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A Review on Current scenario of Lipid Metabolic Disorders

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Abstract

Lipids are mandatory substance readily present in living body. They play a very vital role in maintaining a balance between all the mechanisms of the body. Lipids are almost water insoluble molecules that are transported in a protein capsule, commonly known as lipoprotein. Lipids undergoes a metabolism which is the major energy supplier for a living body. Types of lipids consists of Low-density Lipoprotein [LDL], Very Low-Density Lipoprotein [VLDL], High Density Lipoprotein [HDL], Triglycerides [TG]. Rise in the level of LDL or TG imposes a serious and severe threat to the body. Rise in these levels might lead to several disorders that includes much more severity in the disorders such as dysbetalipoproteinemia, lysosomal storage disorders, nephrotoxicity, menopause, renal disorders, obesity, diabetes, pregnancy toxemia, etc. Adding to these, problems of body such as hypothyroidism, genetic disruptions, etc. makes these disorders worse.

Keywords

Lipids, Triglycerides, Lipid metabolism, Disorders, Familial dysbetalipoproteinemia, Lysosomal Storage Disorder, Nephrotoxicity, Menopause, Renal disorders, Obesity, Diabetes, Pregnancy Toxemia.

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INTRODUCTION:

Lipids, play a vital role in maintaining the balance in a living body. Lipids are water insoluble molecules, transported in a protein capsule or commonly known as lipoprotein. The density of the lipid is determined by the size of the lipoprotein. The core of the lipoprotein consists of cholesteryl esters, commonly known as triglycerides and the outer polar layer is consisting of apolipoproteins, free cholesterols, and phospholipids.

The metabolism of lipids is a vital source for energy for the body. In this metabolism process, it includes synthesis and breakdown of lipids in cells to yield energy for the body. In this, the lipid molecules are either synthesized in cells for energy or are stored in adipocytes as fats for future use.[1,2]

LIPID METABOLISM:

Lipids consists of various types of molecules such as cholesterols, phospholipids, and triglycerides which are commonly known as fats. Lipid metabolism can be described as the synthesis and degradation of lipids in cells, involving the breakdown or storage of fats for energy. Lipid metabolism occurs in adipocytes and liver and in mammary gland during lactation. It also includes synthesis of structural and functional lipids, mainly those are involved in construction of cell membranes. In animals, these fats are obtained from the food they intake, and then, are synthesized in liver. In case of lipid

metabolism, the fats ingested are converted into small particles by the biles in the body. Then, small intestine and lipase from the pancreas, hydrolyzes its fatty acid and results in monoglycerides and free fatty acids. Along with these, a small amount of fatty acids is completely hydrolyzed into glycerol and fatty acids. These hydrolyzed products move into the cells of the epithelium of the intestine. Then, these recombines again to form triglycerides.

Triglycerides are packed along with Cholesterol in large lipoprotein particles known as Chylomicrones. Then, these chylomicrones leaves the enterocytes and they enter the capillaries and then eventually passes into the blood stream. This is a vital way of delivering fats to the tissues.

There is a kind of enzyme in the walls of the blood vessel known as Lipoprotein Lipase [LPL]. These LPL hydrolyzes the chylomicrone molecules. This process breaks the triglyceride molecules into free fatty acids and glycerol, which enables the fatty acids and the glycerol to pass through the capillary walls into the tissues.

In normal body tissues, they are oxidized for energy. In adipose tissues, these are re-esterized for storage, which can be utilized for energy production in future. The fats that are synthesized endogenously in liver, are packed in another type of lipoprotein, i.e., VLDL [Very Low-Density Lipoprotein]. Then, these VLDL are reacted upon by LPL, hydrolyzing them into glycerol and fatty acids and then they are utilized by the tissues in the similar manner of the chylomicrones.

When required, the fats stored in adipose tissues are taken for energy production by the action of Hormone Sensitive Lipase [HSL], which is used to mobilize the stored fats. [3–10]

Lipid metabolism yields energy by the process of-

Lipid metabolism pathway is very closely related and connected to carbohydrate metabolism pathway. Lipolysis occurs to form triglycerides, which breaks down into glycerol and fatty acids by the action of LPL. This glycerol produced is taken up by the glycolysis pathway to convert glucose into pyruvate molecules which is then converted into acetyl CoA. Fatty acids on the other side undergoes β-oxidation to yield acetyl CoA. Each round of β-oxidation eliminates two carbons from the fatty acid chain to yield acetyl CoA. These acetyl CoA are oxidized in the citric acid cycle to yield ATP via Electron Transport System. On the other hand, from β-fatty acid oxidation, 1NADH and 1$FADH_2$ is obtained per round.

