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Review Article

Review Article on Hyperlipidemia

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ABSTRACT

Hyperlipidemia is a prevalent metabolic disorder characterized by elevated levels of plasma lipids, including cholesterol, triglycerides, and various lipoproteins such as low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL), with or without decreased high-density lipoprotein (HDL). It can arise due to genetic factors (primary hyperlipidemia), secondary causes such as diabetes, obesity, hypothyroidism, chronic kidney disease, or be exacerbated by medications and poor lifestyle habits. The condition is largely asymptomatic until significant complications develop, such as cardiovascular diseases, pancreatitis, or visible xanthomas in severe cases, especially among those with familial forms. Hyperlipidemia is a critical risk factor in the development of atherosclerosis, a pathological process involving the accumulation of lipids and formation of fibrous plaques within large and medium arteries. This progression narrows arterial lumen, reducing blood supply and increasing the risk of ischemic cardiovascular events including coronary artery disease, stroke, and peripheral vascular disease. The pathophysiology centers on excessive VLDL and LDL concentrations, which can lead to altered, oxidized LDL uptake by macrophages, foam cell formation, vascular inflammation, and plaque growth. The management of hyperlipidemia revolves around controlling plasma lipid concentrations to prevent adverse cardiovascular outcomes.

INTRODUCTION

Cardiovascular disease is a leading cause of mortality in America, claiming 65,000 lives annually [1]. Cardiovascular disease has been linked to many modifiable risk factors in the literature, particularly blood pressure, low density lipoprotein (LDL), high density lipoprotein (HDL), glucose intolerance, and smoking [2]. (1). Liver synthesizes two-third of the total cholesterol in the body. The rate limiting enzyme is 3-hydroxy-3-methylglutaryl (HMG)-Co A reductase and provides feedback regulation by controlling the cholesterol concentrations in cells. Treatment of hyperlipidemia involves diet control, exercise,

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and the use of lipid-lowering diets and drugs [2]. (2). Hyperlipidemia is considered one of the major risk factors causing to cardiovascular diseases (CVDs). CVDs accounts for 1/3 rd of total deaths around the total world, it is believed that cardiovascular diseases will turn out to be the main cause of death and incapacity worldwide by the year 2020[7-9].(3). In the body, the liver produces about 80% of Cholesterol but the rest is obtained from the food We eat such as fish, eggs, and meat. Hyperlipidemia is the major cause of various cardiovascular diseases which shows greater risk Factors and causes major issues. Various drugs are Used to treat Hyperlipidemia and to reduce Cholesterol levels in the plasma which includes Statins and fibrates (4)

Types of Lipoproteins

1) High-density lipoproteins (HDL)
2) Intermediate-density lipoproteins (IDL)
3) Low-density lipoproteins (LDL)
4) Very Low-Density Lipoproteins (VLDL)
5) Chylomicrons

High-Density Lipoproteins:

HDL is considered a good cholesterol and is Synthesized in the liver. It picks up the excess Amount of cholesterol from the blood and takes it Back to the liver where breakdown happens and Removal from the body. An HDL level ranging From 60mg/dL should be considered desirable and Protect against heart diseases.

Intermediate Density Lipoprotein (IDL):

After the removal of Triglycerides from VLDL by muscles and Adipose tissues, the IDL particles form which have cholesterol molecules.

Low-Density Lipoprotein:

It is sometimes referred to as bad cholesterol because it makes up most of your body's cholesterol. High levels of LDL cholesterol can cause the risk of heart disease and strokes.

❖ **Very Low-Density lipoprotein:**

Very low-density lipoprotein is produced in the liver and released in the bloodstream for supplying fats (triglycerides) to the body tissues.

❖ **Chylomicrons:**

They are the large triglycerides-rich lipoprotein produced in tight junctions of the cells. They Transport dietary triglycerides and cholesterol peripherally.

