

Prognosis of Different Disease Due to Alteration in Lipid Profile

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Abstract

Lipid is one of the most important biomolecules of our body. We need lipid for a number of essential functions. The lipids are needed for the synthesis of cell membranes, some of the vitamins, hormones, energy sources. Any kind of alteration in these lipid content of our body leads to many types of abnormalities like Coronary artery disease, obesity, atherosclerosis and stroke. There are many subfractions of lipid present in our body such as triglycerides, very low-density lipoproteins, high density lipoproteins, low density lipoproteins. Triglyceride have a large affect on HDL cholesterol. Triglyceride is the good marker for obesity and the ratio of total cholesterol to HDL cholesterol is a more specific marker of coronary artery disease than is low-density lipoproteins cholesterol. Total cholesterol is best marker for Stroke.

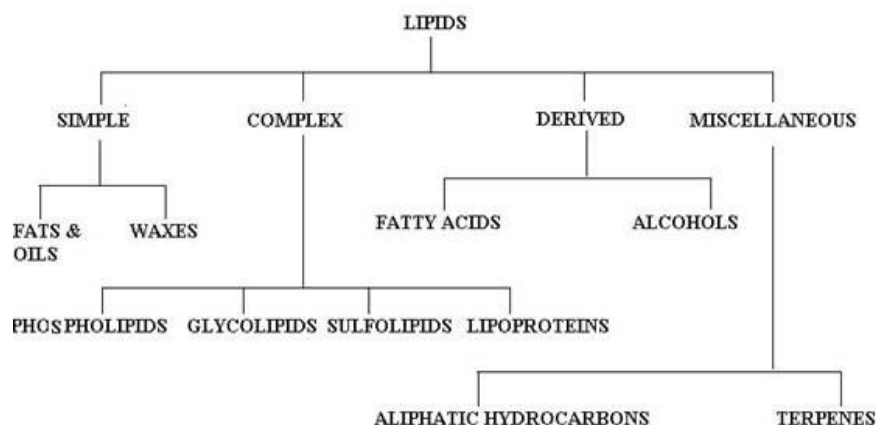
Keywords: Cholesterol, triglyceride, lipoproteins, coronary artery disease, stroke.

Introduction

Lipids are organic compounds that are poorly soluble in water but soluble in organic solvents like ether, chloroform, acetone, benzene. Lipids play a critical role in important physiological function in human body. Lipids are large diverse group of organic compounds including fatty acids and their derivatives, terpenes, steroids and bile acids. Steroid hormones serve as chemical messengers between Cells, tissues and organs. Lipids are structural components in cell and are involved in metabolic and hormonal pathways [1]. Lipids are group of hydrophobic or amphilic molecules. These molecules form structures such as vesicles, liposome's, or membranes in an aqueous environment. Most lipids are amphipatic which interact with other molecules with aqueous solvents by hydrogen bonding and electrostatic interaction. Lipids classified on the bases on their different chemical properties, their chemical composition and their building blocks, including their ability for saponification. We can say saponification is a technique which has ability of lipids to be hydrolyzed by basic solutions into compounds such as glycerol and fatty acids. On the basis of their chemical composition, lipids are classified into two simple lipids and complex lipids. Simple lipids are defined as that hydrolysis yield at most two type of primary product per mole. On the other way complex lipids yield three or more primary hydrolysis products per mole (e.g. glycerol, FAs, and sugar). Lipids are divided into two ketoacyl and isoprene groups one the bases of their building blocks. On the basis of their chemically functional backbone lipids are divided into eight categories FAs, Glycerolipids, Sphingolipids, Glycerophospholipids, Saccharolipids and polyketides. These eight compounds are derived from ketoacyl subunits and sterol lipids and phenol lipids derived from isoprene subunits [2].

Classification of Lipids

On the basis of the nature and structure of lipid, it is divided into four classes.