Fats yield more energy per unit mass as compared to carbohydrates. When acetyl CoA is produced in excessive amount, it is pushed to create ketone bodies. During glucose starvation, ketone bodies are used for excess source of energy for brain. Ketone bodies are acidic in nature, which when produced in excess amount, disturbs the buffering capacity of blood plasma, resulting in metabolic acidosis, which is also known as ketoacidosis, which can lead to coma and death.

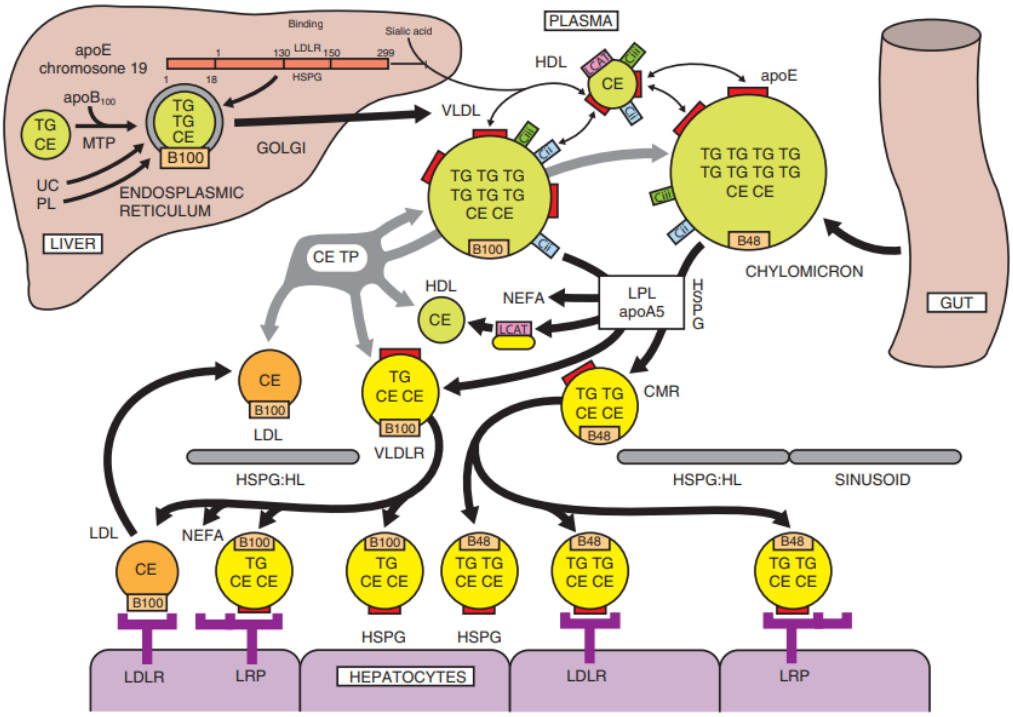

Fig 1: Lipoprotein metabolism [2]

In this above figure, the triglyceride-rich lipoproteins (TGRL) are secreted from the liver (very low-density lipoprotein; VLDL) and gut (Chylomicron). The TGRL contain unesterified cholesterol (UC) and phospholipid in the outer shell and the triglycerides (TG) and cholesterol ester (CE) as neutral lipids situated in the core. VLDL is assembled in the liver by neutral lipid transfer to apolipoprotein B100 (apoB100) by the help of microsomal triglyceride transfer protein (MTP). Chylomicrons are made in the similar manner but contain apolipoprotein B48 (apoB48). ApoE can exchange between lipoproteins, but it is not found in low-density lipoprotein (LDL). The TG in TGRL undergoes hydrolysis by lipoprotein lipase (LPL) and gets retained on the endothelial bed by heparan sulphate proteoglycans (HSPG) and yields non-esterified fatty acids. LPL gets activated by apolipoprotein CII and apolipoprotein A5. Apolipoprotein CIII is an inhibitor of LPL. The remnants of VLDL (VLDLR) and chylomicrons (CMR) passes into the hepatic sinusoidal space where HSPG retains hepatic lipase (HL). This enzyme hydrolyses more TG and converts VLDLR to LDL. Remnants can be taken up by hepatocytes through the low-density lipoprotein receptor (LDLR) or LDLR-related protein (LRP) because Apo-E. HSPG mediates certain uptakes along with this. Only on LDL is apoB100 in the appropriate conformation to bind the LDLR. In the circulation, cholesterol ester transfer protein (CETP) exchanges CE and TG between lipoproteins (HDL). Small discoidal high-density lipoproteins, generated during creation of redundant phospholipid by LPL.[2]

LIPID METABOLISM DISORDERS:

Owing to our present kind of lifestyle and various other diversifying factors, it has led to several types of lipid metabolism disorders.

