50 years in our study. The mean age of the study subjects was 51.24 ± 14.72 years. A study done by Monzani F et al[76] included patients less than 55 years in their study. Another study done by Singh SK et al[77] in north India had included patients of subclinical hypothyroidism and healthy controls with majority age range of 36 to 25 years. Studies conducted by Michishita R et al[78] included the subjects in the age range of 33 to 71 years, Salehi M et al[79] included age range of 25 to 25 years.

Gender distribution:

Majority of the study subjects were males in our study. A study done by Asranna A et al[80] included cases of hypothyroidism and studied the effect of thyroxin on the lipid profile. They had included majority of females in their study. Another study done by Monzani F et al[76] included majority of the females who were having

sub clinical hypothyroidism in their study. Majority of the study subjects were females in the studies conducted by Michishita R et al[78], Salehi M et al[79] and Singh SK et al[77]. This indicates a higher prevalence of sub clinical hypothyroidism in females when compared with males.

Past clinical history:

In our study, 44.50% of them had past history of diabetes, 19% had hypertension, 5% had IHD, 9.50% had hypothyroidism and 25.50% had dyslipidemia. We found a significant difference between the proportions of hypothyroidism and dyslipidemia among the gender.

Interventions studied:

In our study, 52.94% of the people having dyslipidemia used statins but the rest discontinued their statins (47.06%). About 30% of the subjects had lifestyle modification and 17.50% had knowledge about dyslipidemia. Among the diabetics, 27.66% had controlled sugar levels and among the hypertensives, 42.11% had controlled blood pressures. About 84.21% who had elevated TSH levels were started on treatment of hypothyroidism. About 27.50% underwent dietary changes.

Personal history:

The proportions of tobacco use, alcohol and smoking were significantly higher among the males when compared to females. Over all, the prevalence of tobacco use in our study was 23%, alcohol use was 32% and 19% of them were smokers. Majority of the study subjects were having low or sedentary physical activity levels in our study.

Obesity based on body mass index and waist hip ratio:

About 22% of our study subjects were underweight, 51% were normal, 22.50% were overweight and 4.50% were obese in our study. Based on the waist hip ratio, 46% were having abnormal waist: hip ratio i.e. 46% were having central obesity. Subjects with abnormal waist-hip ratio had raised LDL, triglyceride levels by 22.08 % and 27.33 % respectively and decreased HDL levels by 9 % as compared to those who had a normal waist-hip ratio.

Lipid Profile Variation based on age, sex, history, knowledge about dyslipidemia, no.of visits to a doctor:

Subjects more than 40 years of age had raised LDL, triglyceride levels by 18.40 % and 12.44 % respectively and decreased HDL levels by 9.33 % as compared to those less than 40 years of age.

Males had raised LDL, triglyceride levels by 15.11 % and 12.44 % respectively and decreased HDL levels by 3.42 % as compared to females.

Subjects who didn't have knowledge about dyslipidemia had raised LDL, triglyceride levels by 18.17 % and 19.54 % respectively and decreased HDL levels by 9.46 % as compared to those who had knowledge about dyslipidemia.

Subjects who had less than 2 visits to doctor had raised LDL, triglyceride levels by 16.76 % and 23.27 % respectively and decreased HDL levels by 6.92 % as compared to those who had more than 2 visits.

Total cholesterol level variation:

In the present study, between the 1st and 2nd lipid profile, the total cholesterol levels decreased significantly with lifestyle modification, knowledge about dyslipidemia, controlled sugars, controlled blood pressure and dietary changes.

A study done by Michishita R et al[78] compared two interventions and their effect over lipid profile of the dyslipidemia patients. The subjects who were in exercise group showed a significant decrease in the total cholesterol levels after 12 weeks post intervention, but in dietary change group there was no significant change in the total cholesterol levels post 12 weeks intervention. A study conducted by Monazamnezhad A et al[81] on to evaluate the effects of aerobic exercise on lipid profile of patients with Multiple Sclerosis inferred that there was significant decrease in total cholesterol levels.A study done by Ou SM et al[81]to find the impact of physical activity on association of lipid profile with mortality status among the elderly people of China inferred that Older individuals with lowest quintile of total cholesterol were associated with increased risk of all-cause mortality compared to those with other quintile of these lipid profiles. Compared to inactive older individuals, both low and high active older individuals were associated with lower risks of mortality. This highlights the importance of physical activity,a modification which will be helpful in decreasing the lipid parameters and in turn decreasing the mortality.

A study done by Salehi m et al[79] evaluated the importance of long term dietary modification among the subjects and its effect on lipid parameters. Amongst males and females they found a significant decrease in total cholesterol levels after the intervention. A study done by Haghpanah B et al[83]compared the physical fitness and lipid profile in active and inactive middle aged men and found no significant improvement in total cholesterol levels.An analysis of National Health and Nutrition Examination Survey 2003-2012, United states done by Mercado CI et al[84] inferred that diabetic adults had significantly lower TC and LDL-c levels than non-diabetic adults & the percent difference was greater among adults taking cholesterol medication than adults not taking cholesterol medication. Further, mean TC, HDL-c,

and LDL-c levels did not significantly change from 2003 to 2012 in non-diabetic adults taking cholesterol medication or for adults not taking cholesterol medications.A study done by SaedmocheshiS et al[85]inferred that there was significant decrease in the total cholesterol levels in the intervention group (grape seed extract plus aerobic exercise) when compared to control group.

Another study done by Moraleda BR et al[86] inferred that there was a significant decrease in total cholesterol levels, LDL and TG levels among all the interventions they studied. Group 1 had intervention of muscle training plus dietary modification, Group 2 had muscle training plus endurance plus dietary modification, Group 3 had endurance and dietary modification and group 4 had physical activity modifications and dietary changes.A significant change in all the lipid parameters was inferred by a study conducted by Mohammadi HR et al[87]who studied the effect of progressive strength training on lipid profile of in active middle aged men.

Chitra U et al[88] studied the role of lifestyle variables on the lipid profile of selected South Indian subjects and found that there was a significant difference in the total cholesterol levels of subjects who exercised and those who were not involved in any physical activity. There was a significant difference between the high-density lipoprotein (HDL) cholesterol values of the subjects based on exercise levels.

Goyal R et al[89] studied the correlation between hypertension and lipid profile and demonstrated that the serum HDL- cholesterol and LDL-cholesterol levels in hypertensive patients were 38.91 ± 8.02 and 132.16 ± 27.83 mg/dl and 39.91 ± 9.06 and 117.8 ± 34 mg/dl respectively, in healthy volunteers.Ni WQ et al[90] inferred that the presence of dyslipidemia was significantly associated with increasing age, smoking status, hypertension, diabetes, and body mass index.

Present study demonstrated that treatment of hypothyroidism did not find any significant decrease in total cholesterol levels.A study done by Asranna A et al[80] inferred that the total cholesterol levels decreased significantly in their study after thyroxin was started for the patients with hypothyroidism. Monzani F et al[76] conducted a randomised control trial to study the effect of levothyroxine on lipid profile among their patients and they found that there was significant decrease in the total cholesterol levels of their patients after the intervention.A study done Singh SK et al[77] inferred that there was nominal increase in total cholesterol levels after hypothyroidism was treated.

LDL cholesterol level variation:

In the present study, the LDL levels significantly decreased in the patients with lifestyle modification, knowledge about dyslipidemia, use of statins and dietary changes. A study done by Asranna A et al[80] inferred that the LDL cholesterol levels decreased significantly in their study after thyroxin was started for the patients with hypothyroidism. Monzani F et al[76] conducted a randomised control trial to study the effect of levothyroxine on lipid profile among their patients and they found that there was significant decrease in the LDL levels of their patients after the intervention.A study done Singh SK et al[77] inferred that there was nominal increase in LDL cholesterol levels in hypothyroid patients when compared with their healthy controls.A study done by Michishita R et al[78] compared two interventions and their effect over lipid profile of the dyslipidemia patients. The subjects who were in exercise group showed a significant decrease in the LDL cholesterol levels after 12

weeks post intervention, but in dietary change group there was no significant change in the LDL cholesterol levels post 12 weeks intervention.

A study done by DahalS et al[91] compared the LDL cholesterol levels in diabetics with their healthy controls and found that the levels were significantly higher in diabetics when compared to controls. This is an indirect indictor that the controlled diabetes controls the LDL cholesterol levels.A study done by Salehi M et al[79] found among both males and females they found a significant decrease in LDL cholesterol levels after the intervention. A study done by Haghpanah B et al[83]compared the physical fitness and lipid profile in active and in active middle aged men and found no significant improvement in LDL cholesterol levels. A study done by SaedmocheshiS et al[85]inferred that there was significant decrease in the LDL cholesterol levels in the intervention group (grape seed extract plus aerobic exercise) when compared to control group.

HDL cholesterol level variation:

The HDL levels significantly decreased with interventions like lifestyle modification, use of statins and knowledge about dyslipidemia. But there is no significant difference in the HDL levels from the 1st and 2ndlipid profile in controlled sugars, controlled blood pressures, treatment of hypothyroidism and dietary changes.A study done by Asranna A et al[80] inferred that the HDL cholesterol levels increased in their study after thyroxin was started for the patients with hypothyroidism but this decrease was mild and not significant.Monzani F et al[76] conducted a randomised control trial to study the effect of levothyroxine on lipid profile among their patients and they found that there was no significant change in the HDL cholesterol levels of their patients after the intervention.A study done Singh SK et al[77]

inferred that there was nominal decrease in HDL cholesterol levels after hypothyroidism was treated.

A study done by Michishita R et al[78] compared two interventions and their effect over lipid profile of the dyslipidemia patients. The subjects who were in exercise group showed a significant increase in the HDL cholesterol levels after 12 weeks post intervention, but in dietary change group there was no significant change in the HDL cholesterol levels post 12 weeks intervention. A study done by DahalS et al[91] compared the HDL cholesterol levels in diabetics with their healthy controls and found that the levels were significantly lower in diabetics when compared to controls. This is an indirect indicator that the control of diabetes controls the HDL cholesterol levels.

A study done by Salehi m et al[79] found among both males they found a significant increase in HDL cholesterol levels after the intervention but, there was no significant increase among the females. A study done by Haghpanah B et al[83]compared the physical fitness and lipid profile in active and in active middle aged men and found no significant improvement in HDL cholesterol levels.A study done by SaedmocheshiS et al[85]inferred that there was no significant increase in the HDL cholesterol levels in the intervention group (grape seed extract plus aerobic exercise) when compared to control group.

TG level variation:

The changes in triglyceride levels were significantly noted in controlled sugars in past 3 months and dietary changes. But in lifestyle modification, knowledge about dyslipidemia, treatment of hypothyroidism and controlled blood pressures in past 3

months there was no significant difference.A study done by Asranna A et al[80] inferred that the Triglyceride levels decreased significantly in their study after thyroxin was started for the patients with hypothyroidism. Monzani F et al[76] conducted a randomised control trial to study the effect of levothyroxine on lipid profile among their patients and they found that there was no significant change in the triglyceride levels of their patients after the intervention.

A study done by Michishita R et al[78] compared two interventions and their effect over lipid profile of the dyslipidemia patients. The subjects who were in exercise group showed a significant decrease in the triglyceride levels after 12 weeks post intervention, but in dietary change group there was no significant change in the triglyceride levels post 12 weeks intervention. A study conducted by Monazamnezhad A et al[81] on to evaluate the effects of aerobic exercise on lipid profile of patients with Multiple sclerosis inferred that there was significant decrease in triglyceride levels.