Etiology

Sterol, fatty acids, trans fat in the following food may Increase the lipid level in blood:

- Dairy products.
- Ice cream pastries.
- Fried and junk foods.
- Meat etc.20

Other disorders like obesity, diabetes mellitus and Hypothyroidism is major causes for hyperlipidemia. Smoking and low exercising may lead to Hyperlipidemia21.Excessive use of alcohol also increases The risk of hyperlipidemia. Certain drugs as steroids and β– Blockers may cause hyperlipidemia (3) Lipoprotein lipase Mutations22.

Several other causes of hyperlipidemia

- Obesity.
- Genetic or inheritance.

- Smoking.
- Several drugs such as corticosteroids, estrogen, Betablockers may risk for hypertriglyceridemia.
- Alcohol, steroids, hypothyroidism, kidney failure etc.
- Low exercise 23

Clinical presentation

Hypercholesterolemia often lacks overt symptoms but is a major risk factor for cardiovascular disease [3]. Very high cholesterol levels, usually seen in familial hypercholesterolemia, can manifest as xanthomas and corneal arcus. Complications from inadequately managed hypercholesterolemia include carotid artery disease, stroke,peripheral vascular disease, high blood pressure, and type two diabetes mellitus (T2DM) [13, 14].Systemic diseases associated with influencing dyslipidemia include psoriasis, Crohn's disease, inflammatory bowel disease, chronic obstructive pulmonary disease, depression, chronic pain, and chronic kidney disease [14]. A 2017 observational study involving 7,641 Europeans over the age of 50 (1)

- chest pain (angina), heart attack or stroke.
- When levels are exceeded high, cholesterol may be Deposited in tendons or just beneath the skin under the Eyes.
- liver, spleen or pancreas is swelled.
- blood vessels block in brain and heart.
- Higher rate of obesity and glucose intolerance.
- Pimple like lesions across the body25

Pathophysiology

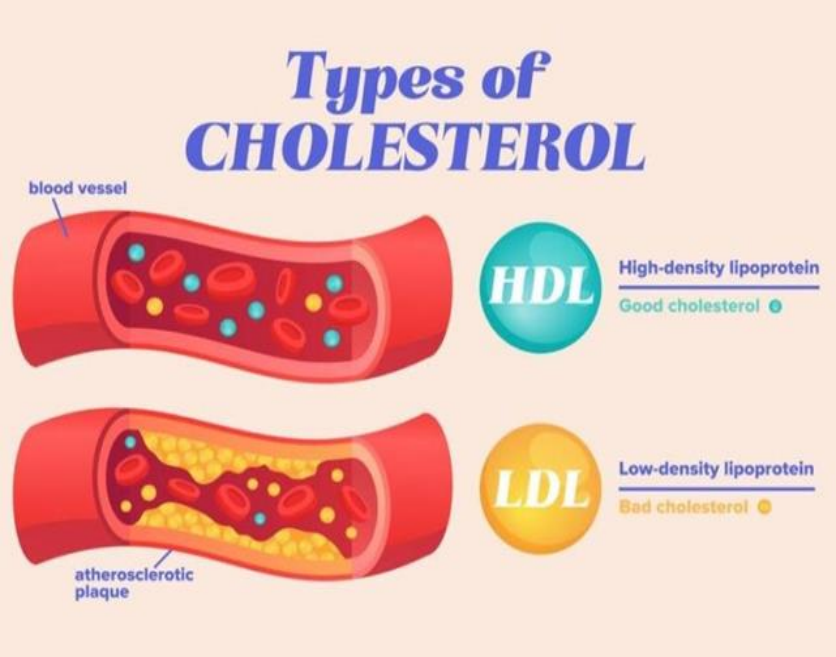
During the early stages of the hyperlipidaemia, blood Monocytes and platelets attach to a vessel wall at the sites of endothelial damage. The release of the mediators such As platelet derived from growth factors leads to a growing Of smooth cells in the intimal and medial lining of the Vessel, collagen synthesis, cholesterol uptake and the Initial for the hyperlipidaemic plaque results. Plaque Ruptures are resulting in the acute syndromes of unstable Angina, myocardial infarction and sudden cardiac death [26.](9)