Familial dysbetalipoproteinemia:

Familial dysbetalipoproteinemia is a rare combined hyperlipidemia, which belong to the type III hyperlipoproteinemia. In this type, the cholesterol and triglyceride levels are high. It consists of accumulation of triglyceride-rich lipoprotein, which includes both chylomicrones and VLDL in plasma.

Familial dysbetalipoproteinemia is majorly a genetic disorder, that might be due to the defect in the gene related to apolipoprotein E. Adding to it, problems like hypothyroidism, obesity and diabetes makes it worse. Either absence of apo E or dysfunctional apo E leads to poor uptake of remnants. (2) This leads to cholesterol depletion in hepatocytes, and this results in constantly upregulation of the LDL receptors, that enhances clearance of the LDL. Due to decrease in lipolytic conversion of VLDL to LDL, accounts for the low LDL cholesterol levels, this is the best available evidence that describes impaired formation of LDL. The metabolic changes that occur inside the body, that either increases the level of VLDL or decreases the functional efficacy of the LDL receptors. Difference in the function of LDL receptor leading to apo E mutation and binding of HSPG might be the reason for the variance in the phenotype of dysbetalipoproteinemia. [1,2,10–15]

Lysosomal storage disorder:

The normal storage capacity of the cell is exceeded, when, glycosphingolipidoses are characterized by the accumulation of GSLs. This causes alteration in the membranes and abnormal lipid vesicles are formed in various organs. Gangliosides are typically component of neuronal plasma membranes; thus they are mainly accumulated in the nervous system, this leads to neuronal dysfunction. Gangliosides accumulates due to their hydrophobic nature and results in several kind of disorders, such as, Gaucher and Krabbe Disease, GM1-Gangliosidosis, Tay–Sachs and Sandhoff Diseases.[16][17]

- Gaucher and Krabbe Disease:

Gaucher disease (GD) is one of the most common Lysosomal Storage Disorder [LSD] with an incidence of 1 in 40,000 in the count of total population. GD is a type of inherited autosomal recessive disorder. It occurs due to mutations in GBA1, which encodes acid-β-glucosidase (GCase). The symptoms of this disease vary and can include brain, liver and spleen, bone marrow and several other organs. There are almost more than 350 mutations are associated with GD. The symptoms of GD involve hepatosplenomegaly, thrombocytopenia, anemia, and in bone involves osteopenia, osteoporosis, and bone pain because of bone infarcts or pathological fractures. GD also increases the chances and risks for Parkinson's Disorder. The successful treatment of GD observed till now are Substrate-reduction and replacement therapy of enzymes.[16][18]

Just as Gaucher disease, Krabbe disease is also an autosomal recessive disorder. This disease includes the mutation of Gal-cerebrosidase gene (GALC). Krabbe disease (KD) is reported to occur early-onset in infants. For this disease, 130 mutations have been reported. Gal-cerebrosidase causes degradation of GalCer, which is an important constituent of myelin, and psychosine, a toxic byproduct of GalCer production. This results in accumulation of these in the nervous system, resulting in progressive loss of myelin, which leads to loss of neural function. Till date there has been no specific treatment discovered for treating the severity of KD, but stem cell

transplantation is being put under test for treatment of the above, and this is being tried in USA. [16][19]

• GM1-Gangliosidosis:

GM1 gangliosidosis is an autosomal recessive disorder, which occurs due to mutation of GLB1 gene, which results in the deficiency of β-galactosidase. It occurs due to deficiency in β-GAL activity that leads to the degradation of GSLs and glycoconjugates which contains terminal β-Gal residues such as GM1, GA1, and muco-polysaccharides. The patients suffering from this has been recorded to have accumulation of GM1 in the grey matter up to 4-fold of GM1 noted from a healthy individual. (16)(20)

There are three types of GM1 gangliosidosis, which are classified as per the onset of the disease. Type 1, also known as classic infantile GM1 gangliosidosis, is the most severe and expresses around 6 months of age, where children start to gain regression developmental milestones leading to rapid deteriorations occurring shortly thereafter. Type 2 is the milder one, which is expressed between the ages of 1–5 years. The symptoms of this includes ataxia, dementia and/or difficulties in speech. Type 3, is least severe and slowest progressing type, where the symptoms develops later during adulthood. The treatment that has seem to work for the treatment of this disease is, enzyme replacement therapy, and the clinical trial for this has begun in 2019. [16,20]