Lipoproteins

Lipoproteins are biochemical transporters, Lipoproteins are composed of protein and lipids. Lipoproteins help all lipids derived from food and synthesized in specific organ to be transported through the body by circulatory system. Lipoproteins are an energy supplier which is used by intestine and liver, they supply energy to other tissues. Intestine and liver also use them as structural materials in their membrane. [2] There is an amphipathic monolayer of lipids in the layer of intestine and liver, this layer is composed of polar head groups of phospholipids, and free cholesterol with Apo proteins which is contact with an aqueous environment and cover the hydrophobic part of their structure the non polar part of layer consist o TAGs and cholesterol esters. Lipoproteins are divided into five major classes [2]. Structure is showing that Lipoproteins have Apo proteins in hydrophobic part and TGs and Cholesterol esters present in the core of the Lipoprotein.

Apo lipoproteins

Apo lipoproteins are the polypeptide found in lipoproteins. Apo lipoproteins are commonly using the abbreviation Apo. Different type of apolipoprotein are A, B, C and E. They have role in transport of Chylomicrons, triglycerides, cholesterol, and fatty acids.

Classification of Lipoproteins

- Chylomicrons:** Chylomicrons are the largest lipoproteins. The diameter of Chylomicrons are 75-600nm. It is formed in the intestinal cell wall by dietary fats and cholesterol. Chylomicrons contain 99% of total lipid and 2% cholesterol.
- VLDL:** It is lipoprotein synthesis by liver transport endogenous lipid from the liver to cells. It contains 91% of total lipids.
- IDL:** Intermediate density lipoproteins which are formed during the conversion of VLDL to LDL. IDL contain 20% of proteins 7% of free cholesterol.
- LDL:** LDL is rich particles of cholesterol. Near about 70% of plasma cholesterol occurs in this form. It contains 80% of total lipids.
- HDL:** HDL is smallest class of lipoproteins. HDL removes the excess cholesterol from cell. It contains 44% of total lipids and 7% of cholesterol. HDL also contain Apo1 and Apo2 proteins. [Joint British Recommendation 2000]

Mechanism of Lipoproteins Metabolism

There are mainly three pathways by which transportation of lipids occur in the body. The pathways are exogenous pathways, the endogenous pathway, and pathway of reverse cholesterol transport. [3-4]

- (a) **Exogenous Pathway:** When we take diet digestion occur than absorption of dietary fat, TG and cholesterol is taking place. These are packaged to form Chylomicrons in the epithelial cells of the intestine through the intestinal lymphatic system. Chylomicrons circulate by circulating system. Chylomicrons interact the capillaries of Adipose tissue, and muscle cells releasing TG to the adipose tissue to be stored for the availability of body's energy. Free fatty acids are released with the hydrolyzation of TG by LPL enzyme. Some components of the Chylomicrons are going back in to the other lipoproteins, like endogenous pathway.
- (b) **Endogenous Pathway:** In this pathway now liver synthesizing lipoproteins. TG and cholesterol ester are released by the liver and add into VLDL particles and it is released into the circulation. Know LPL is working on VLDL in tissues to release Fatty acids and glycerol. Fatty acids are divided according to body need Energy. Muscle cells taken up fatty acids and by the Adipose cells for storage. When the action of LPL is complete VLDL becomes a VLDL remnant. Now there is LDL receptor present by which liver taken up. Majority of VLDL remnants. The remnant which is remaining after this become LDL, it is necessary that some of particles of LDL have to reabsorb by liver with the action of LDL receptor. To form LDL hydrolyzation of IDL particles occur in the liver by hepatic-triglyceride lipase. LDL is smaller than IDL. Cholesterol is circulating in the body and the carrier for this circulating cholesterol is LDL. Cholesterol is used by extra hepatic cells for cell membrane and synthesis of steroid hormones. Most of the LDL particles are taken up by receptor of LDL which is present in liver. At the cellular level remaining LDL is removed by the pathways known as scavenger pathway. LDL is not present because it is taken up by receptors, free cholesterol is released and increase within the cells. LDL receptor become activate and take LDL and regulate plasma LDL concentration by several mechanisms, it also slow down the synthesis of hydroxi-3-methylglutaryl co-enzyme A (HMG-CoA) reductase. This is the enzyme which control the cholesterol synthesis, decrease the rate of new LDL receptor synthesis in the cells, than activation of enzyme occur like acyl-coenzyme A cholesterol acyltransferase, it break down free cholesterol in to cholesterol ester, and storing cholesterol in the cell [5].
- (c) **Reverse Cholesterol transport:** It is working as a transporting system. In this transportation cholesterol is removed from the tissues and returned to the liver [5]. HDL is main lipoprotein which is known as key lipoprotein involved in reverse cholesterol transport and it transfer cholesteryl esters between lipoproteins [1]. HDL is the smallest lipoprotein. Liver and intestine secreted precursor particles also known as nascent HDL. Which formed HDL through a maturation process, and it is proceed through a series of conversions known as HDL cycle. It takes cholesterol from cell membranes and free cholesterol to the core of the HDL particle. HDL2 and HDL3 are sub-classes of HDL particles. The mechanism is not still clear by which the HDL delivers cholesterol esters to the liver, but the many mechanisms have been suggested. One of them is transfer of proteins by the action of cholesteryl ester. This transfer HDL in to a TG rich particle which react with hepatic triglyceride lipase. Cholesterol ester with rich HDL which is directly taken up by the receptor in the liver [5-6].