A study done by DahalS et al[91] compared the triglyceride levels in diabetics with their healthy controls and found that the levels were significantly higher in diabetics when compared to controls. This is an indirect indictor that the controlled diabetes controls the triglyceride levels.A study done by Salehi m et al[79] found among both males and females they found a significant decrease in triglyceride levels after the intervention. A study done by Haghpanah B et al[83]compared the physical fitness and lipid profile in active and in active middle aged men and found no significant improvement in triglyceride levels.A study done by SaedmocheshiS et al[85]inferred that there was significant decrease in the triglyceride levels in the intervention group (grape seed extract plus aerobic exercise) when compared to control group.

Statins and effect of lipid profile

Present study:

- In case of discontinuation of statins, the total cholesterol level significantly increased. Use of statins decreased the total cholesterol levels. Upon detailed analysis, we found that there was significant decrease in the total cholesterol levels of 1st and 2nd reports who had received Rosuva 10mg, Atorva 40mg, Atorva 20mg and Rosuva 5mg but there was no significant difference in cases who had taken Atorva 10mg.
- Discontinuation of statins increased the levels significantly. When the LDL levels were assessed, there was significant decrease in LDL levels in patients who received Rosuva 10mg, Atorva 40mg, Atorva 10mg and Rosuva 5mg but there was no significant decrease in case of Atorva 20 mg.
- The HDL cholesterol levels significantly decreased with discontinuation of statins but use of statins did not yield any significant results. When the HDL levels and the drugs were assessed, there was significant increase the levels only in case of patients who used Atorva 20mg.
- The discontinuation of statins did not yield any significant effects on the levels of triglycerides. Upon detailed analysis, the triglyceride levels were significantly decreased in the patients who used rosuva 10mg, atorva 40mg, atorva 20mg, rosuva 5mg and atorva 10mg.

Following are some studies who have demonstrated similar effects:

Grover A et al[92] studied the correlation of compliance to statin therapy with lipid profile and serum HMGCoA reductase level in dyslipidemic patients and found

that there was significant inverse correlation ($p < 0.05$) between compliance and TC, TG, LDL-C and HMGCoA-R levels and positive correlation ($p < 0.05$) with HDL-C levels. Krause MP et al[93]analysed the lipid profile of elderly women attending their outpatient department. They found that those patients who were having satisfactory treatment based on statins were having lower levels of serum cholesterol when compared with the non satisfactory intake of statins.Valera HR et al[94] studied the plasma level of atorvastatin and its effect on lipid profile and found that Atorvastatin 10 mg/day for 8 weeks with a plasma level range (7.45, 12.08) ng/mL significantly ($P < 0.05$) reduced all the parameters of lipid profile from the study population. Berne C et al[95] compared the effects of rosuvastatin and atorvastatin in their study and its effect of lipid profile and found that rosuvatstatin was better in terms of starting dose and dose titration when compared to atorvastatin. Clearfield MB et al[96] studied the efficacy and safety of rosuva 10mg and atrova 20mg in high risk patients and found that Rosuvastatin 10 mg reduced LDL-C levels significantly more than atorvastatin 20 mg at week 6. Further, High-density lipoprotein cholesterol was increased significantly with rosuvastatin 10 mg versus atorvastatin 20 mg.

CONCLUSION

1. The objective of the study was to study the changes in lipid profile at different time interval and the factors responsible for the changes.
2. Subjects more than 40 years of age had raised LDL, triglyceride levels by 18.40 % and 12.44 % respectively and decreased HDL levels by 9.33 %as compared to those less than 40 years of age.
3. Males had raised LDL, triglyceride levels by 15.11 % and 12.44 % respectively and decreased HDL levels by 3.42 %as compared to females.
4. Diabetic individuals had raised LDL, triglyceride levels by 22.27 % and 33.52 % respectively and decreased HDL levels by 12.52 % as compared to the non diabetics.
5. Subjects who had sedentary lifestyle had raised LDL, triglyceride levels by 23.20 % and 27.79 % respectively and decreased HDL levels by 9.33 % as compared to the individuals who had moderate to vigorous physical activity.
6. Smokers had raised LDL, triglyceride levels by 27.81 % and 22.98 % respectively and decreased HDL levels by 9 % as compared to the non smokers.
7. Subjects who didn't have knowledge about dyslipidemia had raised LDL, triglyceride levels by 18.17 % and 19.54 % respectively and decreased HDL levels by 9.46 % as compared to those who had knowledge about dyslipidemia.
8. Subjects who had less than 2 visits to doctor had raised LDL, triglyceride levels by 16.76 % and 23.27 % respectively and decreased HDL levels by 6.92 % as compared to those who had more than 2 visits.

9. Subjects with abnormal waist-hip ratio had raised LDL, triglyceride levels by 22.08 % and 27.33 % respectively and decreased HDL levels by 9% as compared to those who had a normal waist-hip ratio.
10. Our study revealed that use of statins have a favourable effect on the LDL levels (18% decrease), HDL levels (8.08 % increase) and triglycerides (22.42 % decrease). The change in triglycerides was mainly due to control of sugars.
11. Atorva 20 mg followed by Rosuva 10 mg were the statins used by most of the subjects in our study. However, the percent reduction of LDL levels by the statins used by the subjects in our study were almost same.
12. Discontinuation of statins (either because of statin intolerance or ignorance) increased the LDL levels (by 13%), triglyceride levels (by 19.72 %) and decreased the HDL levels (16.75 %). None of the subjects enrolled in our study were receiving Fibrates.
13. Diabetic patients with controlled blood sugar levels had decreased LDL levels by 9.25 %, increased HDL levels by 13.04 % and decreased Triglyceride levels by 25.04 %.
14. Lifestyle modification along with dietary modification had a favourable effect on LDL, HDL values. Particularly, moderate physical activity, cessation of smoking and tobacco use altered the values favourably. Dietary modification and lifestyle modification decreased the LDL levels by 23.88 % and 13.25 % respectively, increased the HDL levels by 8.08 % and 17.7 % respectively and decreased the triglyceride levels by 22.42% and 7.85 % respectively.

SUMMARY

We conducted a study in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi on patients during the period of January 2017 to December 2017 to study the changes in lipid profile in an individual at different time interval and factors responsible for the changes. Patients attending OPD at the Department of Medicine at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi and having minimum 2 lipid profiles, minimum 3 months apart were recruited sequentially by Convenient sampling method till the sample size of 200 subjects was reached. The selected patients were briefed about the nature of the study and a written informed consent was obtained (Annexure–I). Demographic data like gender and age were collected along with relevant history and recorded on predesigned and pretested proforma (Annexure-II). A thorough clinical examination was conducted and the findings were also recorded.All patient relevant data were noted. History of preexisting diseases like Diabetes Mellitus, Hypertension, Stroke, Ischemic Heart Disease, and previous admission to hospital and present symptomatology was listed and detailed physical examination was done. Details of medical interventions were recorded.The data was analysed using EPI info (version 7.2).

Our study revealed that use of statins have a favourable effect on the LDL levels (18% decrease), HDL levels and triglycerides. The change in triglycerides was mainly due to control of sugars. Discontinuation of statins (either because of statin intolerance or ignorance) increased the LDL levels (by 13%), triglyceride levels and decreased the HDL levels.Lifestyle modification along with dietary modification had a favourable effect on LDL, HDL values. Particularly, moderate physical activity,

cessation of smoking and tobacco use altered the values favourably. Dietary modification and lifestyle modification decreased the LDL levels by 15.5 % and 13.25 % respectively. Our results confirm that diet and exercise routines significantly affect the serum lipid profile. The most important lifestyle factors which affect the serum lipid profile are diet composition, habits and physical activity.

LIMITATIONS

1. Recall Bias.
2. It was a cross sectional study so the results will be difficult to be generalised.
3. It was a single centre study; multi centre longitudinal studies will infer better results.
4. This study was primarily questionnaire focussed. The possibility of subjects concealing information or manipulating data cannot be ruled out.

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ANNEXURE I – CONSENT FORM

INFORMED CONSENT

Title: "FACTORS AFFECTING LIPID PROFILE AMONG PATIENTS ATTENDING OPD AT KLES DR. PRABHAKARKORE HOSPITAL & MRC, BELAGAVI, A ONE YEAR OBSERVATIONAL CROSS SECTIONAL STUDY."

Study investigator

P.G- M.D. GENERAL MEDICINE. J.N. Medical College, KLE Academy Of Higher Education and Research, Belagavi-590010.

INTRODUCTION: You are being invited to participate in this study on Factors affecting lipid profile

EXPLANATION OF PROCEDURE:

POSSIBLE BENEFITS: The investigator does not promise or guarantee that you will receive any benefit being in the study; however, it will be aimed at better understanding of the factors affecting lipid profile

CONFIDENTIALITY: All information collected during the course of study will be kept confidential.

WITHDRAWAL: Participation in this study is voluntary. If you don't wish to participate in this study; you will not lose benefits to which you are entitled. After starting the study, anytime during the study, if you feel to withdraw from the study, you are free to do so.

COST OF PARTICIPATION: The cost of the study will be borne by the researcher. There will be no additional cost to you for participation in the study.

AUTHORIZATION TO PUBLISH THE RESULTS: The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.

In case of the queries during study or in future you may contact following persons,

1. **DR NIKHIL A CHOUGULE**
DEPARTMENT OF GENERAL MEDICINE
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELAGAVI - 590010

Phone number- 8087449342

2. **Dr.V.A. KOTHIWALE,**
VICE-PRINCIPAL &PROFESSOR ,
DEPARTMENT OF MEDICINE,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELAGAVI - 590010

CONSENT STATEMENT:

"I volunteer and consent to participate in this study. I have read the content or it has been read to me in the language I can understand. This study has been fully explained to me and I may ask any questions at any time."

Name and signature of patient:

Name and signature of person obtaining consent:

Name and signature of witness:

Date:

संशोधन में भाग लेने केलिए सम्मती पत्र.