• GM2-Gangliosidosis: Tay–Sachs and Sandhoff Diseases:

This occurs due to decreased levels of β-hexosaminidase. This occurs due to failure in cleave of GalNAcβ residue from GM2, GD2, GT2 and Gb4 and GlcNAcβ- residues from other GSLs. The types of GM-2 include Tay–Sachs Diseases [TSD] variants, Sandhoff Diseases [SD]. It occurs due to deficiency of the GM2 activator protein in AB variants and includes mutations of one of the genes involved in GM2 catabolism. [20] [16,21,22]

There are three isoforms of hexosaminidase [HEX]: HEX-A occurs as an α, β heterodimer while HEX-B is a β, β homodimer, and HEX-S is an α, α homodimer. The α- and β-subunits have an active site with a slightly different substrate specificity - the α-subunit active site is coated with cationic residuesthat allows the accommodation of a negative charge. Both the subunits are generally assoiciated with endoplasmic reticulam, which are targeted with lysosomes for proper degradation of ganglioside. [16,20,23]

Tay–Sachs Diseases is the most common type of GM2 gangliosidosis. The HEX-A and HEX-S activities are reduced, as a result of mutation of the α-subunit. The symptoms are kind of like GM1 gangliosidosis, except visceral pathology from the prior. The common symptoms are seizures, motor impairment, hearing and vision loss and eventually respiratory failure. The characterization of TSD is similar to GM1 gangliosidosis, i.e., classic infantile, juvenile and adult onset. In infantile onset as children begin to face regression in mental development around 6 months of age which results in death by the age of 4. [16,20,22]

SD occurs due to mutation to HEX-B, which includes the β-subunit of HEX-A and HEX-B. The β-subunit has stabilizing properties that is required for the normal HEX-A activity. The symptoms of SD are kind of similar to TSD, but the additional symptom in SD is visceral manifestation. SD is subdivided into three classes on the basis of disease onset with infantile cases presenting as the most severe and rapidly progressing one.

- Other types of LSD: [16]

SL NO.	Name of Disease	Gene Involved	Enzyme Assiociated	Affected GSL
1	Fabry Disease	GLA	α-galactosidase A	Globosides, Blood group B
2	Metachromatic Leukodystrophy	ARSA	Arylsulfatase A	Sulfatide
3	Saposin deficiency	PSAP	Prosaposin (Saposin precursor protein)	GSLs
4	Galactosialidosis, PPCA Deficiency	CTSA	Sialidase I (NEU1) Cathepsin A	GM1
5	Niemann-Pick Disease	SMPD1	Acid sphingomyelinase	Sphingosine
6	Schindler Disease	NAGA	α-N-acetylgalactosaminidase B(α-NAGAL)	Lac-Cer, Blood group A
7	Farber Disease	ASAH1	Acid ceramidase	Ceramides

Triglyceride-rich lipoproteins and their abnormalities in nephrotic syndrome:

Glomerular proteinuria if exceeds more or equal to 3.5 g/day in adults or a urine protein/creatinine ratio of 2/3 mg/mg creatinine or greater in children might result in nephrotic syndrome, which might further lead to disorders like, hypo-albuminemia, edema, and hyperlipidemia.

In nephrotic syndrome, there is an increase in plasma concentration of cholesterol, triglycerides, apolipoprotein B [apoB] which contains lipoproteins (very low-density lipoprotein [VLDL], immediate-density **lipoprotein [IDL], and low-density lipoprotein [LDL]) and lipoprotein-a[Lp-a].[24–28]**

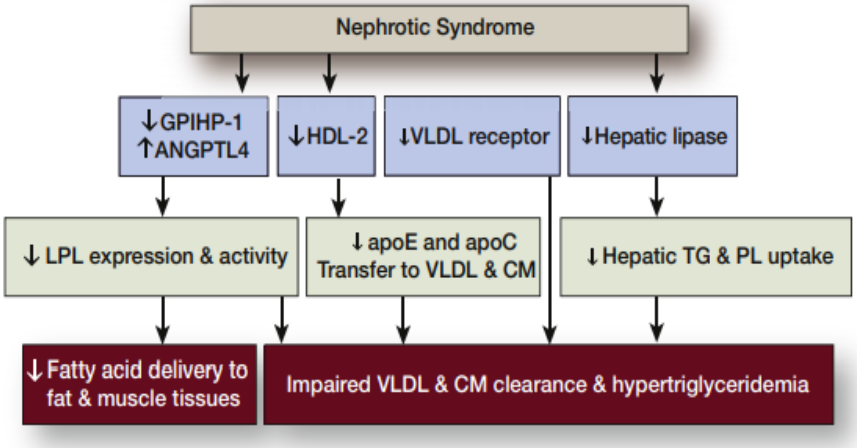

Fig 2: Nephrotic Syndrome via decrease of the lipoprotein lipase (LPL) adapter molecule GPIHP-1 and enhance of the LPL inhibitor molecule ANGPTL4.