Alteration of Lipid profile

- (1) **Obesity:** Obesity is worldwide health problem which affecting increases number of people. Obesity is defined as excessive accumulation of energy in the form of body fat. The main cause of obesity is our eating habits. We have no control on food, it causes obesity. Especially foods which are rich in fats, overweight and obesity has a direct correlation with cardiovascular disease. In obesity always there is an increase in plasma triglycerides [7-8]. If we compare obese person and non-obese person's serum value, then the obese person has high serum TNF α , triglyceride, and insulin and CRP levels than non-obese person. We can say that obesity is an increased

risk for metabolic syndrome. On the basis of central distribution of body fat intra- abdominal fat is more risk factor than distribution of peripheral obesity. According to weight and height we estimate the body fat. The formula which we use for the calculating body fat is known as BMI. By using the value of BMI we can see difference between overweight and obesity, it gives the information about body fatness [8-9]. Our fat cells (adipocytes) produced leptin hormone. When the fat which is stored in adipocytes, when it increases, leptin is act as a lipostat. Leptin come in blood flow and gives signals to the brain that the body has enough to eat. mostly the people who are overweight, they have increase level of leptin in their blood stream, it indicating that other molecules of body also effect feeling of satiety and it is regulate the body weight [10] . Early onset obesity is controlled by gives the leptin injections subcutaneously; significantly it is helpful in weight loss without any alteration in energy expenditure. Decrease level of basal metabolic rate was counter balanced by during more physical activity [11]. Leptin is helpful in weight loss because it have suppressive effect on food intake [12]. Obesity effect on cardiovascular function and it also cause sleep breathing abnormalities. According to waist circumference and waist hip ratio HDL-C is decreased in obese person [13]. In obesity there is a metabolic defect occur. In obese person the level of free fatty acids become high because of insulin resistance, there is also increases the level of LDL cholesterol, VLDL and triglycerides also become high, but the level of HDL-cholesterol become low. In obesity when the level of free fatty acids is high in liver then there is over production of VLDL. Because the level of VLDL is known become high so the level of production of LDL is also become high. Via the sequence: VLDL production of intermediate density lipoprotein (IDL). Then production of LDL [14]. The production of VLDL is related to insulin level in our body [15] and % of body fat [16].

