

Hyperlipidemia Characterized by Abnormal High Level of Lipids

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Abstract: *Hyperlipidemia is a family of disorders that are characterised by abnormally high levels of lipida (fats) in the blood. While fats play a vital role in the body's metabolic processes, high blood levels of fats increase the risk of coronary heart disease (CHD). Cardiovascular diseases, especially coronary heart disease (CHD), are epidemic in India. According to American Heart Association, the Centres for Disease Control and Prevention, the National Institutes of Health and other government sources, cardiovascular disease is the leading global cause of death, accounting for more than 17.3 million deaths per year, a number that is expected to grow to more than 23.6 million by 2030. India has seen a rapid transition in its heart disease burden over the past couple of decades. Of the 30 million heart patients in India, 14 million reside in urban areas and 16 million in rural areas. If the current trend continues, by the year 2020, the burden of atherothrombotic cardiovascular diseases in India will surpass that of any other country in the world. The Registrar General of India reported that CHD led to 17% of total deaths and 26% of adult deaths in 2001-2003, which increased to 23% of total and 32% of adult deaths in 2010-2013. The global increase in the prevalence of hyperlipidemia is due to unhealthy eating habits, obesity and physical inactivity. The emergencies, risk factors and remedies are described in the literature..*

Keywords: Hyperlipidemia, Coronary heart disease, lipoproteins.

I. INTRODUCTION

Hyperlipidemia disease has afflicted humankind since antiquity. In 2002, coronay heart Epidemiological evidence strongly supported the positive correlation between blood lipids, hyperlipidemia and its complications, mainly CHD [1]. This relationship has been shown between and within cultures [2-4]. The hyperlipidemia is traditionally defined as conditions in which the concentration of cholesterol or triglyceride-carrying lipoproteins in plasma exceeds an arbitrary normal limit [5]. These lipoproteins deposit in the interstitial space of arteries arising from aorta, restricting the blood supply to the heart. This phenomenon is known as atherosclerosis. Higher deposition of lipoproteins completely blocked the blood supply to the heart, and thus myocardial infarction (MI) occurs, which is commonly known as heart attack.

Cholesterol

It is a vital component of the mammalian cell membrane of all tissues and is a precursor of steroid hormones and bile acids. It occurs, either free or as many fatty esters in all animal cells, but is absent in plant fats. Its structure is depicted

Triglycerides

These are the most abundant of all lipids. It is found abundantly in adipocytes. These are major components of storage fats in plant and animal cells. Excess calories, alcohol and sugar in the body get converted into triglycerides and stored in fat cells throughout the body [6]. Chemically triglycerides are esters of glycerol with 3 fatty acid molecules. The generic formula is shown in fig. 2. Data obtained from National Institute of Health, limits triglycerides value to 200 mg/dl as the normal range and 500 mg/dl as an abnormal range. Range higher than 500 mg/dl is considered dangerous for the development of cardiovascular diseases [7].



VLDL: Very low-density lipoproteins are smaller particles carrying lesser triglyceride contents than chylomicrons, and are secreted from the liver. VLDL carries cholesterol from the liver to organ and tissues in the body. They are formed from the combination of cholesterol and triglycerides [8].

IDL: VLDL particles after degradation by lipase enzyme in the capillaries of adipose tissue and muscle give rise to intermediate density lipoprotein.

LDL: According to Lee et al., and Galeano et al., low-density lipoproteins are synthesised partly in intestinal chyle and partly after lipolysis of VLDL. It is directly correlated to CHD [9, 10]

HDL: HDL is commonly referred as good cholesterol. High-density lipoproteins are synthesised in the liver. It carries cholesterol and other lipids from tissues back to the liver for degradation [11]. HDL plays an antiatherogenic role.

Lp(a): It is secreted from the liver. Berg defined lipoprotein (a) as a cholesterol-rich plasma lipoprotein, which is directly correlated with atherosclerosis [12]. The risk of CHD is increased 2 to 5 fold with higher Lp(a) plasma concentration level.

Studies by Nago et al., concluded that Lp(a) levels were higher in females in contrary to males and statistically significant increase were observed in Lp(a) plasma level concentration with age. They also reported the lower Lp(a) plasma levels in alcohol drinkers, contrary to non-drinkers [13].

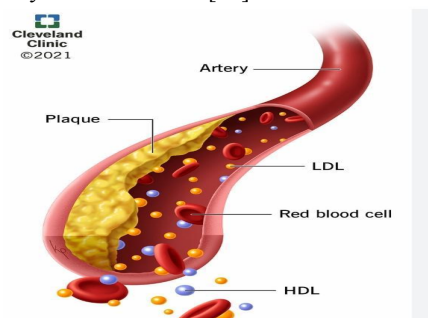


Fig 1 Hyperlipidemia

Classification

Familial (Primary) hyperlipidemia—On the basis of causing factors hyperlipidemia can be designated as either primary or secondary [14]. According to Fredrickson familial hyperlipidemia is classified into five types (table 2) on the basis of electrophoresis or ultracentrifugation pattern of lipoproteins [15].

