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Lipid Profile and the Growing Concern on Lipid Related Diseases

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Abstract: *The lipids can be classified as Total Cholesterol (TC) and its derivatives such as; Triglycerides (TAG), Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL) and Very Low Density Lipoprotein (VLDL) cholesterol. Lipids are insoluble in water but are soluble in alcohol and other solvents. Hence, they are transported around the body as lipoproteins. Lipids originate from two sources: endogenous lipids, synthesized in the liver, and exogenous lipids, which are ingested and absorbed in the intestine. Approximately 7% of body's cholesterol circulates in plasma in the form of low density lipoproteins (LDL) and it is well known that he level of plasma cholesterol is influenced by its synthesis and catabolism in which liver plays a crucial role (Robbins and Cotran, 2004).A lipid profile or lipid panel is a panel of blood tests that serves as an initial broad medical screening tool for abnormalities in lipids, such as cholesterol and triglyceride. The results may identify certain genetic diseases and also determine risks for cardiovascular disease, (Anderson et al., 1987). A lipid profile measures TC, HDL-C, LDL-C and TAG. The results of the lipid profile are considered along with other known risk factors of heart disease to develop a plan of treatment and follow up. Depending on the result and other risk factors, treatment options may involve life-style changes such as diet and exercise or lipid - lowering medications such as statin (Bitcher et al., 2000). However, even normal and especially high levels of cholesterol are strongly associated with progression of atherosclerosis. Of interest in this review are cholesterol, VLDL, LDL, HDL, and triglyceride and few related diseases such as hyperlipidemia and hypocholesterolemia.*
Key words: *Lipid profile, cholesterol, atherosclerosis and hypelipidemia.*

I. Introduction

Before we consider the lipid profile and the growing concern of lipid related diseases, we would like to explore the classes of lipid, its physiology and their mode of transport to other organs (parts) of the body.

Basic Classification of lipids

The lipids can be classified as Total Cholesterol (TC) and its derivatives such as; Triglycerides (TAG), Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL) and Very Low Density Lipoprotein (VLDL) cholesterol. The cholesterol along with some other types of fats cannot dissolve in the blood. In order to be transported to and from cells, they have to be specially carried by certain molecules called lipoproteins, which consist of an outer layer of protein with an inner core of cholesterol and triglycerides (Kritchevsky, 1988 and Dargel, 1989). In addition, the lipoproteins have been found essential for cholesterol to move around the body.

Total cholesterol (TC)

According to guidelines of National Cholesterol Education Program USA (NCEP), TC concentrations below 200 mg/dL have been regarded as desirable, whereas, concentrations greater than 240 mg/dL are referred to as hyperlipidemic. However, epidemiological evidence suggests that the risk of cardiac events decreases as TC levels fall approximately to 150 mg/dL. Moreover, TC should be less than 180 mg/dL for children (Ahmed et al., 1998, Ginsberg and Goldberg, 2001 and Fryar et al., 2010).

Triglyceride

Triglycerides are another type of fat that is carried in the blood by lipoproteins. The excess calories, alcohol or sugar in the body get converted into triglycerides and stored in fat cells throughout the body (Smelt, 2010). The triglyceride concentration less than 150 mg/dL is regarded as normal, whereas, concentrations of 200-499 mg/dL are considered as high. Moreover, concentrations of 500 mg/dL or higher are considered dangerous for the development and progression of various Cardio-vascular diseases (CVDs) (Ginsberg and Goldberg, 2001).

LDL cholesterol (LDL-C)

LDL-C is commonly known as the bad cholesterol, which is produced by the liver and transported to different areas of the body like muscles, tissues, organs and heart. High levels

of LDL indicate much more cholesterol in the blood stream than necessary and hence,increase the risk of heart disease (Ahmed et al., 1998 and Costet, 2010). According to NCEP guidelines, LDL cholesterol concentrations below 100mg/dL are considered optimal, whereas concentrations in the range of 160-189mg/dL are considered to be on the high side. However, increasing evidence supports that normal human LDL cholesterol concentration can be as low as 50 to 70 mg/dL (Ginsberg and Goldberg, 2001). It has been generally accepted that the risk of CVDs decreases as LDL cholesterol concentration decreases.

HDL cholesterol (HDL-C)

HDL-C is commonly referred to as the good cholesterol, which is produced by the liver to carry cholesterol and other lipids from tissues back to the liver for degradation (Ridker et al., 2010). High levels of HDL cholesterol have been considered as a good indicator of a healthy heart. The concentrations of 60 mg/dL or higher have been considered as optimal, whereas, HDL concentrations below 40 mg/dL are considered as major risk factor for CVDs. However, HDL is often interpreted in the context of TC and LDL concentrations, and hence may be regarded as less significant when LDL is low (Ginsberg and Goldberg, 2001 and Ridker et al., 2010).