आपको इस संशोधन **"फ्याक्टर्स अफ्याक्टिंग लीपिड फ्रोपैल अमंग पेसेन्ट्स अटेन्डिन्ग ओ.पि.डि एट के.एल.ई. एस. डॉ. प्रभाकर कोरे हास्पिटल और एम.आर.सी. बेलगावि में एक क्रास सेक्शनल अध्ययन"** में भाग लेने के लिये निमंत्रित करता हु । ये संशोधन , **डॉ. चौगले निखिल अशोक** पी.जी. विद्यार्थी, औषध वैद्यक शास्त्र विभाग, जे. एन. मेडीकल कालेज बेळगावि. और मार्गदर्शक : **डॉ. क्वि. ए. कोठिवाले**. प्रोफेसर अंड व्हायिस प्रिन्सिपाल औषध वैद्यक शास्त्र विभाग, जे.एन. मेडीकल कालेज बेळगावि. द्वारा किया जा रहा है ।

मुझे इस संशोधन के बारे में और इसके फायदे और इसके रिस्क पुरे तरिके से बतादिये गये है ।

मै अपनी मरजी से संशोधन में भाग लेना चाहता हुं और इसके लिये मेरी सहमती है । मैं अपनी मरजी से कभी भी संशोधन में भाग लेने के लिये मना कर सकता हुँ । मेरे पास संशोधन के बारे मे प्रश्न पुछने के लिये पूरा समय है और इसके लिय मैं कभी भी प्रश्न पुछ सकता हुँ ।

मेरा साइन / अगूंठा साक्षी है कि मै सहमति पत्र के लिय तैयार हूँ ।

इस विषय पर और अधिक जानकारि केलिये या संपर्क किजिए

१. **मुख्य तपासक, डॉ. चौगले निखिल अशोक** पी.जी. विद्यार्थी, औषध वैद्यक शास्त्र विभाग,

डा. गंगा. एस. पाल्ल. चअरमन, इन्स्टटूशनल एथक्स कामटाम, प्राफसर, पथालाज विभाग, जे.एन. मेडीकल कालेज, बेळगावि । मो–९४८०२७५६०१

सम्मती पत्र

मै निचे सही करनेवाला स्वइच्छेसे इस अभ्यासमें भाग लेने के लिए मान्यता देता हूँ । मै अपना नाम किसी भी वक्त इसमेसे वापस ले सकता हूँ और इस सम्मती के कारण मै मेरे कोई भी कानूनी हक नहीं छोड रहा हूँ। यह सब उपर के विषय के बारे में स्वयं पढकर या पढने के, सुनने के बाद मैं इस सम्मती पत्र पर अपने हस्ताक्षर कर के सभी प्रश्नों का उत्तर दिया हूँ ।

सहभागी का नाम :

हस्ताक्षर :

साक्षीदार :

हस्ताक्षर :

संशोधक :

हस्ताक्षर :

दिनांक :

स्थळ :

ಸಂಶೋಧನಾ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವಿಕೆಗಾಗಿನ ಸಮ್ಮತಿ ಪತ್ರ

ನಾವು ನಿಮ್ಮನ್ನು ಸಂಶೋಧನೆಯಲ್ಲಿ ತೊಡಗಿಸಿಕೊಳ್ಳಲು ವಿನಂತಿಸುತ್ತಿದ್ದೇವೆ **ಪ್ಯಾಕ್ಟರ್ಸ ಅಫ್ಯಾಕ್ಟಿಂಗ್ ಲೀಪಿಡ್ ಪ್ರೋಫೈಲ್ ಅಮಂಗ್ ಪೆಸೆಂಟ್ಸ್ ಅಟೆಂಡಿಂಗ್ ಓ.ಪಿ.ಡಿ. ಆಟ್ ಕೆ.ಎಲ್.ಇ.ಎಸ್. ಡಾ|| ಪ್ರಭಾಕರ ಕೋರೆ ಹಾಸ್ಪೀಟಲ್ ಮತ್ತು ಎಮ್.ಆರ್.ಸಿ. ಬೆಳಗಾವಿಯಲ್ಲಿ ಮಾಡುವ ಒಂದು ಕ್ರಾಸ್ ಸೆಕ್ಷನಲ್ ಅಧ್ಯಯನ" ಡಾ|| ಚೌಗುಲೇ ನಿಖಿಲ್ ಅಶೋಕ, ಸ್ನಾತಕೋತ್ತರ ವಿದ್ಯಾರ್ಥಿ ಜೆ.ಎನ್.ಮೆಡಿಕಲ್ ಕಾಲೇಜ, ಬೆಳಗಾವಿ ಇವರು [illegible], ವ್ಹಾಯಿಸ್ ಪ್ರಿನ್ಸಿಪಾಲ್ & ಪ್ರೊಫೇಸರ, ವೈದ್ಯಕೀಯ ವಿಭಾಗ, [illegible]ಗಾವಿ,** ಇವರ ಮಾರ್ಗದರ್ಶದಲ್ಲಿ ನಡೆಸುತ್ತಿದ್ದೇವೆ.

ಗೌರವಾನ್ವಿತರೇ ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ಅರ್ಹರಿದ್ದಿರಿ.

ಸಂಶೋಧನೆಯಲ್ಲಿ ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆ ವೈಯಕ್ತಿಕವಾಗಿದ್ದು, ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವುದು ನಿಮ್ಮ ನಿರ್ಧಾರವಾಗಿರುತ್ತದೆ. ಇದರಿಂದ ಜೆ.ಎನ್ ಮೇಡಿಕಲ್ ಕಾಲೇಜಿಗೆ ನಿಮಗಿರುವ ಸಂಬಂಧಕ್ಕೆ ಪರಿಣಾಮ ಬೀರುವುದಿಲ್ಲ. ನೀವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ಹಿಂದೆ ಸರಿಯಬಹುದು.

ನೀವು ನನ್ನ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮನ್ನು ತೊಡಗಿಸಿಕೊಳ್ಳಲು ಒಪ್ಪಿದ ನಂತರ ಪ್ರಾಯೋಗಿಕವಾಗಿ ವಿಚಾರಣೆ ಹಾಗೂ ಅದಕ್ಕೆ ತಕ್ಕಂತೆ ತನಿಖೆ ನಡೆಸಲಾಗುವುದು. ನಿಮ್ಮ ಹಾಗೂ ಕುಟುಂಬದ ಇತಿಹಾಸದ ಬಗ್ಗೆ ಸಂಧರ್ಶನ ನಡೆಯಿಸಲಾಗುವುದು.

ತಾವುಗಳು ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವಾಗ ಮುನ್ನೆಚ್ಚರಿಕೆ ಕ್ರಮಗಳನ್ನು ಅನುಸರಿಸಲಾಗುವುದು. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವುದರಿಂದ ಖಾಯಿಲೆಯ ಸಂಪೂರ್ಣ ಮಾಹಿತಿ ಪಡೆಯಬಹುದು. ಇದರಿಂದ ಇದೇ ಖಾಯಿಲೆಯಿಂದ ಬಳಲುತ್ತಿರುವ ಇತರರಿಗೆ ತುಂಬಾ ಸಹಾಯವಾಗುವುದು.

ಈ ಪರೀಕ್ಷೆಯ ವೆಚ್ಚವನ್ನು ಆಸ್ಪತ್ರೆಯ ನಿಯಮದಂತೆ ತಾವೇ ಭರಿಸಬೇಕು. ಆದರೆ ಇದರಲ್ಲಿ ಯಾವುದೇ ಇತರ ವೆಚ್ಚುಗಳು ಇರುವುದಿಲ್ಲ.

ತಾವು ಈ ಪರೀಕ್ಷೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವುದನ್ನು ಸಂಪೂರ್ಣವಾಗಿ ಗೌಪ್ಯವಾಗಿ ಇಡಲಾಗುವುದು.

ತಮ್ಮ ಖಾಯಿಲೆ ಹಾಗೂ ಸಂಶೋಧನೆಯ ವಿವರಗಳನ್ನು ಎಲ್ಲಿಯೂ ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ಸಂಶೋಧನೆಯ ವಿವರಗಳನ್ನು ಪ್ರಕಟಿಸಲಿಕ್ಕೆ ಉಪಯೋಗ ಮಾಡಬಹುದು. ಆದರೆ ಇಲ್ಲಿ ನಿಮ್ಮ ಗೌಪ್ಯತೆಯನ್ನು ಕಾಪಾಡಲಾಗುವುದು. ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ಆಗುವ ಯಾವುದೇ ವ್ಯತಿರಿಕ್ತ ಪರಿಣಾಗಳಿಗೆ ಕೆ.ಎಲ್.ಇ.ಆಸ್ಪತ್ರೆಯ ಮೂಲಕ ಚಿಕಿತ್ಸೆ ನೀಡಲಾಗುವುದು.

ತಮಗೆ ಯಾವುದಾದರೂ ಸಂಶಯಗಳಿದ್ದಲ್ಲಿ ಅಥವಾ ಹೆಚ್ಚಿನ ಮಾಹಿತಿ ಬೇಕಾಗಿದ್ದಲ್ಲಿ ಈ ಕೆಳಗಿನ ವೈದ್ಯರನ್ನು ಸಂಪರ್ಕಿಸಬಹುದು.

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವವರ ಹಕ್ಕುಗಳ ವಿವರಗಳಿಗಾಗಿ ಈ ಕೆಳಗಿನ ವೈದ್ಯರನ್ನು ಸಂಪರ್ಕಿಸಬಹುದು.
ಡಾ॥ ಗಂಗಾ ಎಸ್. ಪಿಳ್ಳಿ, ಚೇರಮನ್, ಇನಸ್ಟಿಟ್ಯೂಶನಲ್ ಎಥಿಕ್ಸ್ ಕಮಿಟಿ, ಪ್ರೊಫೇಸರ, ಪೆಥಾಲಾಜಿ ವಿಭಾಗ, ಜೆ.ಎನ್.ಮೇಡಿಕಲ್ ಕಾಲೇಜ, ಬೆಳಗಾವಿ. (ಮೋ) 9480275601.

ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ಸ್ವ–ಒಪ್ಪಿಗೆ ಪ್ರಮಾಣ ಪತ್ರ :

ಈ ಸಂಶೋಧನೆಯ ಬಗ್ಗೆ ನನ್ನ ಸ್ವಂತ ಭಾಷೆಯಲ್ಲಿ ಸಂಪೂರ್ಣ ವಿವರವಾಗಿ ನನಗೆ ಅರ್ಥವಾಗಿರುತ್ತದೆ. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ನನಗೆ ಸಂಪೂರ್ಣವಾದ ಒಪ್ಪಿಗೆ ಇರುತ್ತದೆ. ಈ ಸಂಶೋಧನೆಯ ವಿವರಗಳು ಹಾಗೂ ಪರಿಣಾಮಗಳ ಬಗ್ಗೆ ನನಗೆ ಸಂಪೂರ್ಣವಾದ ಮಾಹಿತಿ ಇರುತ್ತದೆ. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಸ್ವ ಇಚ್ಛೆಯಿಂದ ಪಾಲ್ಗೊಳ್ಳಲು ಬಯಸುತ್ತೇನೆಂದು ಈ ಮೂಲಕ ದೃಢೀಕರಿಸುತ್ತೇನೆ. ನಾನು ಈ ಸಮ್ಮತಿ ಪತ್ರಕ್ಕೆ ಸಹಿ ಮಾಡುವುದರಿಂದ ನನಗೆ ಲಭ್ಯವಿರುವ ಕಾನೂನಿನ ಯಾವುದೇ ಹಕ್ಕುಗಳನ್ನು ಬಿಟ್ಟುಕೊಟ್ಟಿರುವುದಿಲ್ಲ. ನಾನು ಮೇಲಿನ ವಿಷಯ ಓದಿ ಅಥವಾ ಓದಿಸಿ ಕೇಳಿ ಸಮ್ಮತಿ ಪತ್ರದಲ್ಲಿರುವ ಎಲ್ಲ ಪ್ರಶ್ನೆಗಳಿಗೆ ಉತ್ತರಿಸಿರುತ್ತೇನೆ.