Type I—Raised cholesterol with high triglyceride levels.

Type II—High cholesterol with normal triglyceride levels.

Type III—Raised cholesterol and triglycerides.

Type IV—Raised triglycerides, atheroma and uric acid.

Type V—Raised triglycerides.

This classification was later adopted by WHO. This method does not directly account for HDL and also does not distinguish among the different genes that may be partially responsible for some of these conditions. It remains a popular system of classification but is considered dated by many [16].

Acquired (Secondary) hyperlipidemia—Acquired hyperlipidemia (secondary dyslipoproteinemias) results from underlying disorders and lead to alterations in plasma lipid and lipoprotein metabolism [17]. This type of hyperlipidemia may mimic primary forms of hyperlipidemia and can have similar consequences. They may result in increased risk of premature atherosclerosis, pancreatitis and other complications of the chylomicronemia syndrome. The most common causes of acquired hyperlipidemia are given below [18].

Several prospective studies have identified hypertension [19] higher concentration of lipids in serum [20-22] and cigarette smoking [23, 24] as the three treatable risk factors that have the highest association with CHD. The association of total plasma cholesterol levels (TC) with the incidence of CHD is well established [25, 26]. The low-density lipoprotein cholesterol (LDL-C) is directly correlated [27-29], while high-density lipoprotein cholesterol (HDL-C) is inversely related [30-32] to CHD incidence. Human plasma IDL-C are a heterogeneous collection of particles which



vary in buoyant density, size, lipid and protein composition [33, 34]. The presence of estrogens in female lowers serum lipids [35].

Complications of hyperlipidaemia

Atherosclerosis: It is a common disorder and occurs when fat, cholesterol and calcium deposits in the arterial linings [36]. This deposition results in the formation of fibrous plaques. A plaque normally consists of three components: 1) atheroma which is a fatty, soft, yellowish nodular mass located in the centre of a larger plaque that consists of macrophages, which are cells that play a role in immunity; 2) a layer of cholesterol crystals; and, 3) calcified outer layer. Atherosclerosis is the leading cause of cardiovascular disease.

Coronary Artery Disease (CAD): Atherosclerosis is the major cause of CAD. It is characterised by the narrowing of the arteries that supply blood to the myocardium and results in limiting blood flow and insufficient amounts of oxygen to meet the needs of the heart. The narrowing may progress to the extent that the heart muscle would sustain damage due to lack of blood supply. Elevated lipid profile is correlated to the development of coronary atherosclerosis [37].

Myocardial Infarction (MI): MI is a condition which occurs when blood and oxygen supplies to the cardiac arteries are partially or completely blocked, resulting in damage or death of heart cells. The blockage is usually due to the formation of a clot in an artery. This condition is commonly known as heart attack. The studies show that one-fourth of survivors of myocardial infarction were hyperlipidemic [38].

Angina Pectoris: Angina is not a disease but a symptom of an underlying heart condition. It is characterised by chest pain, discomfort or a squeezing pressure. Angina occurs as a result of a reduction or a lack of blood supply to a part or the entire heart muscle. Poor blood circulation is usually due to CHD when partial or complete obstruction of the coronary arteries is present.

Ischemic stroke or Cerebrovascular Accident (CVA): It occurs when blood circulation in part of the brain is blocked or diminished. When blood supply, which carries oxygen, glucose, and other nutrients, is disrupted, brain cells die and become dysfunctional. Usually, strokes occur due to blockage of an artery by a blood clot or a piece of atherosclerotic plaque that breaks loose in a small vessel within the brain. Clinical trials revealed that lowering of LDL and total cholesterol by 15% significantly reduced the risk of first stroke [39].

Causes of hyperlipidemia

A diet rich in saturated fat and cholesterol increases blood cholesterol and triglyceride levels.

Other disorders as obesity, diabetes mellitus and hypothyroidism increase the risk of hyperlipidemia.

Smoking and not exercising may lead to hyperlipidemia [40].

Excessive use of alcohol also increases the risk of hyperlipidemia.

Certain drugs as steroids and β -blockers may cause hyperlipidemia.

Hereditary factor is also one of the common causes for hyper-lipidemia.

In some cases hyperlipidemia occurs during pregnancy.

Lipoprotein lipase mutations [41].