VLDL cholesterol (VLDL-C)

VLDL-C is similar to LDL-C in the sense that it contains mostly fat and not much protein. VLDL cholesterol is the lipoproteins that carry cholesterol from the liver to organs and tissues in the body (Sundaram and Yao, 2010).They are formed by a combination of

cholesterol and triglycerides. Moreover, VLDLs are heavier than LDL, and are also associated with atherosclerosis and coronary heart disease (Sundaram and Yao, 2010). Physiology of cholesterol and its derivatives

Cholesterol is a lipid (fat) which is produced by the liver and vital for normal body function.

Every cell in our body has cholesterol in its outer layer. Cholesterol is a waxy steroid and is transported in the blood plasma of all animals. It is the main sterol synthesized by animals; small amounts are also synthesized in plants and fungi (Hanukoglu, 1992). Since cholesterol is essential for all animal life, each cell synthesizes it from simpler molecules, a complex 37 - step process which starts with the intracellular protein enzyme HMG - CoA reductase. However, normal and especially high levels of fats (including cholesterol) in the blood circulation depending on how it is transported within lipoproteins are strongly associated with progression of atherosclerosis.

Most ingested cholesterol is esterified, which is poorly absorbed, the body compensates for any absorption of additional cholesterol by reducing cholesterol synthesis (Lecerf et al., 2011). For this reasons, cholesterol intake in food has little, if any, effect on total body cholesterol content or concentrations of cholesterol in the blood. Some plants make cholesterol in very small amounts in the form of phytosterols (substances chemically similar to cholesterol), which can compete with cholesterol for re-absorption in the intestinal tract, thus potentially reducing cholesterol re-absorption (Lecerf et al., 2011). When intestinal epithelial cells absorb phytosterol in place of cholesterol, they usually secrete it back into the GIT, an important protective mechanism.

II. Functions of cholesterol

Cholesterol is required to build and maintain cell membranes (outer layer); it modulatesnmembrane fluidity over the range of physiological temperatures. The structure of the tetracyclic ring of cholesterol contributes to the decreased fluidity of the cell membrane as the molecule is in a trans conformation making all but the side chain of cholesterol rigid and planar (Ohvo-Rekila et al., 2002). In this structural role, cholesterol reduces the permeability of the plasma membrane to neutral solutes (Yeagle, 1991), protons, (positive hydrogen ions) and sodium ions (Haines, 2001).

Within the cell membrane, cholesterol also functions in intracellular transport, cell signaling and nerve conduction (Haines, 2001). Cholesterol is essential for the structure and function of invaginated caveolae and clathrin-coated pits, including cavedae-dependent and clathrin-dependent endocytosis. Recently, cholesterol has been implicated in cell signaling processes, assisting in the formation of lipid rafts in the plasma membrane (Incardona et al., 2000). Lipid raft formation brings receptor proteins in close proximity with high concentration of second messenger molecules (Incardona et al., 2000). In many neurons, a myelin sheath, rich in cholesterol, since it is derived from compacted layers of Schwann cell membrane, provides insulation for more efficient conduction of impulses (Pawlina et al., 2006).

Within cells, cholesterol is the precursor molecule in several biochemical pathways in the liver, cholesterol is converted to bile, which is then stored in the gallbladder. Bile contains

bile salts, which solubilize fats in the digestive tract and aid in the intestinal absorption of fat molecules as well as the fat-soluble vitamins, A, D, E and K. Cholesterol is an important precursor molecule for the synthesis of vitamin D and the steroid hormones, including the adrenal gland hormones (cortisol and aldosterone), as well as the sex hormones (progesterone, estrogen and testosterone), and their derivatives (Hanukoglu, 1992). Some research indicates cholesterol may act as an antioxidant (Smith, 1991).

Blood lipids and lipid transport

Lipids are insoluble in water but are soluble in alcohol and other solvents. Hence, they aretransported around the body as lipoproteins. A lipoprotein is any complex or compound containing both lipid (fat) and protein (Nordqvist, 2004). Lipids originate from two sources: endogenous lipids, synthesized in the liver, and exogenous lipids, which are ingested and absorbed in the intestine. Approximately 7% of body's cholesterol circulates in plasma in the form of low density lipoproteins (LDL). The level of plasma cholesterol is influenced by its synthesis and catabolism in which liver plays a crucial role (Robbins and Cotran, 2004).