In Nephrotic Syndrome, there is a decrease in the activity of the lipoprotein lipase [LPL] adapter molecule, i.e. GPIHP-1 and there is an enhancement in the activity of LPL inhibitor molecule ANGPTL4. Along with these, there is a scarcity of cholesterol ester–rich high-density lipoprotein (HDL), which serves as a donor for apoE and apoC to the nascent very low-density lipoprotein (VLDL) and chylomicrons (CM), that enhances their ability to bind to the endothelial lining and activate LPL. But LPL deficiency and dysfunction decreases the amount of transfer of lipids to the e muscles for generation of energy and to the adipose tissue for storage of energy. Adding to it, nephrotic syndrome causes deficiency in hepatic lipase, that causes impairment with the ability of the liver to extract triglyceride (TG) and phospholipid (PL) contents of immediate-density lipoprotein (IDL) and HDL. All of these together causes hypertriglyceridemia, that leads to increase of serum VLDL, and also causes accumulation of atherogenic IDL, CM remnants, and triglyceride (TG)-rich LDL in patients suffering from nephrotic syndrome. [24,29–32]

LDL and cholesterol metabolism in nephrotic syndrome:

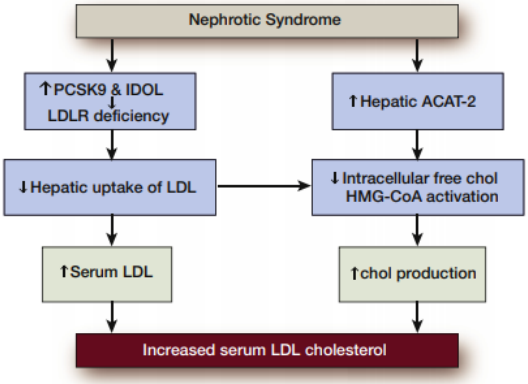

Fig 3: Nephrotic Syndrome via a marked increase in serum proprotein convertase subtilisin kexin type 9 (PCSK9) and the liver tissue inducible degrader of the LDL receptor (IDOL), which are potent degraders of low-density lipoprotein (LDL) receptor (LDLR), nephrotic syndrome results in acquired LDLR deficiency.

In Nephrotic syndrome, there is a marked increase in the levels of serum proprotein convertase subtilisin kexin type 9 [PCSK9] and in the liver tissues inducible degrader of the LDL receptor [IDOL], which is a potent degrader of LDL receptor [LDLR], that results in acquired LDLR deficiency. This causes impairment in the clearance of increased serum LDL in patients suffering from nephrotic syndrome. Adding to it, this disease leads in the increase of expression and work of Acyl-CoA cholesterol acyltransferase-2 [ACAT-2] in liver. This results in the increase esterification of cholesterol and decrease of intracellular free cholesterol. The decrease in cholesterol uptake takes place due to LDLR deficiency and the decrease in intracellular free cholesterol due to ACAT-2 to promote activation of sterol regulatory element-binding protein-2 (SREBP-2) and SREBP-1. Enhancement of the activity of SREBP-2 heightens 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase–mediated cholesterol production and increase in the activity of SREBP-1 that increases production of fatty acids, and that leads to hypercholesterolemia and hypertriglyceridemia in nephrotic syndrome. [24,26,29,33–37]

HDL metabolism and its abnormalities in nephrotic syndrome:

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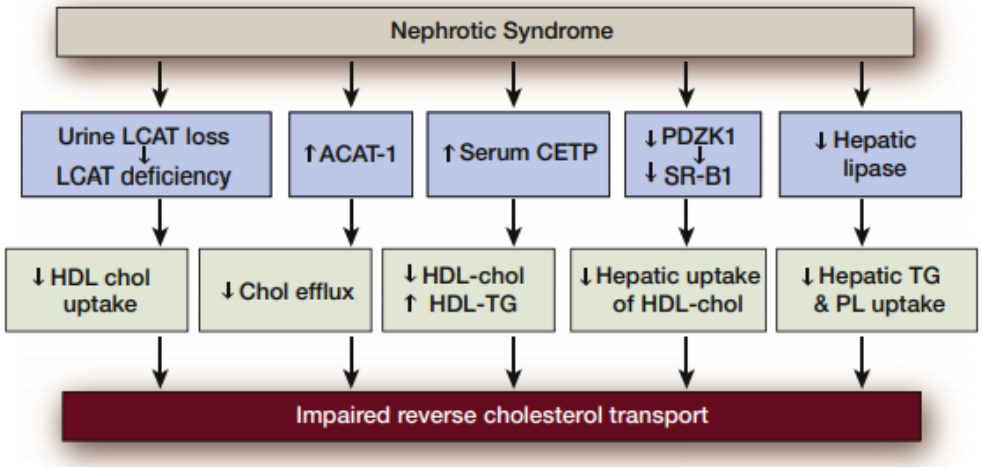