- Diabetes Mellitus
- Use of drugs such as diuretics, β -blockers and estrogens.
- Alcohol consumption.
- Some rare endocrine disorders and metabolic disorders.
- Hypothyroidism
- Renal failure
- Nephrotic syndrome
- Major primary and secondary forms of hyperlipidemia, their lipoprotein abnormalities and drugs used for their treatment chest pain (angina), heart attack or stroke.
- When levels are exceedingly high, cholesterol may be deposited in tendons or just beneath the skin under the eyes.



- Swelling of organs such as liver, spleen or pancreas.
- Blockage of blood vessels in brain and heart.
- Higher rate of obesity and glucose intolerance.
- Pimple like lesions across the body.
- Pathogenesis of hyperlipidemia

Cholesterol, triglycerides, and phospholipids are transported in the bloodstream as complexes of lipid and proteins known as lipoproteins. Elevated total and low-density lipoprotein (LDL) cholesterol and reduced high-density lipoprotein (HDL) cholesterol are associated with the development of coronary heart disease (CHD).

During the early stages of the hyperlipidemia, blood monocytes and platelets attach to a vessel wall at the sites of endothelial damage. The release of the mediators such as platelet derived growth factors leads to a proliferation of smooth cells in the intimal and medial lining of the vessel, collagen synthesis, cholesterol uptake and the beginning of the hyperlipidemic plaque results. Plaque ruptures are resulting in the acute syndromes of unstable angina, myocardial infarction and sudden cardiac death [44].

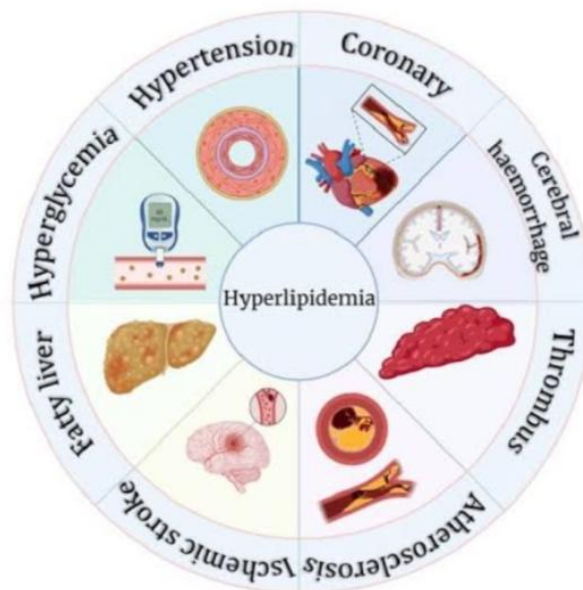


Fig 2 Causes of Hyperlipidemia

Diagnosis of hyperlipidemia

Hyperlipidemia typically shows no symptoms and can only be detected by a blood test. Screening for hyperlipidemia is done with a blood test called a lipid profile. According to National Cholesterol Education Program (NECP) screening [45] should start at age 20, and if the report is normal, it should be repeated at least every five years. Normal levels for a lipid profile [46, 47] are listed below (table 5).

Prevention of hyperlipidemia

Low fats and cholesterol diet should be taken.

Eat foods high in soluble fiber such as oats, beans and certain fruits.

Exercise regularly to maintain a healthy weight.

Controllable lifestyle changes are the best way to fight hyperlipidaemia. But when lifestyle changes fail to control the disease then treatment with cholesterol-lowering drugs is required.



Treatment of hyperlipidemia

In 1987 the National Institute of Health (NIH) established the National Cholesterol Education Program (NCEP) to be directed by the Adult Treatment Panel (ATP) for the purpose of issuing information for health professionals and the general public concerning testing, evaluating, monitoring and treating hyper-lipidemia. An important criterion of ATP guidelines is the development of treatment goals for hyperlipidemia based on patient's risk of CHD.

ATP recommends two methods of treatment:

- 1) Therapeutic lifestyle changes;
- 2) Drug therapy.

Therapeutic lifestyle changes

Diet modification, regular physical activity, smoking cessation, and weight reduction should be tried as initial treatment, especially in mild cases of hyperlipidemia and in persons without CHD or CHD risk equivalent and <2 risk factors. It should be kept in mind that when dieting, cholesterol intake is reduced. At the same time, production of cholesterol, especially by the liver, increases. It is recommended that the intake should be restricted to 25%-35% of energy intake and that saturated fatty acids make up less than 7% of energy intake and that cholesterol intake should be less than 200 mg daily. The intake of plant sterol esters and soluble fibre is advisable. A healthy diet can result in 10% to 15% reduction of cholesterol blood level.