When dietary fats are digested and absorbed into the small intestines, they eventually reform into triglycerides, which are then packaged into lipoproteins (Birtcher et al., 2000). For this reason, there are several types of lipoprotein in blood, called in order of increasing density, chylomicrons, very - low-density lipoprotein (VLDL), intermediate-density lipoprotein

(IDL), LDL, and HDL. Of interest in this review are cholesterol, VLDL, LDL, HDL, and triglycerides. The more lipids and less protein a lipoprotein has, the less dense it is. Dietary fat, are absorbed from the small intestines and transported into the liver by lipoproteins called chylomicrons. Chylomicrons are large droplets of lipids with a thin shell of phospholipids, cholesterol, and protein. Once chylomicrons enter the bloodstream, an enzyme called lipoprotein lipase breaks down the triglycerides into fatty acid and glycerol. After a 12-14 hours fast, chylomicrons are absent from the bloodstream. Thus individuals who are having a lipid profile done should fast overnight to ensure that chylomicrons have been cleared (Wardlaw et al., 2004).

The liver removes the chylomicrons fragments, and the cholesterol is repackaged for transport in the blood in VLDLs which eventually turn into LDL. LDL cholesterol (LDL-C) the "bad cholesterol" consists mainly of cholesterol. Most LDL particles are absorbed from the bloodstream by receptor cells in the liver. If too much is carried, than can be used by cells, there can be a harmful building of LDL. This lipoprotein can increase the risk of arterial disease (atherosclerosis) if levels rise too high (Tymoczko et al., 2002). Diets high in

saturated fats and cholesterol decrease the uptake of LDL particles by the liver. LDL particles are also removed from the bloodstream by scavenger cells, preventing cholesterol fromreentering the bloodstream, but they deposit the cholesterol in the inner walls of blood vessels, eventually leading to the development of plaque (Wardlaw et al., 2004).

High - density lipoproteins are a separate group of lipoproteins that contain more protein and less cholesterol than LDL. HDL cholesterol (HDL-c) is also called "good cholesterol". HDL is produced primarily in the liver and intestine, and it travels in the bloodstream, picks up cholesterol, and gives the cholesterol to other lipoproteins for transport back to the liver, so HDL particles are thought to transport cholesterol back to the liver for excretion or to other tissues that use cholesterol to synthesize hormones in a process known as reverse cholesterol transport (RCT) (Lewis et al., 2005). Having large numbers of large HDL particles correlates with better health outcomes (Gordon et al., 1989). In contrast, having small numbers of large HDL particles is independently associated with atheromatous disease progression in the arteries (Lewis et al., 2005).

Lipid profile

A lipid profile or lipid panel is a panel of blood tests that serves as an initial broad medical screening tool for abnormalities in lipids, such as cholesterol and triglyceride. The results of this test can identify certain genetic diseases and can determine approximate risks for cardiovascular disease, certain forms of pancreatitis and other diseases (Anderson et al., 1987). A lipid profile measures TC, HDL-C, LDL-C and TAG. Lipid panels are commonly ordered as part of a physical examination, along with other panels such as the complete blood count (CBC) and basic metabolic panel (BMP). The results of the lipid profile are considered along with other known risk factors of heart disease to develop a plan of treatment and follow up. Depending on the result and other risk factors, treatment options may involve life-style

changes such as diet and exercise or lipid - lowering medications such as statin (Bitcher et al., 2000).

The NCEP (2002) recommends that individuals age twenty and over have a fasting lipoprotein profile every five years. A lipid profile should be done after nine - to twelve - hours fast without food, liquids or medication. If fasting is not possible the values for total cholesterol and HDL - C may still be useful (Sidhu et al., 2012). If total cholesterol is 200 mg/dl or higher or HDL -C is less than 40 mg/dl, the individual will need to have a follow - up lipoprotein profile done to determine LDL-c and triglyceride levels. Depending on the physician's request, the lipid profile may include the ratio of cholesterol to HDL. This ratio is sometimes used in place of total blood cholesterol. Most of lipid related disorders are discussed in the next sections.

III. Lipid related diseases or conditions

Hyperlipidemia

Hyperlipidemia is a medical condition characterized by an elevation of any or all lipid profile and/or lipoproteins in the blood. It is also called hypercholesterolemia/hyperlipoproteinemia (Amit et al., 2011). Although elevated low density lipoprotein cholesterol (LDL) is thought to be the best indicator of atherosclerosis risk, (Amit et al., 2011) dyslipidemia (abnormal amount of lipids in the blood) can also describe elevated total cholesterol (TC) or

triglycerides (TG), or low levels of high density lipoprotein cholesterol (HDL).