- Excess intake or endogenous production of fats leads to increased circulating triglycerides and cholesterol, especially low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL).
- Impaired clearance of these lipoproteins, often from reduced activity of enzymes like lipoprotein lipase, is a frequent cause, particularly in diabetes.
- In genetic forms, such as familial hypercholesterolemia, mutations reduce LDL receptor function, impairing LDL clearance.
- Elevated lipids trigger oxidative stress and inflammation, promoting endothelial damage, atherosclerosis, and tissue fibrosis.
- Intracellularly, excess lipid accumulation disrupts normal cell signaling, mitochondrial function, and energy metabolism, especially in the heart and vascular system.
- Hyperlipidemia also suppresses autophagy in tissues, promotes apoptosis, and can independently alter cardiac electrophysiology, making the myocardium more susceptible to damage.

Histopathology

In the presence of hyperlipidaemia, not only the vascular structures are negatively involved but also other tissues. Fort example, research has

demonstrated through patellar tendon shear wave velocities that there is a direct relationship between the intrinsic alteration of the patellar tendon and the presence of hyperlipidaemia. The tendon becomes stiffer with morphological alteration of the tissue and changes in the type of cells present. Increases the number of macrophages in the tendon tissue, damaged collagen fibres, replacement of collagen cells with lipid cells; collagen type III increases, which is less elastic, matrix metalloproteinases increase. The tendon in the presence of hyperlipidaemia becomes mechanically less effective and more prone to injury.



High Blood Cholesterol

Hyperlipidemia is dangerous because the extra cholesterol circulating in the bloodstream forms the basis for plaque lining the arteries. Plaque slows the flow of blood through the arteries, which is especially dangerous when it occurs in the heart. Coronary artery disease can result in angina or a heart attack. During a heart attack, a section of the heart muscle receives no oxygen because blood circulation in the heart arteries is blocked by plaque. Plaque can also break off from an artery wall and circulate in the body, causing a stroke or peripheral arterial disease. Treatment for high cholesterol includes lifestyle changes and cholesterol-lowering medication. Weight Loss, regular exercise, smoking cessation, and a healthful diet low in saturated fats, trans fats, and cholesterol can lower bad cholesterol significantly. The recommended target cholesterol level depends upon The patient's overall health and the presence of other risk factors for heart disease, such as diabetes and High blood pressure. If lifestyle changes are not effective in reducing cholesterol to the target level, various Medications are available that are safe and effective for lowering cholesterol, including statins, fibrates, Bile acid sequestrants, the selective cholesterol-absorption inhibitor ezetimibe, and nicotinic acid.

Diagnosis

No any other specific symptom for Hyperlipidemia it can Be only detected by a blood test. Screening for Hyperlipidemia is done with a blood test called a lipid Profile.39Hyperlipidemia

may be diagnosed by a regular Checkup of LDL, HDL, VLDL and Triglycerides in blood test.40. A high cholesterol level (>200 mg/dL) alone does not cause symptoms, but the health problems that Result from high cholesterol can cause symptoms. A blood test can be used to diagnose hyperlipidemia Long before symptoms arise. There are normal ranges for total cholesterol (≤200 mg/dL), LDL cholesterol (<100 mg/dL), and HDL cholesterol (>60 mg/dL), but these may be adjusted based on individual factors such as the patient's age and the presence of other health problems, such as diabetes or heart disease (11)

Prevention Of Hyperlipidemia

- Low fatty acid and cholesterol diet should be taken.
- Intake of foods high in soluble fiber such as oats, beans and certain fruits.
- Exercise regularly to maintain a healthy weight.3

Treatment

The following lifestyle modification may lower the cholesterol level

- Proper diet.
- Less weight of the body.
- Regular exercise.
- Having non-oily food

Management: Lifestyle Modification

Lifestyle changes are the cornerstone of hyperlipidaemias management and are often the first line of treatment, especially for individuals with moderately elevated lipid levels. These modifications can significantly reduce lipid Levels and lower the risk of cardiovascular disease.

Dietary Changes

Emphasise a diet rich in Fruits, vegetables, whole Grains, lean proteins, and Healthy fats (monounsaturated and Polyunsaturated). Limit Saturated and trans fats, Cholesterol, and refined Sugars. The Mediterranean Diet is often recommended.