ಭಾಗವಹಿಸುವವರ ಹೆಸರು : _____

ಭಾಗವಹಿಸುವವರ ಸಹಿ : _____

ಭಾಗವಹಿಸುವವರ ಹೆಬ್ಬಟ್ಟಿನ ಗುರುತು : _____

ಸಾಕ್ಷಿದಾರರ ಹೆಸರು : _____

ಸಾಕ್ಷಿದಾರರ ಸಹಿ : _____

ಸಂಶೋಧಕರ ಹೆಸರು : _____

ಸಂಶೋಧಕರ ಸಹಿ : _____

ಸ್ಥಳ : _____
ದಿನಾಂಕ : _____

संशोधन अभ्यास सहभाग संमती

संशोधन अध्ययन: **"फ्याक्टर्स अफ्याक्टिंग लीपिड फ्रोपैल अमंग पेसेन्ट्स अटेन्डिन्ग ओ.पि.डि एट के. एल. ई. एस. डॉ. प्रभाकर कोरे हास्पिटल आणि एम.आर.सी. बेलगावि, मधील एक क्रास सेक्शनल अध्ययन" डॉ. चौगुले निखिल अशोक** पी.जी. विद्यार्थी, औषध वैद्यक शास्त्र विभाग,, जे.एन. मेडीकल कालेज बेळगावि, द्वारा आयोजित डॉ. प्रोफेसर, अंड व्हायिस प्रिन्सिपाल औषध वैद्यक शास्त्र विभाग, जे.एन. मेडीकल कालेज, जे.एन. मेडीकल कालेज बेळगावि यांच्या मार्गदर्शनाखाली करत आहेत.

प्रक्रिया सहभाग:

तुम्ही माझ्या अभ्यासात स्वत: नावनोंदणी सहमत असल्यास, नंतर वैद्यकीय तपशील केली जाईल, आणि त्यानुसार तपास, तुमच्या सध्याच्या गेल्या आणि कुटुंब इतिहास संबंधित मुलाखत घेतली जाईल.

धोके आणि फ़ायदे

या अभ्यासातील धोके आणि फ़ायदे मला समजावले गेले आहेत.

स्वय्मसेवी सहभाग/काढणे:

सहभाग ऐच्छिक आहे. आपण स्वत: ला या अभ्यासात नाही निवडू शकता. रूग्णालयाशी असलेल्या सबंधात काही फरक पडणार नाही. तुम्ही या अभ्यासातून कधीही माघार घेऊ शकता

पर्याय : आपण अभ्यास सहभाग सोडला तरी आपलेला व्यवस्थापन नियमा प्रमाणे मिळेल.

गोपनीयता : तुमही. दिलेली संशोधनदरम्यानची माहिती ही फक्त संशोधन संघाती लोकांनाच माहित असेल. तुमच्या लेखी परवानगीशिवाय कोणतीच माहिती उघड केली जाणार नाही.

परिणाम छापण्याबाबत : संशोधनच्या परिणामांबाबत चर्चा करताना, तुमची ओळख पटेल अशी माहिती उघड केली जाणार नाही.

नुकसानभरपाई : काहीही आरोग्यिक नुकसान झाल्यास रूग्णालय कोणतीहीं आर्थिक नुकसानभरपाई देण्यास बद्ध नाही.

संशोधनाबाबत काहीही प्रश्न असल्यास संपर्क साधावा :

३. डॉ. गंगा. एस. पिल्लि. चेअरमन, इन्स्टिट्यूशनल एथिक्स कमिटीम, प्रोफेसर, पेथोलाजि विभाग, जे.एन. मेडीकल कालेज, बेळगावि । मो–९४८०२७५६०१

सम्मती पत्र

मी खाली सही करणारा स्वत:हून आभ्यासामध्ये भाग घेण्यासाठी हे मान्य करत आहे. मी माझे नांव यातून कोणत्याही क्षणी काढून घेवू शकतो. हा नमूना फार्म सही केल्यामुळे मी माझे कोणतेही नैतिक अधिकार सोडून देत नाही आहे. हे वाचून पाहिल्यानंतर किंवा ते वाचून दाखविल्या नंतर मी माझी सही या सम्मती पत्रावर करत आहे. व अशा प्रकारे मी सर्व प्रश्नाची उत्तरे देत आहे.

भाग घेणार्याचे नांव :

सही अथवा डाव्या हाताचा अंगठा :

साक्षीदाराचे नांव :

साक्षीदाराची सही :

तपासणान्याचे नांव :

तपासणान्याचे सही :

तारीख: ठिकाण :

ANNEXURE-II

PROFORMA

QUESTIONNAIRE

NAME: **GENDER:**

AGE: **MARRIED:**

QUALIFICATION: **DESIGNATION:**

WEIGHT: kgs **;** **HEIGHT:** cms **;** **BMI:**

1. Do you have knowledge about Dyslipidemia?
   Ans:

2. Family history of dyslipidemia?
Ans:

3. Did you ever suffer from acute coronary syndrome or coronary artery disease?
   Ans:

4. Do you suffer from Dyslipidemia? Duration?
   Ans:

5. Are you on any medication for Dyslipidemia? Which? Dose? Whether taking regularly?

Ans:

6. Have you modified your food habits?

Ans:

7. Have you brought about any change in your Physical activity? Elaborate.

Ans:

8. Do you have Hypertension?

Ans:

9. Do you have Diabetes Mellitus? Rx?

Ans:

10. Do you suffer from any other disease? If yes, Rx?

Ans:

11. Do you suffer from stress because of work?

Ans:

12. Do you have any habits? If yes, Elaborate.

Ans:

13. Have you lost or gained weight?

Ans:

14. Change in waist circumference?

Ans:

ANNEXURES III - MASTER CHART

Sl no	Reg No.	Gender	Age	Diabetes	Duration of diabetes (Years)	Hypertension	Duration of hypertension (Years)	Dyslipidemia	IHD	Hypothyroidism	TC1	LDL1	HDL1	TGs1	TC2	LDL2	HDL2	TGs2	Treatment of hy pothyroidism	Lifestyle modification	Control of Blood sugars	Control of Hypertension	Use of statins	Discontinuation of statins	Diet modification	Physical activity modification	Dyslipidemia Knowledge	Height (cms)	Weight (Kg)	Body mass index	Waist circumference	Hip circumference	SBP	DBP	Waist:Hip ratio	Physical activity	Smoker
1	4009056	M	59	N	N/A	Y	2	Absent	N	Absent	190	116	52	109	200	112	50	110	N/A	Not done	N/A	Done	N/A	N/A	Not done	Not done	Absent	145	56	26.63	56	78	120	80	0.717948718	2.19	Y
2	3983084	M	85	N	N/A	Y	3	Absent	N	Absent	98	55	28	76	101	52	29	87	N/A	Done	N/A	Done	N/A	N/A	Not done	Not done	Absent	166	65	23.59	93	98	128	70	0.948979592	1.83	N
3	3022253	M	65	Y	8	Y	4	Absent	N	Absent	213	166	25	111	245	178	23	134	N/A	Not done	N/A	Not done	N/A	N/A	Done	Not done	Present	168	63	22.32	94	90	124	80	1.044444444	2.1	N
4	2374046	M	33	Y	1	N	N/A	Present	N	Absent	188	104	30	271	176	100	35	256	N/A	Not done	Done	N/A	Not done	Yes	Not done	Done	Absent	170	63	21.80	92	91	130	76	1.010989011	1.88	N
5	4087130	M	42	Y	1	N	N/A	Absent	N	Absent	271	147	35	443	265	142	38	383	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Not done	Absent	163	57	21.45	87	88	140	90	0.988636364	1.89	N
6	824456	M	55	N	N/A	N	N/A	Absent	N	Absent	150	97	25	141	152	101	23	156	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	166	61	22.14	84	93	138	92	0.903225806	1.7	Y
7	3417630	F	40	Y	1	Y	1	Absent	N	Present	139	77	29	166	141	76	30	171	Done	Not done	Done	Not done	N/A	N/A	Not done	Not done	Absent	166	67	24.31	92	96	126	86	0.958333333	1.91	N
8	4120611	F	65	Y	1	Y	2	Present	N	Absent	234	169	17	242	244	172	20	223	N/A	Not done	Not done	Done	Done	N/A	Done	Not done	Absent	171	70	23.94	89	99	140	90	0.898989899	2.01	N
9	4429009	F	50	Y	3	N	N/A	Absent	N	Absent	291	202	59	150	301	178	56	165	N/A	Done	Not done	N/A	N/A	N/A	Not done	Not done	Present	149	43	19.37	76	82	120	82	0.926829268	2.09	N
10	821126	M	60	Y	2	N	N/A	Absent	N	Present	230	170	47	64	210	165	34	68	Done	Not done	Not done	N/A	N/A	N/A	Not done	Done	Absent	160	56	21.88	84	87	130	76	0.965517241	1.89	Y
11	821107	M	42	Y	2	N	N/A	Present	N	Absent	174	86	22	332	186	88	23	312	N/A	Not done	Done	N/A	Not done	Yes	Not done	Not done	Absent	162	29	11.05	55	70	90	70	0.785714286	1.88	N
12	3343463	M	63	Y	3	N	N/A	Absent	N	Present	234	155	42	182	193	47	19	635	Done	Not done	Not done	N/A	N/A	N/A	Not done	Not done	Absent	162	75	28.58	103	101	130	80	1.01980198	2.29	N
13	785744	M	55	Y	1	N	N/A	Absent	N	Absent	193	47	19	635	265	154	33	291	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Not done	Absent	167	72	25.82	92	96	160	106	0.958333333	2.06	N
14	4215031	M	21	Y	5	N	N/A	Present	N	Absent	265	154	33	291	268	178	33	286	N/A	Not done	N/A	N/A	Done	N/A	Not done	Not done	Present	170	66	22.84	81	98	140	80	0.826530612	1.87	N
15	4144303	M	41	Y	2	N	N/A	Absent	N	Absent	268	178	33	286	250	183	37	151	N/A	Done	Not done	N/A	N/A	N/A	Not done	Done	Present	156	50	20.55	76	85	124	80	0.894117647	2.01	N
16	732878	M	62	Y	4	Y	2	Present	N	Absent	250	183	37	151	150	82	35	167	N/A	Not done	N/A	Not done	Not done	Yes	Not done	Not done	Absent	166	75	27.22	96	95	146	94	1.010526316	1.93	N
17	782734	M	73	Y	3	N	N/A	Present	N	Absent	150	82	35	167	118	65	21	156	N/A	Done	Not done	N/A	Done	N/A	Not done	Not done	Absent	158	49	19.63	74	84	140	78	0.880952381	2.24	N
18	4206588	M	65	Y	2	N	N/A	Absent	N	Absent	251	150	37	318	178	111	36	157	N/A	Not done	Not done	N/A	N/A	N/A	Done	Not done	Absent	163	63	23.71	89	97	118	78	0.917525773	1.78	Y
19	578989	M	54	Y	2	N	N/A	Present	N	Absent	166	100	35	154	137	76	22	197	N/A	Not done	Not done	N/A	Done	N/A	Done	Done	Absent	168	46	16.30	72	87	154	88	0.827586207	1.89	N
20	3884742	M	58	N	N/A	N	N/A	Absent	N	Absent	242	95	32	114	196	126	36	172	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	164	57	21.19	88	91	150	98	0.967032967	1.51	N
21	493907	M	65	Y	1	N	N/A	Absent	N	Absent	118	65	21	156	123	62	24	167	N/A	Done	Not done	N/A	N/A	N/A	Not done	Not done	Absent	172	70	23.66	92	96	130	88	0.958333333	2.26	Y
22	787230	F	49	Y	1	Y	3	Absent	N	Absent	178	111	36	157	146	80	54	61	N/A	Done	Done	Not done	N/A	N/A	Not done	Not done	Present	166	60	21.77	87	93	110	90	0.935483871	1.97	N
23	1655114	M	50	Y	2	N	N/A	Absent	N	Absent	137	76	22	197	196	140	36	102	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Not done	Absent	160	71	27.73	99	93	140	74	1.064516129	2.3	Y
24	632013	F	34	Y	2	N	N/A	Present	N	Present	196	126	36	172	154	99	42	67	Done	Not done	Not done	N/A	Not done	Yes	Done	Done	Absent	172	45	15.21	66	83	160	110	0.795180723	1.79	N
25	3148055	F	40	Y	3	N	N/A	Absent	N	Absent	188	106	36	230	118	75	28	75	N/A	Not done	Done	N/A	N/A	N/A	Done	Not done	Absent	159	73	28.88	103	99	146	80	1.04040404	2.19	N
26	623902	M	56	Y	1	N	N/A	Present	N	Absent	155	85	27	214	194	131	35	140	N/A	Not done	Not done	N/A	Not done	Yes	Not done	Not done	Absent	163	67	25.22	97	96	146	66	1.010416667	2.12	N
27	2432102	M	17	Y	1	Y	2	Present	N	Absent	118	65	21	156	166	57	24	424	N/A	Done	Done	Done	Done	N/A	Not done	Not done	Absent	154	47	19.82	78	89	210	120	0.876404494	2.12	N
28	2100114	F	32	Y	3	N	N/A	Absent	Y	Absent	178	102	60	77	123	61	40	107	N/A	Not done	Not done	N/A	N/A	N/A	Done	Done	Present	171	73	24.96	93	98	146	90	0.948979592	2.18	N
29	3790994	F	39	Y	2	N	N/A	Absent	N	Absent	188	133	42	66	123	64	48	57	N/A	Not done	Not done	N/A	N/A	N/A	Done	Not done	Absent	163	60	22.58	85	90	116	70	0.944444444	2.05	N
30	3910813	F	26	Y	3	N	N/A	Absent	N	Absent	146	80	54	61	113	66	33	71	N/A	Done	Not done	N/A	N/A	N/A	Not done	Not done	Absent	165	46	16.90	73	83	122	86	0.879518072	1.87	N