Human body is complex machine for maintaining the homeostasis of various organ and organ system. Any undesirable change will disturb the balance resulting in diseased state (Virchow and Thrombose, 1856). Lipids are fats in the blood stream, commonly divided into

cholesterol and triglycerides. Cholesterol circulates in the bloodstream and is involved in the structure and function of cells. Triglycerides (TG) are best viewed as energy that is either used immediately or stored in fat cells. TG is manufactured in the liver from the foods or by being absorbed from the intestine (Ankur et al., 2012). Virchow in 19th century who

identified cholesterol crystals in atherosclerotic lesion and stated that endothelial cell injury initiates atherogenesis (Virchow and Thrombose, 1856).

In a modification of this hypothesis it was proposed that the endothelium normally influences the behaviour of arterial smooth muscle cells by providing a barrier to the passage of plasma proteins,and that the major effect of haemodynamic or other factors that injure endothelium is to reduce the effectiveness of the barrier (Ross and Glomset, 1976). Arteries are normally smooth and unobstructed on the inside, but in case of increased lipid level, a sticky substance called plaque is formed inside the walls of arteries. This leads to reduced blood flow, leading to stiffening and narrowing of the arteries. It has been proved that elevated plasma levels of cholesterol and of LDL are responsible for atherosclerosis in man, and epidemiological data suggests that elevated plasma levels of HDL have a protective effect (Grundy and Vega, 1998).

This medical condition or problem is divided into two subtypes: primary hyperlipidemia and secondary hyperlipidemia detailed in one of one paper in press (Onwe et.al.). Primary hyperlipidemia: This usually take place as a result of genetic problems i.e., mutation within receptor protein,
which may be due to single (monogonic) gene defect or multiple (polygenic) gene defect. This type may occur as a result of change in dietary and lack of proper physical activities. See table below for summaries the various classes of primary hyperlipidemia.

Secondary hyperlipidemia

This arises as a result of other underlining diseases like diabetes, myxoedema, nephritic syndrome, chronic alcoholism, with use of drugs like corticosteroids, oral contraceptives, Beta blockers (Joseph, 2005).

IV. Causes of hyperlipidemia

The main cause of hyperlipidemia includes changes in lifestyle habits (Kelly, 2010), diabetes, kidney disease, pregnancy, underactive thyroid gland, hereditary factor (Durrington, 1995) and female hormones like estrogen. In addition, drugs like diuretics, beta-blockers and medicines used to treat depression have also been reported to raise cholesterol levels (Lipman et al., 2000). Other illnesses that may elevate cholesterol levels include polycystic ovarian syndrome and kidney disease.

Possible Treatment

The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) recommends that a fasting lipoprotein profile and risk factor assessment be used in the initial classification of adults. There are three categories of risk that modify the goals and modalities of LDL-lowering therapy. The highest risk category

is having known CHD or CHD risk equivalents; the risk for major coronary events is equal to or greater than that for established CHD (i.e., more than 20% per 10 years, or 2% per year). The intermediate category includes two or more risk factors, in which the 10-year risk for CHD is 20% or less. The lowest risk category is persons with zero to one risk factor, which is usually associated with a 10-year risk of CHD of less than 10% (Barbara et al., 2005).

Over the past few years guidelines for the use of lipid-lowering therapy have become more aggressive following the results of major trials showing mortality benefit for the use of statins. Most guidelines recommend statin treatment for a patient with CAD with a 10-year risk that is greater than 20% (high risk) once a trial of dietary therapy has been unsuccessful.

However, treatment can be cost effective with a 10-year risk of 10% (Barbara et al., 2005). The goals of therapy are the reduction of LDL cholesterol levels and the level of initiation of therapeutic lifestyle change (TLC) and proper drug therapy are for adults and children. While these goals are surrogate end points, the primary reason to institute TLC and drug therapy is to reduce the risk first or recurrent events such as MI, angina, heart failure, ischemic stroke, or other forms of peripheral arterial disease such as carotid stenosis or abdominal aortic aneurysm (Amit et al., 2011).

Basically Treatment therapy involves two approaches, which are Non-pharmacological therapy and Pharmacological therapy. See reviewed work on possible treatment in one of our unpublished work (Onwe et.al 2015)

V. Hypocholesterolemia

Abnormally low levels of cholesterol are termed hypocholesterolemia. Research into the causes of this state is relatively limited, but some studies suggest a link with depression, cancer, and cerebral hemorrhage. In general, the low cholesterol levels seem to be a consequence rather than a cause, of an underlying illness (Lewington et al., 2007).

VI. Conclusion

Lipid profile is a group of blood tests which are carried out to determine the risk of coronary artery diseases (CAD). It is considered as good indicators of whether someone is prone to develop stroke or heart attack caused by atherosclerosis. For proper treatment of dyslipidemia, the results of the lipid profile are correlated with age, sex and other risk factors.

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