Regular Physical Activity

Aim for at least 150 minutes Of moderate-intensity Aerobic exercise or 75 Minutes of vigorous intensity exercise per week. Exercise helps lower LDL, Raise HDL, and reduce Triglycerides.

Weight Management

Achieving and maintaining a Healthy weight can Significantly improve lipid Profiles. Even a modest Weight loss can have a Positive impact on Cholesterol and triglyceride Levels.

Smoking Cessation

Quitting smoking is one of The most impactful steps to Improve cardiovascular Health. It helps increase HDL cholesterol and Reduces damage to blood Vessels.

Moderate Alcohol Consumption

If you drink alcohol, do so in Moderation. Excessive Alcohol intake can Significantly raise Triglyceride levels.

Management: Pharmacological Treatment

When lifestyle modifications alone are insufficient to achieve target lipid levels, pharmacological interventions Become necessary. Several classes of medications are available, each targeting different aspects of lipid Metabolism.

1 Statins

The most commonly prescribed drugs for high cholesterol. They work by inhibiting an enzyme in the Liver that produces cholesterol, thereby lowering LDL cholesterol and triglycerides, and modestly Increasing HDL.

2 Ezetimibe

Works by blocking the absorption of cholesterol from the small intestine. It is often used in combination With statins or as an alternative for those who cannot tolerate statins.

3 PCSK6 Inhibitors

A newer class of injectable drugs that significantly lower LDL cholesterol by increasing the number of LDL receptors on liver cells. Used for individuals with very high LDL or those who cannot tolerate Statins.

4 Fibrates

Primarily used to lower very high triglyceride levels and can also modestly increase HDL cholesterol. Examples include gemfibrozil and fenofibrate.

5 Niacin (Nicotinic Acid)

Can lower LDL cholesterol and triglycerides while raising HDL cholesterol. However, its use is limited by Side effects such as flushing.

6 Omega-3 Fatty Acid Supplements

High doses of prescription omega-3 fatty acids can significantly lower very high triglyceride levels.

Differential Diagnosis

It is imperative for diagnosing providers to assemble a comprehensive list of differentials when screening a patient for hyperlipidemia. Primary disorders should always be considerations; these include familial hypercholesterolemia, familial combined hyperlipidemia, dysbetalipoproteinemia, familial defective apo B-100, and PCSK9 gain of function mutations. Then, these secondary disease processes must also be in the differential when diagnosing a patient with hyperlipidemia: obstructive liver disease or biliary obstruction,hypothyroidism, nephrotic syndrome, chronic renal insufficiency, anorexia, obesity, metabolic syndrome, and diabetes.[4] A full history and physical complete with comprehensive labs should be obtained to narrow down the differential and make the correct diagnosis.

CONCLUSION

Hyperlipidemia remains a significant public health challenge, contributing substantially to the global burden of cardiovascular disease. Comprehensive management, encompassing both lifestyle modifications and pharmacological therapies, is crucial for preventing its devastating complications.Hyperlipidemia, a primary cause of coronary Heart disease, is quite common in India. The link Between hyperlipidemia and the development of Cardiovascular disease has long been known. Antioxidants, fibrates, bile acid binding resins, And other treatments for hyperlipidemia have Been described in a number of trials. Diet, Physical exercise, and smoking are all Controllable risk factors. Age and gender are two Non-modifiable characteristics. Non-healthy People cause adiposopathy. Diet and a low Active lifestyle are harmful to the environment, And persons who are genetically prone Prior to The event, The majority of patients have physical Results that appear to be abnormal. Regardless, Various lipid disorders frequently coexist, Management strategies are determined by the

Situation. Irregularity of lipids There are several Nations or regions that have their own Dyslipidaemia guidelines were produced. Dyslipidemia prevention and therapy consists of A large number of operations. These methods Involve risk assessment, treatment goal Establishment, increased activity level, food Change, medical therapy, follow-up, Reassessment, and procedure adjustment as Needed. Raise awareness of the disease and the Actions that must be taken by all family Members. Future research is needed to identify The mechanobiological mechanisms that govern The response of lipid profiles to dietary loading.

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