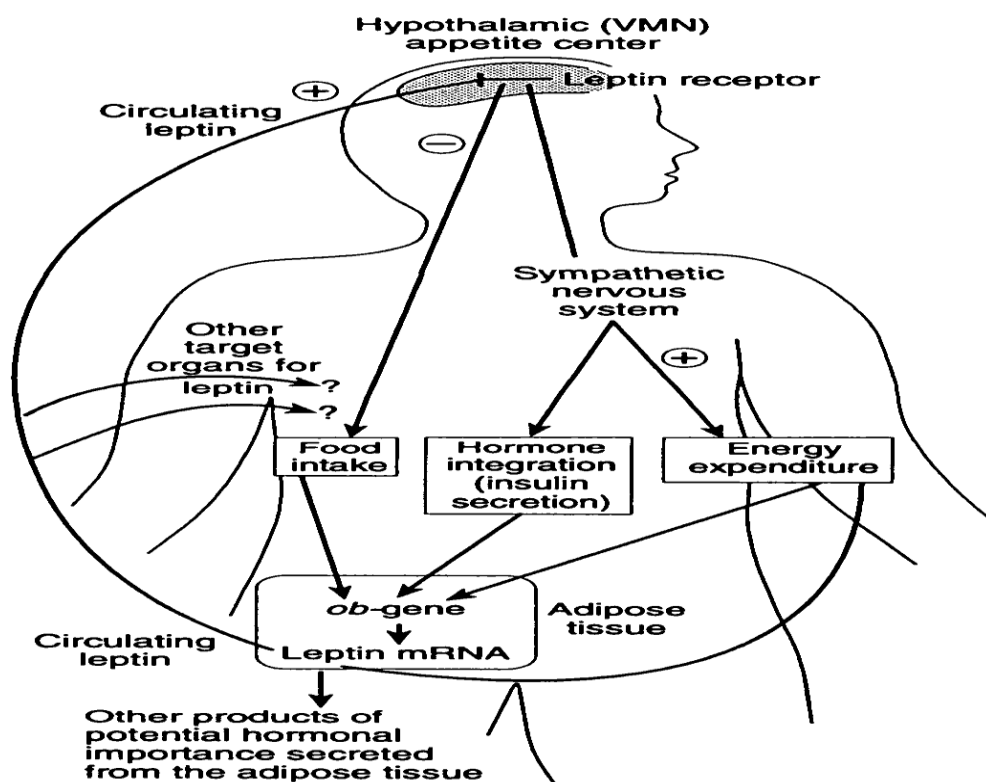


Figure. 1. In this picture it shows the role of the leptin. Adipose tissue secretes leptin. Leptin binds to db gene receptor.

Mechanism of Obesity Adiposity and TGs

Lipoproteins in adiposity with hyperglyceridemia. TG level is used to measure the TG content of all lipoproteins which is circulating in our body, this have majority of apoprotein B containing Lipoproteins. The main function of

these particles they act like a primary carrier of TG in blood, they transport TG to the periphery. Lipoproteins which are containing Apo B are subdivided into two classes. Apo B48 and Apo B100. Apo B48 have Chylomicrons and the remnant of their particles taking from dietary lipid, it is compile with enterocytes of the gut. second Apo B is known as Apo B100, it have VLDL, intermediate density lipoprotein (IDL), also have LDL and a glycoprotein derivative LDL like particle, lipoprotein. Lipoproteins are formed in liver. Lipoproteins which are secreted from liver they are VLDL with postsecretory action of various Lipase when the particles circulate through peripheral tissues. Adiposity means in the liver and peripheral tissues the action of insulin is resistance, it causes the alteration in intracellular signalling, resulting in the level of secretion of TG is increased [17]. This is combined with LPL is and the activity decreases or insufficient.

(b) Coronary artery disease Coronary artery disease is a condition in which build up of plaque in the pericardial coronary arteries. In this disease plaque grows in the coronary arteries and it limited the blood flow to the heart's muscle. When the plaques formed then the formation of occlusive thrombi and the precipitation of acute events, and increase risk of myocardial infarctions, these all problems increase the oxidative stress in the pathophysiology of coronary artery disease [18-20]. Rise in the prevalence of CAD in developing countries like India. Prevalence of CAD in India is increased due to their lifestyle, neo-affluence and mainly due to changes in food habits. Stress and strain is also responsible for CAD but besides of this, food habits, like they use to eat high lipid, salt with less of fibre and one of the main determinants is intake of green vegetable [21].