31	682418	M	64	N	N/A	N	N/A	Absent	N	Absent	196	140	36	102	166	57	24	424	N/A	Done	N/A	N/A	N/A	N/A	Done	Done	Absent	166	55	19.96	76	90	116	82	0.844444444	1.83	Y
32	3213286	F	26	Y	2	Y	4	Present	N	Absent	154	99	42	67	82	34	19	143	N/A	Not done	Done	Not done	Done	N/A	Done	Not done	Absent	165	67	24.61	98	94	130	66	1.042553191	1.93	N
33	816682	M	63	Y	3	N	N/A	Present	N	Absent	118	75	28	75	151	99	37	74	N/A	Not done	Not done	N/A	Not done	Yes	Not done	Not done	Present	170	72	24.91	90	98	160	70	0.918367347	2.17	N
34	694466	M	72	Y	2	N	N/A	Absent	N	Absent	173	91	71	58	158	77	58	115	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Done	Absent	157	60	24.34	87	84	124	80	1.035714286	1.83	N
35	1858630	F	49	Y	5	N	N/A	Absent	N	Absent	194	131	35	140	82	34	19	143	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Done	Absent	150	50	22.22	77	84	130	90	0.916666667	1.82	N
36	3774463	M	59	Y	10	N	N/A	Absent	N	Absent	166	57	24	424	178	56	22	412	N/A	Done	Done	N/A	N/A	N/A	Done	Not done	Absent	168	65	23.03	96	95	104	68	1.010526316	1.84	N
37	680879	M	69	Y	1	Y	1	Absent	N	Absent	136	69	32	172	151	99	37	74	N/A	Not done	Not done	Not done	N/A	N/A	Done	Not done	Present	165	79	29.02	100	94	150	90	1.063829787	1.72	N
38	3608528	M	52	N	N/A	N	N/A	Absent	N	Absent	123	61	40	107	190	116	52	109	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Done	Absent	162	40	15.24	77	80	110	70	0.9625	1.9	N
39	4336568	M	68	N	N/A	N	N/A	Absent	N	Absent	123	64	48	57	98	55	28	76	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	166	56	20.32	85	91	124	70	0.934065934	1.73	N
40	4207500	F	61	N	N/A	N	N/A	Present	N	Absent	113	66	33	71	213	166	25	111	N/A	Not done	N/A	N/A	Not done	Yes	Done	Done	Present	155	44	18.31	74	80	120	80	0.925	1.87	N
41	2042381	F	43	Y	2	N	N/A	Present	N	Absent	166	57	24	424	188	104	30	271	N/A	Done	Done	N/A	Done	N/A	Done	Not done	Absent	162	58	22.10	83	89	106	88	0.93258427	1.84	N
42	4024270	F	57	Y	5	Y	0.5	Absent	Y	Present	82	34	19	143	150	97	25	141	Done	Not done	N/A	Not done	N/A	N/A	Not done	Not done	Absent	180	64	19.75	92	88	120	84	1.045454545	1.77	N
43	4146301	M	18	Y	6	N	N/A	Absent	Y	Absent	151	99	37	74	139	77	29	166	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	167	60	21.51	91	93	150	94	0.978494624	1.83	Y
44	3297044	F	46	Y	3	N	N/A	Present	N	Absent	133	66	40	137	234	169	17	242	N/A	Not done	Not done	N/A	Done	N/A	Done	Done	Absent	158	53	21.23	88	88	120	88	1	2.03	N
45	3632850	F	57	Y	2	N	N/A	Absent	N	Absent	119	47	43	144	291	202	59	150	N/A	Done	Not done	N/A	N/A	N/A	Done	Done	Present	168	60	21.26	95	94	160	100	1.010638298	1.94	N
46	3448274	F	60	Y	1	N	N/A	Present	N	Absent	158	77	58	115	174	86	22	332	N/A	Not done	Done	N/A	Not done	Yes	Not done	Not done	Present	161	37	14.27	66	75	120	80	0.88	1.64	N
47	1472597	F	40	Y	4	Y	0.5	Present	N	Present	309	232	44	165	193	47	19	635	Not done	Not done	N/A	Done	Done	N/A	Not done	Not done	Absent	153	59	25.20	84	91	116	90	0.923076923	1.84	N
48	731434	M	46	N	N/A	N	N/A	Absent	N	Absent	82	34	19	143	265	154	33	291	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	167	70	25.10	97	92	140	90	1.054347826	2.05	N
49	583261	F	46	N	N/A	N	N/A	Absent	N	Absent	166	57	24	424	268	178	33	286	N/A	Done	N/A	N/A	N/A	N/A	Done	Done	Absent	161	49	18.90	77	81	160	110	0.950617284	1.98	N
50	597610	F	54	Y	1	Y	2	Present	Y	Absent	151	99	37	74	211	151	43	85	N/A	Not done	Not done	Done	Not done	Yes	Not done	Done	Absent	162	53	20.20	85	85	170	90	1	1.87	N
51	4174467	M	58	Y	1	N	N/A	Absent	Y	Present	190	116	52	109	142	82	38	113	Done	Done	Not done	N/A	N/A	N/A	Not done	Not done	Absent	161	50	19.29	71	81	132	96	0.87654321	1.85	N
52	3322233	M	26	Y	4	N	N/A	Absent	N	Absent	98	55	28	76	155	96	31	141	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Present	167	60	21.51	100	83	140	100	1.204819277	1.7	N
53	2476805	M	57	N	N/A	N	N/A	Absent	N	Absent	213	166	25	111	133	73	38	108	N/A	Not done	N/A	N/A	N/A	N/A	Done	Not done	Absent	165	34	12.49	65	74	110	80	0.878378378	2.02	N
54	803866	F	63	Y	2	Y	2	Present	N	Absent	188	104	30	271	205	138	40	136	N/A	Not done	Not done	Done	Not done	Yes	Not done	Not done	Absent	172	60	20.28	79	91	100	70	0.868131868	2.14	N
55	981719	F	40	Y	2	N	N/A	Absent	N	Present	271	147	35	443	190	116	52	109	Done	Not done	Done	N/A	N/A	N/A	Not done	Done	Present	167	75	26.89	98	97	140	96	1.010309278	2	N
56	775757	M	58	N	N/A	N	N/A	Absent	Y	Present	150	97	25	141	98	55	28	76	Not done	Done	N/A	N/A	N/A	N/A	Not done	Done	Absent	171	53	18.13	84	88	102	68	0.954545455	2.12	Y
57	719695	F	58	Y	5	N	N/A	Absent	N	Absent	139	77	29	166	213	166	25	111	N/A	Not done	N/A	N/A	N/A	N/A	Done	Not done	Absent	174	52	17.18	77	85	124	82	0.905882353	2.08	N
58	592849	M	55	Y	4	Y	5	Present	Y	Absent	234	169	17	242	188	104	30	271	N/A	Done	N/A	Not done	Done	N/A	Not done	Done	Absent	169	67	23.46	99	98	190	100	1.010204082	2.03	N
59	2918718	F	29	Y	2	N	N/A	Absent	Y	Absent	291	202	59	150	271	147	35	443	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Not done	Present	164	51	18.96	73	82	110	86	0.890243902	1.83	N
60	3855206	M	61	Y	1	N	N/A	Present	N	Absent	230	170	47	64	150	97	25	141	N/A	Not done	Not done	N/A	Done	N/A	Not done	Done	Absent	163	46	17.31	60	81	160	120	0.740740741	1.74	Y
61	3695518	F	67	N	N/A	N	N/A	Absent	N	Present	174	86	22	332	139	77	29	166	Done	Not done	N/A	N/A	N/A	N/A	Done	Not done	Absent	157	44	17.85	75	80	150	80	0.9375	1.75	N
62	3205955	F	72	Y	1	Y	5	Present	N	Absent	193	47	19	635	234	169	17	242	N/A	Done	Done	Not done	Not done	Yes	Not done	Not done	Absent	176	55	17.76	74	83	104	76	0.891566265	1.87	N
63	1621427	F	30	N	N/A	N	N/A	Absent	N	Absent	265	154	33	291	230	170	47	64	N/A	Done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	165	44	16.16	74	82	114	80	0.902439024	2.03	N
64	732077	F	78	Y	1	N	N/A	Absent	Y	Absent	268	178	33	286	174	86	22	332	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Not done	Absent	158	55	22.03	89	90	130	78	0.988888889	1.83	N
65	782600	M	62	Y	3	N	N/A	Absent	N	Absent	211	151	43	85	193	47	19	635	N/A	Not done	Not done	N/A	N/A	N/A	Done	Done	Absent	165	76	27.92	106	104	180	120	1.019230769	2	Y
66	3476050	F	49	Y	4	Y	6	Present	N	Absent	142	82	38	113	133	73	38	108	N/A	Not done	N/A	Not done	Not done	Yes	Not done	Done	Absent	160	47	18.36	84	85	126	78	0.988235294	1.75	N
67	3262115	F	25	N	N/A	N	N/A	Present	N	Absent	155	96	31	141	234	155	42	182	N/A	Done	N/A	N/A	Done	N/A	Not done	Not done	Absent	152	50	21.64	86	84	130	95	1.023809524	1.74	N
68	3323287	F	53	Y	3	N	N/A	Absent	N	Absent	133	73	38	108	193	47	19	635	N/A	Done	Not done	N/A	N/A	N/A	Done	Done	Absent	167	64	22.95	92	92	136	70	1	1.88	N
69	625734	M	61	Y	3	N	N/A	Absent	N	Absent	205	138	40	136	265	154	33	291	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Not done	Absent	170	67	23.18	88	97	130	64	0.907216495	2.1	Y
70	750293	M	67	Y	3	Y	1	Absent	N	Absent	190	116	52	109	133	73	38	108	N/A	Not done	Not done	Done	N/A	N/A	Not done	Not done	Absent	174	60	19.82	88	86	116	78	1.023255814	2.1	N
71	3304686	M	69	Y	1	N	N/A	Absent	N	Absent	98	55	28	76	198	130	45	117	N/A	Not done	Done	N/A	N/A	N/A	Not done	Not done	Absent	154	35	14.76	66	78	114	82	0.846153846	2.17	Y
72	755290	F	60	Y	2	N	N/A	Present	Y	Absent	213	166	25	111	204	125	57	112	N/A	Done	Not done	N/A	Not done	Yes	Done	Not done	Absent	168	50	17.72	81	87	160	82	0.931034483	1.94	N
73	742070	M	60	Y	3	N	N/A	Present	N	Absent	188	104	30	271	136	74	48	71	N/A	Not done	Not done	N/A	Done	N/A	Not done	Done	Present	157	62	25.15	100	93	124	80	1.075268817	1.47	N
74	2863622	M	58	N	N/A	N	N/A	Absent	N	Absent	271	147	35	443	194	95	54	226	N/A	Done	N/A	N/A	N/A	N/A	Not done	Done	Absent	168	75	26.57	105	99	160	100	1.060606061	1.97	N
75	4166615	M	65	Y	5	N	N/A	Absent	Y	Absent	150	97	25	141	214	155	34	124	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	162	59	22.48	84	94	120	86	0.893617021	1.78	Y
76	3451044	F	42	N	N/A	N	N/A	Absent	N	Present	139	77	29	166	223	144	46	167	Done	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Present	175	36	11.76	57	77	104	64	0.74025974	2.12	N
77	789112	M	48	Y	1	Y	5	Present	Y	Absent	234	169	17	242	228	124	89	77	N/A	Not done	Done	Not done	Not done	Yes	Done	Not done	Absent	166	65	23.59	94	90	150	126	1.044444444	2.19	Y
78	3892647	F	27	Y	3	N	N/A	Present	N	Present	291	202	59	150	186	117	32	187	Done	Done	Not done	N/A	Not done	Yes	Not done	Done	Absent	155	29	12.07	57	72	104	60	0.791666667	1.76	N
79	4091075	M	48	Y	2	N	N/A	Absent	N	Absent	230	170	47	64	234	153	44	184	N/A	Done	Not done	N/A	N/A	N/A	Not done	Done	Absent	159	44	17.40	66	82	124	86	0.804878049	1.86	N
80	1378178	M	60	Y	2	N	N/A	Absent	Y	Absent	174	86	22	332	208	154	44	52	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Done	Present	161	65	25.08	98	99	160	85	0.98989899	1.86	N