Drug therapy

High LDL, the presence of risk factors, and documentation of CHD should qualify initiating drug therapy along with TLC. Monotherapy has been shown to be effective in treating hyperlipidemia, but combination therapy may be required for a comprehensive approach. Current lipid-lowering drugs include statins, ezetimibe, bile acid sequestrants or bile binding resins, niacin, fibric acid derivatives, and plant sterols.

Medication specially designed to reduce blood cholesterol levels may be prescribed when dietary modifications prove inadequate. In rare patients with extremely high cholesterol levels, repeated removal of blood plasma may be recommended to lower blood cholesterol levels. Most people require lifelong treatment of hyperlipidemia with both lifestyle measures and medications.

Pharmacological treatment

Numbers of hypolipidemic drugs are available in the market for the treatment of hyperlipidemia. The existing hypolipidemic drugs are listed in table 6. In 1975, the results of the Coronary Drug Project indicated that the drugs are relatively ineffective for preventing myocardial infarction in patients with pre-established CHD.

This project examined the effects of estrogens, D-thyroxin, clofibrate and nicotinic acid. The high-dose estrogens were discontinued in 1970 because of an increased number of fatal cardiovascular events without any indication of benefit.

The low-dose estrogens were discontinued in 1975 because of suggestion of an excess incidence of mortality from cancer. D-thyroxin was discontinued in 1971 because of increased mortality in this group [48].

Ayurvedic treatment

Ayurvedic medicine is one of the world's oldest medical systems. Ayurvedic therapeutics is based on the "laws" of nature. Its approach to health-care is based on understanding the interrelationship of body, mind and spirit. The aim of ayurveda medicine is to integrate and balance these elements to prevent illness and promote wellness through diet, nutrition, herbs, yoga, meditation and daily seasonal routines [49].

There is no term for hyperlipidemia in Ayurveda. But distinct nomenclature is used, e. g., Rasagata Sneha Vriddhi (increased lipid plasma level), Rasa Raktagata Sneha Vriddhi (increased lipid plasma and lipid blood level), Medovriddhi (generalised lipid increase), Medoroga (obesity), AAMA Medo Dhatu (abnormally formed adipose tissue).



AAMA is the primary cause of all metabolic disorders in Ayurveda. A detailed study of hyperlipidemia reveals its similarity to Asthaya Medo Dhatu Vriddhi (abnormal increase in circulating lipids). This excessively increased circulating lipid is AAMA in nature, resulting in further complications [50].

Ayurvedic medicine has been used for thousands of years for treatment of various metabolic disorders. However, few studies have been conducted to evaluate the effectiveness of Ayurveda herbal medicine formulae on hyperlipidemia. Higher quality studies, such as randomised clinical trials, are lacking [51].

Ayurveda also prescribes “Yoga” as a beneficial tool for proper blood circulation and elimination of the cholesterol build up in the body [52]. Some of the useful asanas for the treatment of hyperlipidemia are-Ardhamatsyendrasana, Shalabhasana, Padmasana, Vajrasana.

Home medications

Besides, pharmacological and ayurvedic treatment, some home remedies are also beneficial in the treatment of hyperlipidemia.

Plants having hypolipidemic activity

Medicinal plants have always been considered as a healthy source of life for all people due to its rich therapeutic properties and being 100% natural [53]. Medicinal plants are widely used by the majority of populations to cure various diseases and illness and have a high impact on the world's economy [54].

Over the past decade, herbal medicine has become a topic of global importance, making an impact on both world health and international trade. Continuous usage of herbal medicine by a large proportion in the developing countries is largely due to the high cost of Western Pharmaceuticals and Healthcare [55]. Medicinal plant-based drug industries is progressing very fast in India. The medicinal plants play a major role in hypolipidemic activity [56]. The advantages of herbal medicines are effectiveness, safety, affordability and acceptability.

II. CONCLUSION

The prevalence of hyperlipidemia, a major cause for coronary heart disease is very high in India. The relation between hyperlipidemia and occurrence of cardiovascular diseases has been already established. Various studies have reported the treatment of hyperlipidemic patients with antioxidants, fibrates, bile acid binding resins, etc.

Though many Ayurvedic formulations and herbal remedies are available to treat hyperlipidemia, the problem of enhanced cholesterol levels in the blood is still prevailing and is being a cause for many coronary disorders.

Recently, certain medicinal plants and herbs have seen light in treating these elevated lipid levels and reducing the risk of heart attacks. To reduce the risk of cardiovascular diseases due to hyperlipidemia requires urgent lifestyle intervention strategies and drugs that can reduce the cholesterol and triglyceride levels in the blood. Further studies are mandatory in order to provide more information about the safety and efficacy of novel anti-hyperlipidemic agents.

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