In CAD there is lower level of HDL Cholesterol with higher levels of serum triglycerides [22-23]. Smallest Lipoprotein is a HDL, it is present in outer layer of phospholipids and free cholesterol it is controlled by Apo-lipoproteins and in the core of lipid cholesterol ester and triglycerides are present [24], by the action of several enzymes and interactions with specific receptor HDL components are modified along its biogenesis [24]. the main HDL protein is Apo A-1, it is produced by hepatocytes, it is also synthesized in the intestine, with the help of phospholipids and free cholesterol form lipid poor complex [24], the enzyme which is known as lecithin cholesterol acyl- transferase increases the spherical HDL particles which generate the cholesterol esters in the lipid core pool, they exchange lipids with other VLDL and LDL Lipoproteins, resolve by phospholipids transfer protein, and cholesterol ester transfer protein [24-26]. The level of LDL is involved in the risk of coronary disease

and myocardial infarction.

Mechanism of action

Active oxygen species which have free radicals they are involved in CAD [23-25]. In CAD production of free radical and capacity of antioxidant is altered in favour of the former, it is become to oxidative stress. On the basis of "Oxidation hypothesis" LDL absorbed in the intima, under the oxidative modification binding to proteoglycans by the free radicals [27]. when Oxidation of LDL is done then there is chemical modification of some moieties of apolipoprotein by the products of lipid peroxidation. in the lipid fraction of atheroma lipid hydroperoxides, carbonyl compounds and lysophospholipids are localised [28] for activate expression of Adhesion molecules, immune response is enhance by oxidised LDL. it activate the Adhesion molecules, Cytokines, chemokines and many mediators of LDL particles which are oxidatively modified, enhance the level of triglycerides, along with oxidative stress HDL-C is decreased which is the major risk of CAD.

(c) Stroke Stroke is a clinical Syndrome, in this condition people loss of cerebral functions. Its symptoms show more than 24 hours it leads to death with no appropriate cause other than vascular origin [28]. We defined stroke as the stoppage of blood flow to the brain and it is a leading cause of death. 12% of strokes are hemorrhagic. In hemorrhagic cerebral blood vessel is become rupture, and 88% are ischemic. When there is blockage in cerebral artery stop the blood flow and also interrupt the supply of nutrients, glucose and oxygen to the brain. The metabolism of glucose and oxygen supply energy to brain for the phosphorylation of ADP to ATP. The ATP which is generated by brain is used to maintain intracellular homeostasis and transmembrane ion. These are gradients of sodium, potassium and calcium. When the energy is not delivered then ion gradients are collapse and high secretion of neurotransmitters such as dopamine and glutamate [26-28], result in neuronal death and develop an infarction. Increase release of glutamate and the receptor are stimulate then the activation of phospholipase/ sphingomyelinase hydrolysis of phospholipids occur and it secrete second messengers ArAc and ceramide the process which mentioned above lead to necrotic cell death. Some scientific community see the difference between blood lipids levels and cardiovascular disease. So they found the main difference between levels of cholesterol, the level of serum cholesterol found high, mainly low-density lipoprotein cholesterol, which develop the atherosclerosis. When they see the level of High density Lipoprotein cholesterol which play a protective role [27-28]. Mostly the change in diet and Life style cause, increased hyperlipidemic, which is the risk factor for stroke. In cerebrovascular disease relationship of serum lipids and lipoproteins they are risk factors in coronary heart disease. Some clinical trials see difference between high concentrations of serum cholesterol and ischemic stroke.

Conclusion

One of the most important biomolecules is lipid which is compulsory for a number of cellular functions. These lipids not only do the normal physiological functions but also helps in immunity development and other no usual function of body. Several common reasons are also responsible for the alteration of lipid profile like, their sedentary lifestyle. Here am concluded my study we can reduced chance of alteration of lipid profile by changing our eating habits, life style and by doing physical activities once in a day. The management of lipid and homeostasis maintenance leads to protect body from many metabolic disorders. Any kind of fluctional in blood parameters of lipid profile results in the abnormal situation.

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