81	2107020	M	37	N	N/A	N	N/A	Absent	Y	Absent	234	155	42	182	112	45	33	171	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Present	172	55	18.59	76	82	118	70	0.926829268	1.76	Y
82	4260485	F	60	Y	1	N	N/A	Present	Y	Absent	193	47	19	635	239	146	54	193	N/A	Done	Done	N/A	Done	N/A	Done	Not done	Absent	156	43	17.67	76	77	112	80	0.987012987	1.62	N
83	799462	F	68	Y	1	Y	1	Present	N	Absent	265	154	33	291	231	170	36	125	N/A	Done	Not done	Done	Done	N/A	Not done	Not done	Absent	115	40	30.25	66	78	150	112	0.846153846	2.06	N
84	2579054	F	50	N	N/A	N	N/A	Absent	Y	Absent	133	73	38	108	215	128	38	243	N/A	Done	N/A	N/A	N/A	N/A	Not done	Done	Present	155	41	17.07	76	84	124	76	0.904761905	2.3	N
85	655957	F	53	Y	2	N	N/A	Absent	N	Absent	234	155	42	182	174	99	45	146	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Done	Absent	168	70	24.80	91	95	140	100	0.957894737	2.13	N
86	3680644	F	36	Y	2	N	N/A	Absent	Y	Present	193	47	19	635	175	129	28	92	Done	Not done	Not done	N/A	N/A	N/A	Done	Not done	Absent	168	56	19.84	79	89	118	75	0.887640449	2.08	N
87	4267236	F	50	Y	1	Y	1	Present	N	Absent	265	154	33	291	212	133	46	166	N/A	Not done	Not done	Done	Done	N/A	Not done	Not done	Present	148	43	19.63	80	83	144	78	0.963855422	1.67	N
88	3589824	M	50	Y	2	Y	5	Absent	N	Absent	133	73	38	108	167	98	42	136	N/A	Done	Done	Not done	N/A	N/A	Not done	Not done	Absent	155	58	24.14	93	94	140	84	0.989361702	1.78	N
89	1682689	M	57	Y	4	Y	5	Absent	Y	Absent	88	40	23	125	177	127	37	63	N/A	Done	N/A	Not done	N/A	N/A	Not done	Done	Present	168	64	22.68	89	90	126	78	0.988888889	2.28	Y
90	3422377	M	41	Y	4	N	N/A	Present	Y	Absent	226	136	45	236	204	125	57	112	N/A	Not done	N/A	N/A	Not done	Yes	Done	Done	Present	166	78	28.31	98	104	120	90	0.942307692	1.84	N
91	4270672	F	28	N	N/A	N	N/A	Absent	Y	Absent	198	130	45	117	136	74	48	71	N/A	Not done	N/A	N/A	N/A	N/A	Done	Not done	Absent	153	45	19.22	75	85	170	90	0.882352941	2.1	N
92	4269012	M	77	N	N/A	N	N/A	Absent	N	Absent	204	125	57	112	194	95	54	226	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	148	56	25.57	86	91	132	90	0.945054945	1.85	N
93	789417	M	66	Y	1	N	N/A	Present	N	Absent	136	74	48	71	223	144	46	167	N/A	Done	Not done	N/A	Not done	Yes	Not done	Not done	Present	175	78	25.47	106	104	128	90	1.019230769	2.28	Y
94	792828	F	64	Y	1	N	N/A	Absent	N	Absent	194	95	54	226	214	155	34	124	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Not done	Absent	163	73	27.48	101	104	116	80	0.971153846	2.15	N
95	1998165	M	49	Y	2	Y	1	Present	N	Absent	223	144	46	167	182	71	44	334	N/A	Not done	Not done	Not done	Done	N/A	Not done	Done	Present	166	45	16.33	71	98	114	84	0.724489796	1.86	N
96	2135172	M	39	Y	2	Y	1	Present	Y	Absent	214	155	34	124	164	114	32	89	N/A	Not done	Not done	Done	Not done	Yes	Done	Done	Absent	155	54	22.48	82	90	110	80	0.911111111	1.76	N
97	732509	M	41	Y	1	N	N/A	Absent	N	Absent	223	144	46	167	151	75	47	147	N/A	Not done	Done	N/A	N/A	N/A	Done	Not done	Present	167	86	30.84	116	110	124	84	1.054545455	2.22	N
98	6403995	M	61	Y	2	N	N/A	Present	Y	Absent	228	124	89	77	191	120	40	157	N/A	Not done	Not done	N/A	Not done	Yes	Not done	Not done	Absent	163	73	27.48	95	98	130	80	0.969387755	2.08	Y
99	3340304	M	69	Y	3	Y	2	Absent	N	Absent	186	117	32	187	88	40	23	125	N/A	Not done	Not done	Not done	N/A	N/A	Not done	Not done	Absent	171	69	23.60	98	91	190	110	1.076923077	1.7	N
100	1460559	F	51	Y	2	N	N/A	Absent	N	Absent	234	153	44	184	226	136	45	236	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Not done	Present	156	63	25.89	96	95	110	70	1.010526316	1.64	N
101	777458	M	55	Y	1	Y	3	Present	N	Absent	176	118	34	121	198	130	45	117	N/A	Done	Done	Not done	Done	N/A	Not done	Done	Absent	177	80	25.54	88	100	150	66	0.88	1.9	N
102	3649721	M	62	N	N/A	N	N/A	Present	Y	Absent	220	144	44	159	250	136	45	236	N/A	Done	N/A	N/A	Not done	Yes	Done	Done	Present	161	46	17.75	66	82	110	76	0.804878049	2.19	Y
103	660812	F	48	N	N/A	N	N/A	Absent	Y	Absent	140	90	33	85	120	41	35	222	N/A	Not done	N/A	N/A	N/A	N/A	Done	Not done	Absent	158	81	32.45	109	108	150	78	1.009259259	1.83	N
104	703862	F	53	Y	1	Y	2	Absent	Y	Absent	208	154	44	52	175	116	47	62	N/A	Not done	Not done	Done	N/A	N/A	Not done	Not done	Absent	163	68	25.59	91	94	118	86	0.968085106	2.1	N
105	750869	M	51	Y	1	N	N/A	Present	N	Absent	112	45	33	171	118	68	36	71	N/A	Done	Not done	N/A	Done	N/A	Not done	Not done	Absent	159	60	23.73	90	95	138	70	0.947368421	1.88	N
106	2533855	M	58	Y	4	N	N/A	Absent	N	Absent	239	146	54	193	195	143	34	90	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	173	62	20.72	83	82	148	90	1.012195122	1.89	N
107	3905037	F	65	Y	1	Y	1	Absent	N	Present	231	170	36	125	189	139	34	79	Done	Not done	Done	Done	N/A	N/A	Not done	Done	Absent	162	48	18.29	73	80	114	68	0.9125	1.7	N
108	785261	M	61	N	N/A	N	N/A	Present	N	Absent	215	128	38	243	163	105	29	144	N/A	Not done	N/A	N/A	Not done	Yes	Not done	Done	Present	152	53	22.94	84	83	140	90	1.012048193	1.91	N
109	1454738	M	21	Y	2	Y	1	Present	N	Absent	174	99	45	146	190	84	28	392	N/A	Not done	Not done	Not done	Done	N/A	Not done	Not done	Absent	169	54	18.91	70	85	102	64	0.817647059	2.01	Y
110	4293324	F	19	Y	0.5	N	N/A	Absent	N	Absent	175	129	28	92	185	84	28	392	N/A	Done	Not done	N/A	N/A	N/A	Done	Not done	Absent	165	66	24.24	83	101	112	69	0.821782178	2.09	N
111	3268371	M	71	N	N/A	N	N/A	Absent	N	Absent	212	133	46	166	264	187	62	72	N/A	Done	N/A	N/A	N/A	N/A	Done	Not done	Absent	170	53	18.34	70	86	119	74	0.813953488	1.89	N
112	794304	M	77	Y	0.75	Y	2	Absent	N	Absent	129	77	34	92	143	94	29	98	N/A	Not done	Done	Not done	N/A	N/A	Not done	Not done	Absent	173	53	17.71	73	86	99	61	0.848837209	1.88	N
113	4295441	F	38	N	N/A	N	N/A	Absent	Y	Absent	167	98	42	136	163	105	29	144	N/A	Done	N/A	N/A	N/A	N/A	Not done	Done	Present	161	46	17.75	64	85	114	80	0.752941176	2.29	N
114	3719025	M	26	Y	1	N	N/A	Present	N	Absent	177	127	37	63	166	89	61	81	N/A	Done	Not done	N/A	Done	N/A	Not done	Not done	Absent	173	80	26.73	92	103	142	89	0.897560976	2.06	N
115	4270255	F	52	Y	3	N	N/A	Absent	N	Absent	204	125	57	112	190	84	28	392	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Done	Absent	150	59	26.22	73	87	126	77	0.83908046	1.87	N
116	2804479	M	60	N	N/A	N	N/A	Absent	N	Absent	136	74	48	71	185	84	28	392	N/A	Done	N/A	N/A	N/A	N/A	Done	Not done	Absent	175	55	17.96	69	70	138	78	0.985714286	2.01	N
117	547730	M	55	Y	0.5	N	N/A	Absent	Y	Absent	194	95	54	226	264	187	62	72	N/A	Done	Done	N/A	N/A	N/A	Done	Not done	Present	176	64	20.66	80	96	128	70	0.833333333	1.93	N
118	3460694	F	48	N	N/A	N	N/A	Present	N	Present	223	144	46	167	143	94	29	98	Done	Not done	N/A	N/A	Done	N/A	Not done	Not done	Present	171	63	21.55	76	90.5	118	63	0.839779006	2.24	N
119	829134	F	47	Y	1	N	N/A	Absent	N	Absent	214	155	34	124	170	107	40	117	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Not done	Absent	168	67	23.74	85	92	140	86	0.923913043	1.78	N
120	897923	F	50	Y	1	N	N/A	Present	N	Absent	182	71	44	334	218	141	42	174	N/A	Done	Not done	N/A	Not done	Yes	Not done	Not done	Absent	174	60	19.82	73	86.5	133	58	0.838150289	1.89	N
121	796720	M	65	N	N/A	N	N/A	Absent	N	Absent	164	114	32	89	146	97	32	83	N/A	Done	N/A	N/A	N/A	N/A	Not done	Done	Present	177	65	20.75	82	93.5	127	82	0.877005348	1.51	Y
122	2094682	F	34	Y	2	N	N/A	Absent	N	Absent	151	75	47	147	173	96	51	129	N/A	Not done	Not done	N/A	N/A	N/A	Done	Done	Absent	174	79	26.09	96	108	138	70	0.888888889	2.26	N
123	3670283	F	49	N	N/A	N	N/A	Absent	N	Absent	230	107	45	481	203	127	37	196	N/A	Done	N/A	N/A	N/A	N/A	Done	Not done	Absent	178	61	19.25	84	91	132	81	0.923076923	1.97	N
124	791465	M	62	Y	2	N	N/A	Present	Y	Absent	191	120	40	157	217	127	37	196	N/A	Done	Not done	N/A	Done	N/A	Not done	Not done	Absent	172	57	19.27	76	90	131	75	0.844444444	2.3	N
125	774364	M	57	Y	3	N	N/A	Present	N	Absent	88	40	23	125	238	173	33	162	N/A	Done	Done	N/A	Done	N/A	Not done	Not done	Absent	165	60	22.04	80	93	111	79	0.85483871	1.79	N
126	3203790	M	47	Y	2	N	N/A	Absent	N	Absent	226	136	45	236	215	129	33	267	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Done	Present	162	49	18.67	70	85.5	121	71	0.81871345	2.19	Y
127	668375	M	56	N	N/A	N	N/A	Absent	N	Absent	198	130	45	117	138	73	18	237	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Done	Absent	180	62	19.14	79	91.5	123	80	0.863387978	2.12	N
128	1164962	F	40	N	N/A	N	N/A	Absent	N	Absent	250	136	45	236	142	58	40	219	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	173	64	21.38	83	94	119	59	0.882978723	2.12	N
129	3746592	M	29	N	N/A	N	N/A	Absent	N	Absent	120	41	35	222	260	214	24	108	N/A	Not done	N/A	N/A	N/A	N/A	Done	Not done	Present	170	55	19.03	74	88	123	75	0.840909091	2.18	Y
130	4324843	F	24	N	N/A	N	N/A	Absent	N	Absent	175	116	47	62	153	109	24	98	N/A	Done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	174	50	16.51	65	84	119	65	0.773809524	2.05	N