Fig 4: Nephrotic Syndrome and HDL Metabolism

As a result of Nephrotic Syndrome, there is a marked increase of vascular and renal tissue Acyl-CoA cholesterol acyltransferase-1[ACAT-1] expression and heavy urinary losses and significantly decrease of serum lecithin cholesteryl ester acyltransferase [LCAT] level, that functions to regulate high-density lipoprotein [HDL]–mediated extraction of cholesterol from lipid-laden macrophages and mesangial and other cell types. This is followed by a significant increase in the level of serum cholesterol ester transfer protein [CETP]. This leads to further decrease in the level of HDL cholesterol and enhancement of its high-density lipoprotein triglyceride [HDL-TG]. Adding to it, by inducing inhibition and decrease of PDZ-containing kidney protein 1 (PDZK1), this disease results in a significant decrease in liver HDL docking receptor (scavenger receptor class B, type 1 [SR-B1]), that leads to unloading of HDL's cholesterol cargo and hepatic lipase-mediated extraction of its TG and phospholipid (PL) cargo. Altogether, all these abnormalities debilitate reverse cholesterol transport and contributes to the atherogenic diathesis for nephrotic syndrome. [24,29,33,38,39]

Menopause and Lipids:

Menopause is such a clinical condition, that is generally tracked in the women typically within age group of 45-55 years. It is a clinically diagnosed condition in which, the women due loss in the follicular activity of the ovaries has not been able to menstruate for nearly or over a year. Before arrival of the stage of menopause, women experiences perimenopause, or menopausal transition, where in order to cope up with the cessation of oocyte production in the ovaries, women experience irregular menstrual cycle. [6]

Estrogen, a primary female sex hormone, significantly regulates the development and function of the female reproductive system. Along with estrogen, estradiol [E2] and estriol [E3] is also present in body. E2 is found in almost every woman in reproductive age but E3 is produced by placenta. During reproductive age of women, the average level of total estrogen is 100–250 pg/mL, but post-

menopause, the level of E2 decreases to 10 pg/mL. [6,40]

In women with menopause, are at the highest risk for cardiovascular disease [CVD] due to deficiency in the level of estrogen and dysregulated metabolism of lipids. Owing to the menopausal status of women, there is a huge alteration in the various body fats. This alteration occurs due to decrease in the level of estrogen and follicle-stimulating hormone [FSH]. These changes are often noted during later menopause. Lipids that are majorly affected during menopause or perimenopause or post-menopause are, Lipoproteins, Apolipoproteins [Apo], Low-Density Lipoprotein-Cholesterol [LDL-C], High-Density Lipoprotein [HDL], High-Density Lipoprotein-Cholesterol [HDL-C], and TG[Triglycerides]. These lipids show a significant rise in level in perimenopause and early postmenopausal phase. By a study conducted, it was noted that in women of middle-age were noted to have lowest quartile FSH levels and the highest levels of total cholesterol and LDL-C. This fluctuation in the levels sex hormone and lipid metabolism increases the risk of CHD in women. The ratio of total cholesterol to HDL is a major indicator for cardiovascular disease in comparison with total cholesterol.

As per the studies reported, HDL-C levels gets elevated after menopause. As per the study reports, the HDL-C levels increase gradually from pre-menopause and peak during perimenopause. Gradually, HDL-C level declines until late post-menopause. But as per studies conducted, middle-aged healthy women, showed a decline in HDL-C level and gradual rise in LDL-C level. This rise in LDL-C level significantly increases the chance of cardiovascular diseases in women after menopause. [6,40–42] [43–51]

Lipid Metabolism and Renal Disorder:

Out of all the organs in the body, kidney is such an organ that requires high amount of energy. But, compared to its energy demand, it has relatively low glycolytic capacity. Thus, β-oxidation of free fatty acids (FFAs) in the mitochondria especially for proximal tubule cells is the major source of energy. Albumin contains >99% of plasma long-chain fatty acids (LCFAs). In chronic kidney disease [CKD] (especially in case of diabetic kidney disease), the circulating levels of LCFAs increases significantly, that leads to an increase in the LCFA load per albumin molecule. Serum LCFAs binds to albumin during glomerular filtration and those are reabsorbed by the proximal tubular cells via fatty acid transport CD36 and this mediates renal tubular fibrosis. This highlights the role of hypertriglyceridemia and high level of FFAs for tubular fibrosis. In CKD, the accumulation of tri-acyl-glycerol and FFAs with lower fatty acid oxidation (FAO) has important roles for the formation of foam cell and its pathogenesis for the case of kidney fibrosis. Several factors induce severe disbalance between fatty acid uptake and its consumption in CKD, such as oxidative damage of mitochondria, that results in reduction in FAO. The genes related to fatty acid metabolism along with their key transcriptional regulator complex (PPARα/PGC-1α) were seen to decrease significantly in human chronic kidney disease (CKD) samples with higher accumulation of lipids in diseased renal TECs. [52–55]

CD36 binds with context-specific binding partners [like Toll-like receptor 2 (TLR2), TLR4, TLR6 and Na +/K + ATPase] to activate multiple signal pathways. The interaction of CD36 with TLR2, tetraspanin and integrin, stimulates the uptake of ox-LDL and leads to the formation of foam cells during atherosclerosis. Hypertriglyceridemia is also stated as an independent risk factor for development of proteinuria and CKD. [52,56]

Pathophysiological Changes Caused by Lipid Overloading in Kidney:

- Oxidative Stress- Though initially n lipid-mediated renal damage is not clear, but oxidative stress plays an important role. Hyperlipidemia causes a rise in the rates of production of reactive oxygen species (ROS). This impairs with the relaxation of endothelium in kidney and leads to rise in plasma Ox-LDL level. In CKD, HDL cholesterol levels along with its antioxidant property in reduced in plasma. Inflammatory mediators such as TNFα and IL-1β, are commonly ROS activating factors in the kidney and may stimulate oxygen radical formation. Oxidative stress leads to decrease in renal NO production and it causes stimulation of angiotensin II synthesis, which leads to renin–angiotensin system (RAS) activation causes lipid-induced renal injury. Angiotensin II causes rise in the expression of TGF-β and plasminogen activator inhibitor-1 (PAI-1), that results in glomerular fibrosis. [52,53,56–63]
- Endoplasmic Reticulum (ER) Stress- The stress in ER induces a coordinated unfolded protein response (UPR), that helps the ER to adjust the accumulation of misfolded proteins. As per the recent study, intracellular accumulation of saturated fatty acids and cholesterol leads to ER stress, that result in apoptosis of macrophages. ER stress leads to dysregulation of endogenous sterol response mechanism and along with it activates oxidative stress pathways. [9,24,31,52,61–68]. Inflammatory Stress- The

presence of oxidative and ER stress activates the NF-κB pathway, which is related with the inflammatory events in glomerulonephritis, and stimulates the severity of CKD. [52,56].

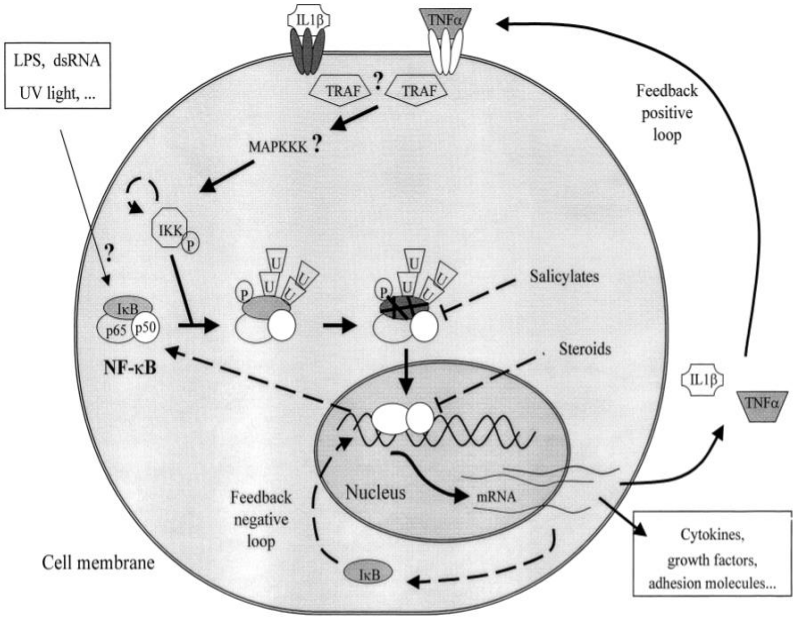

Fig: The pathway of NF-kB activation [69]