131	4324337	F	22	N	N/A	N	N/A	Absent	N	Absent	118	68	36	71	174	151	107	121	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	177	98	31.28	108	120	138	87	0.9	1.87	N
132	4288515	M	20	N	N/A	N	N/A	Absent	N	Absent	195	143	34	90	279	190	53	182	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	166	50	18.14	17	87	134	64	0.195402299	1.83	N
133	770936	M	56	Y	1	N	N/A	Absent	N	Absent	105	56	37	62	116	67	32	76	N/A	Not done	Not done	N/A	N/A	N/A	Not done	Done	Present	168	65	23.03	82	93	144	89	0.88172043	1.93	Y
134	4330611	F	68	N	N/A	N	N/A	Absent	Y	Absent	189	139	34	79	101	48	33	99	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Done	Absent	164	47	17.47	67	83	102	59	0.807228916	2.17	N
135	4336915	F	30	N	N/A	N	N/A	Absent	N	Absent	163	105	29	144	174	103	47	122	N/A	Done	N/A	N/A	N/A	N/A	Done	Done	Absent	174	65	21.47	80	96	114	64	0.833333333	1.83	N
136	752827	M	73	Y	2	N	N/A	Present	N	Absent	166	89	61	81	218	141	42	174	N/A	Done	Done	N/A	Done	N/A	Done	Not done	Absent	166	54	19.60	74	92	114	61	0.804347826	1.82	Y
137	4337592	M	24	N	N/A	N	N/A	Absent	Y	Absent	190	84	28	392	146	97	32	83	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	173	66	22.05	92	101	131	76	0.915422886	1.84	N
138	3281625	F	20	N	N/A	N	N/A	Absent	N	Present	185	84	28	392	173	96	51	129	Done	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	173	60	20.05	81	92.5	119	66	0.875675676	1.72	N
139	3283106	F	56	N	N/A	N	N/A	Absent	N	Absent	264	187	62	72	203	127	37	196	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	179	69	21.53	83	97	110	62	0.855670103	1.9	N
140	4347897	M	74	Y	1	N	N/A	Absent	N	Absent	143	94	29	98	217	127	37	196	N/A	Done	Not done	N/A	N/A	N/A	Done	Not done	Absent	155	54	22.48	79	90	138	80	0.877777778	1.73	Y
141	4349455	F	18	N	N/A	N	N/A	Absent	N	Present	163	105	29	144	177	99	38	200	Done	Not done	N/A	N/A	N/A	N/A	Done	Not done	Absent	177	60	19.15	74	91	116	65	0.807692308	1.87	N
142	3647136	F	25	Y	4	N	N/A	Absent	N	Absent	166	89	61	81	238	173	33	162	N/A	Done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	173	58	19.38	76	89.5	146	98	0.849162011	1.84	N
143	640608	M	59	N	N/A	N	N/A	Absent	N	Absent	190	84	28	392	215	129	33	267	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	174	79	26.09	96	108	138	70	0.888888889	1.77	N
144	783794	M	47	N	N/A	N	N/A	Absent	Y	Present	185	84	28	392	138	73	18	237	Done	Not done	N/A	N/A	N/A	N/A	Not done	Done	Absent	178	61	19.25	84	91	132	81	0.923076923	1.83	Y
145	4074622	M	27	Y	2	N	N/A	Absent	Y	Absent	264	187	62	72	142	58	40	219	N/A	Not done	Done	N/A	N/A	N/A	Done	Not done	Absent	172	57	19.27	76	90	131	75	0.844444444	2.03	Y
146	1425406	M	67	N	N/A	N	N/A	Absent	N	Absent	143	94	29	98	260	214	24	108	N/A	Done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	165	60	22.04	80	93	111	79	0.85483871	1.94	N
147	3589824	M	50	Y	1	N	N/A	Present	Y	Absent	170	107	40	117	153	109	24	98	N/A	Done	Not done	N/A	Done	N/A	Not done	Not done	Absent	162	49	18.67	70	85.5	121	71	0.81871345	1.64	Y
148	4354196	F	68	N	N/A	N	N/A	Absent	Y	Absent	218	141	42	174	199	140	30	143	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Done	Absent	180	62	19.14	79	91.5	123	80	0.863387978	1.84	N
149	809750	F	53	Y	3	N	N/A	Absent	N	Absent	146	97	32	83	125	69	28	142	N/A	Not done	Not done	N/A	N/A	N/A	Done	Not done	Absent	175	36	11.76	57	77	104	64	0.74025974	2.05	N
150	4411905	M	48	Y	2	N	N/A	Absent	N	Absent	173	96	51	129	127	68	29	148	N/A	Not done	Done	N/A	N/A	N/A	Not done	Not done	Absent	166	65	23.59	94	90	150	126	1.044444444	1.98	Y
151	4049861	F	56	N	N/A	N	N/A	Absent	N	Absent	203	127	37	196	279	190	53	182	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	155	29	12.07	57	72	104	60	0.791666667	1.87	N
152	3546461	M	52	N	N/A	N	N/A	Absent	N	Absent	217	127	37	196	116	67	32	76	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Done	Absent	159	44	17.40	66	82	124	86	0.804878049	1.85	Y
153	2952803	M	66	N	N/A	N	N/A	Absent	N	Absent	177	99	38	200	101	48	33	99	N/A	Not done	N/A	N/A	N/A	N/A	Done	Not done	Absent	161	65	25.08	98	99	160	85	0.98989899	1.7	Y
154	824780	F	64	N	N/A	N	N/A	Absent	Y	Absent	238	173	33	162	174	103	47	122	N/A	Done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	175	36	11.76	57	77	104	64	0.74025974	2.02	N
155	824848	M	53	Y	1	N	N/A	Absent	N	Absent	215	129	33	267	218	141	42	174	N/A	Done	Not done	N/A	N/A	N/A	Not done	Not done	Absent	166	65	23.59	94	90	150	126	1.044444444	2.14	N
156	817782	F	35	Y	4	N	N/A	Absent	N	Absent	138	73	18	237	279	190	53	182	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Done	Absent	155	29	12.07	57	72	104	60	0.791666667	2	N
157	821507	F	70	Y	1	N	N/A	Absent	N	Absent	142	58	40	219	116	67	32	76	N/A	Not done	Not done	N/A	N/A	N/A	Done	Not done	Absent	156	63	25.89	96	95	110	70	1.010526316	2.12	N
158	821497	M	44	N	N/A	N	N/A	Absent	N	Absent	260	214	24	108	101	48	33	99	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	177	80	25.54	88	100	150	66	0.88	2.08	N
159	824455	M	65	N	N/A	N	N/A	Absent	N	Absent	153	109	24	98	174	103	47	122	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	161	46	17.75	66	82	110	76	0.804878049	2.03	Y
160	823463	M	43	N	N/A	N	N/A	Absent	N	Absent	174	151	107	121	218	141	42	174	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	158	81	32.45	109	108	150	78	1.009259259	1.83	Y
161	823989	F	59	N	N/A	N	N/A	Absent	N	Absent	279	190	53	182	263	187	51	176	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Done	Absent	163	68	25.59	91	94	118	86	0.968085106	1.74	N
162	888706	M	73	N	N/A	Y	3	Absent	N	Absent	116	67	32	76	121	72	36	98	N/A	Done	N/A	Not done	N/A	N/A	Done	Not done	Absent	155	41	17.07	76	84	124	76	0.904761905	1.75	N
163	889513	M	76	N	N/A	Y	1	Present	Y	Absent	101	48	33	99	112	43	45	121	N/A	Done	N/A	Done	Not done	Yes	Not done	Not done	Absent	168	70	24.80	91	95	140	100	0.957894737	1.87	Y
164	889307	M	41	N	N/A	Y	2	Absent	Y	Absent	174	103	47	122	186	113	50	120	N/A	Done	N/A	Not done	N/A	N/A	Not done	Not done	Absent	168	56	19.84	79	89	118	75	0.887640449	2.03	N
165	889700	M	61	N	N/A	N	N/A	Absent	N	Absent	218	141	42	174	212	137	43	176	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	148	43	19.63	80	83	144	78	0.963855422	1.83	N
166	888353	M	52	N	N/A	N	N/A	Absent	N	Absent	146	97	32	83	151	101	30	97	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	155	58	24.14	93	94	140	84	0.989361702	2	N
167	890426	M	63	Y	0.5	Y	1	Absent	N	Present	173	96	51	129	192	101	47	126	Not done	Not done	Not done	Not done	N/A	N/A	Done	Not done	Absent	168	64	22.68	89	90	126	78	0.988888889	1.75	Y
168	890359	M	39	N	N/A	N	N/A	Absent	N	Absent	203	127	37	196	200	123	34	187	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Done	Absent	166	78	28.31	98	104	120	90	0.942307692	1.74	N
169	889535	F	68	N	N/A	N	N/A	Absent	N	Absent	217	127	37	196	222	132	34	212	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	153	45	19.22	75	85	170	90	0.882352941	1.88	N
170	889861	M	60	Y	1	N	N/A	Present	N	Absent	177	99	38	200	187	101	36	213	N/A	Not done	Not done	N/A	Done	N/A	Not done	Not done	Absent	148	56	25.57	86	91	132	90	0.945054945	2.1	N
171	890099	M	40	N	N/A	N	N/A	Absent	N	Absent	238	173	33	162	235	172	32	167	N/A	Not done	N/A	N/A	N/A	N/A	Done	Not done	Absent	175	78	25.47	106	104	128	90	1.019230769	2.1	Y
172	891093	M	55	N	N/A	Y	0.5	Absent	N	Absent	215	129	33	267	223	131	34	250	N/A	Not done	N/A	Done	N/A	N/A	Not done	Done	Absent	163	73	27.48	101	104	116	80	0.971153846	2.17	Y
173	891160	F	59	N	N/A	N	N/A	Absent	N	Absent	138	73	18	237	199	140	30	143	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	166	45	16.33	71	98	114	84	0.724489796	1.94	N
174	890288	F	52	N	N/A	N	N/A	Absent	N	Absent	142	58	40	219	134	45	67	209	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	155	54	22.48	82	90	110	80	0.911111111	1.47	N
175	890529	M	70	Y	2	N	N/A	Absent	N	Absent	260	214	24	108	265	223	22	125	N/A	Not done	Done	N/A	N/A	N/A	Done	Not done	Absent	167	86	30.84	116	110	124	84	1.054545455	1.97	N
176	890992	M	51	N	N/A	N	N/A	Absent	N	Absent	153	109	24	101	151	102	25	103	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Done	Absent	163	73	27.48	95	98	130	80	0.969387755	1.78	Y
177	889531	F	57	N	N/A	Y	0.5	Absent	N	Absent	199	140	30	143	203	145	32	132	N/A	Not done	N/A	Not done	N/A	N/A	Not done	Not done	Absent	171	69	23.60	98	91	190	110	1.076923077	2.12	N
178	889687	F	66	Y	1	Y	1	Present	N	Absent	125	69	28	142	135	78	26	165	N/A	Not done	Not done	Done	Not done	Yes	Not done	Not done	Absent	156	63	25.89	96	95	110	70	1.010526316	2.19	N
179	825607	M	56	N	N/A	N	N/A	Absent	N	Absent	127	68	29	148	131	67	34	142	N/A	Not done	N/A	N/A	N/A	N/A	Done	Not done	Absent	177	80	25.54	88	100	150	66	0.88	1.76	N
180	832581	F	28	N	N/A	N	N/A	Absent	N	Absent	279	190	53	196	200	123	34	187	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Done	Absent	161	46	17.75	66	82	110	76	0.804878049	1.86	N

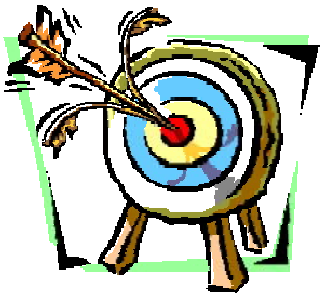
181	867543	F	75	N	N/A	N	N/A	Absent	N	Absent	116	67	32	196	222	132	34	212	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	158	81	32.45	109	108	150	78	1.009259259	1.86	N
182	829697	F	66	N	N/A	N	N/A	Absent	N	Absent	101	48	33	200	187	101	36	213	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	163	68	25.59	91	94	118	86	0.968085106	1.76	N
183	830376	M	60	N	N/A	N	N/A	Absent	N	Absent	174	103	47	196	200	123	34	187	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	159	60	23.73	90	95	138	70	0.947368421	1.62	Y
184	854698	F	35	N	N/A	N	N/A	Absent	N	Absent	218	141	42	196	222	132	34	212	N/A	Done	N/A	N/A	N/A	N/A	Done	Not done	Absent	173	62	20.72	83	82	148	90	1.012195122	2.06	N
185	829551	M	48	N	N/A	N	N/A	Absent	N	Absent	279	190	53	196	200	123	34	187	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Done	Absent	156	63	25.89	96	95	110	70	1.010526316	2.3	N
186	829350	F	61	N	N/A	N	N/A	Absent	N	Absent	116	67	32	196	222	132	34	212	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	177	80	25.54	88	100	150	66	0.88	2.13	N
187	829087	M	40	N	N/A	N	N/A	Absent	N	Absent	101	48	33	200	187	101	36	213	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	161	46	17.75	66	82	110	76	0.804878049	2.08	Y
188	828365	M	22	N	N/A	N	N/A	Absent	N	Absent	174	103	47	162	235	172	32	167	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	158	81	32.45	109	108	150	78	1.009259259	1.67	N
189	829122	M	57	N	N/A	N	N/A	Absent	N	Absent	218	141	42	196	200	123	34	187	N/A	Not done	N/A	N/A	N/A	N/A	Done	Done	Absent	163	68	25.59	91	94	118	86	0.968085106	1.78	Y
190	830755	M	50	N	N/A	N	N/A	Absent	N	Absent	279	190	53	196	222	132	34	212	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	177	80	25.54	88	100	150	66	0.88	2.28	Y
191	830340	M	40	N	N/A	N	N/A	Absent	N	Absent	116	67	32	200	187	101	36	213	N/A	Done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	161	46	17.75	66	82	110	76	0.804878049	1.84	N
192	824600	F	45	N	N/A	N	N/A	Absent	N	Absent	101	48	33	162	235	172	32	167	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	158	81	32.45	109	108	150	78	1.009259259	2.1	N
193	825607	M	56	N	N/A	N	N/A	Absent	N	Absent	174	103	47	267	223	131	34	250	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	163	68	25.59	91	94	118	86	0.968085106	1.85	Y
194	829121	M	55	N	N/A	N	N/A	Absent	N	Absent	218	141	42	237	199	140	30	143	N/A	Not done	N/A	N/A	N/A	N/A	Done	Done	Absent	155	41	17.07	76	84	124	76	0.904761905	2.28	N
195	827928	F	31	N	N/A	N	N/A	Absent	N	Absent	146	97	32	219	134	45	67	209	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	168	70	24.80	91	95	140	100	0.957894737	2.15	N
196	828387	M	35	N	N/A	N	N/A	Absent	N	Absent	173	96	51	196	200	123	34	187	N/A	Done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	168	56	19.84	79	89	118	75	0.887640449	1.86	Y
197	827010	M	50	N	N/A	N	N/A	Absent	N	Absent	203	127	37	196	222	132	34	212	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Done	Absent	148	43	19.63	80	83	144	78	0.963855422	1.76	Y
198	828010	F	45	N	N/A	N	N/A	Absent	N	Absent	217	127	37	200	187	101	36	213	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	155	58	24.14	93	94	140	84	0.989361702	2.22	N
199	828041	F	65	N	N/A	N	N/A	Absent	N	Absent	177	99	38	162	235	172	32	167	N/A	Done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	168	64	22.68	89	90	126	78	0.988888889	2.08	N
200	828022	M	54	N	N/A	N	N/A	Absent	N	Absent	238	173	33	267	223	131	34	250	N/A	Not done	N/A	N/A	N/A	N/A	Not done	Not done	Absent	166	78	28.31	98	104	120	90	0.942307692	1.7	Y

ANNEXURE-IV

KEY TO MASTER CHART

Male	-	M
Female	-	F
Not Applicable	-	N/A
IHD- Y	-	YES; N-NO

Introduction



Objectives

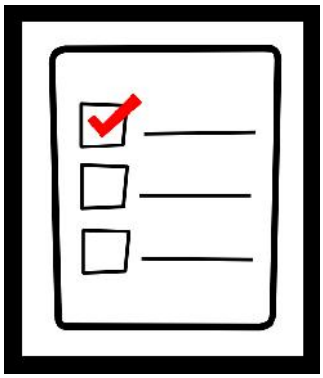
Review of Literature

Methodology

Results

Discussion

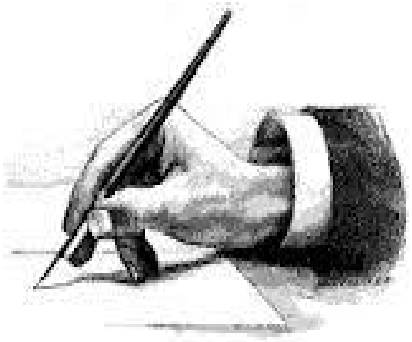
Conclusion



Limitations

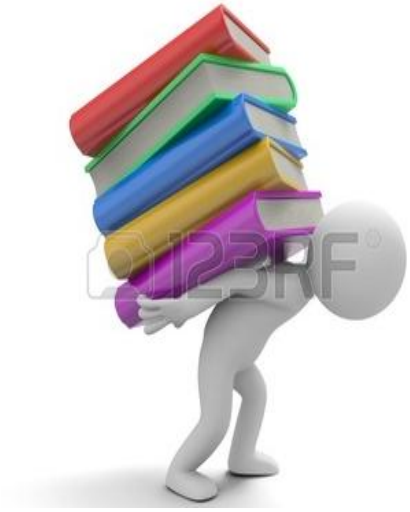
Summary

Bibliography



Annexure-I

Annexure-II



Annexure-III

Annexure-IV

Annexure-V