Lipids acts as pro-inflammatory mediators. LDL, VLDL, and IDL at a specific concentration, significantly increase in the secretion of inflammatory cytokines by MCs, that includes IL-6, PDGF, and TGF-β. As per studies, HDL has the capability to downregulate VCAM-1 and E-selectin on endothelial surfaces and this in turn reduces NF-κB. Thus, low HDL cholesterol levels enhance the chances of inflammatory responses. Absence of Apo-E blocks IL-6 receptor that prevents the risk of severity of proteinuria and renal lipid deposition. This also manages the mesangial cell proliferation that associates with severe hyperlipoproteinemia. This in turn manages pathogenesis of hyperlipidemia-induced glomerular injury. Inflammation also increases both medial and intimal calcifications which stimulates vascular and renal injury. [30,31,52,54,55,70–75]

Renal Fibrosis- Renal fibrosis is the major pathological change in the process of end-stage renal disease and it is the final pathological outcome of various chronic progressive renal diseases. [52,62,76,77]

Other Disorders Associated with Lipid Metabolism:

Some other disorders associated with lipid metabolism are diabetes, pregnancy toxemia, obesity, etc.

- Diabetes- Diabetes induced due to disorder of lipid metabolism occurs mainly in 75% of patients with type-2 diabetes mellitus. This is also known as diabetic dyslipidemia. It is mixed [atherogenic]hyperlipidemia. It causes the major risk for cardiovascular disease. It mainly occurs due to insulin resistance, and it is followed by moderate increase in the level of LDL-C, and rise in the level of TGs, level of HDL-C lowers. [1,75,78–81]
- Obesity- As we know that dyslipidemia includes rise in plasma levels of low-density lipoprotein cholesterol [LDL-C], very low-density lipoprotein cholesterol [VLDL-C], triglyceride [TG], and reduction in plasma levels of high-density lipoprotein cholesterol [HDL-C]. Thus, this is a confirmed hallmark for obesity and cardiovascular diseases (CVD), that imposes serious risks to the future of human health. Hence, the molecular metabolism of dyslipidemia, is associated with the morbidity and mortality of obesity and CVD. [7,15,32,43,61,62,75,82–84]
- Pregnancy toxemia- As per the recent studies conducted, there is an underlying mechanisms of lipid metabolism disorder in the livers that leads to pregnancy toxemia [PT]. Any disruption associated with lipid metabolism might be a reason for the pathogenesis of pregnancy toxemia. [85–89]

DISCUSSION:

Lipids thus plays some vital roles in maintaining the body balance in a living organism. Lipids thus are compounds that are water insoluble molecules and transported in a protein capsule or commonly known as lipoprotein. The density of the lipid is determined by the size of the lipoprotein. The core of the lipoprotein consists of cholesteryl esters, commonly known as triglycerides and the outer polar layer is consisting of apolipoproteins, free cholesterols, and phospholipids. Lipid metabolism thus can be described as the synthesis and degradation of lipids in cells, involving the breakdown or storage of fats for energy. It occurs in adipocytes and liver and in mammary gland during lactation. Lipid metabolism pathway is very closely related and connected to carbohydrate metabolism pathway. Lipolysis occurs to form triglycerides, which breaksdown into glycerol and fatty acids by the action of LPL. This glycerol produced is taken up by the glycolysis pathway to convert glucose into pyruvate molecules which is then converted into acetyl CoA. Fatty acids on the other side undergoes β-oxidation to yield acetyl CoA. Each round of β-oxidation eliminates two carbons from the fatty acid chain to yield acetyl CoA. These acetyl CoA are oxidized in the citric acid cycle to yield ATP via Electron Transport System. On the other hand, from β-fatty acid oxidation, 1NADH and 1FADH2 is obtained per round.

Fats yield more energy per unit mass as compared to carbohydrates. When acetyl CoA is produced in excessive amount, it is pushed to create ketone bodies. During glucose starvation, ketone bodies are used for excess source of energy for brain. Ketone bodies are acidic in nature, which when produced in excess amount, disturbs the buffering capacity of blood plasma, resulting in metabolic acidosis, which is also known as ketoacidosis, which can lead to coma and death. [1,2]

CONCLUSION:

From the above discussed disorders of lipid metabolism, we can draw a line that, lipid metabolism is a very vital process in a living body. It is such a function whose little disruption might lead to severe damages. These damages can sometimes be reversed via various medications and therapies, but sometimes these disorders are irreversible and might lead to permanent damage in body.

Conflict of interest statement

We declare that we have no conflict of interest.

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