

A Review on Hyperlipidemic

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Abstract

Hyperlipidemia disease has afflicted humankind since antiquity. The treasure house of plant kingdom has a number of plants to treat this ailment. The indigenous system of medicine provides an abundant data about plants available for treatment of hyperlipidemia. A lot work has been carried out by researches on various plants to evident their effectiveness in hyperlipidemia. But still lots many are left which are used in the indigenous system but no systematically studies regarding their pharmacology have been carried out. One such natural medicine in indigenous system claimed to be useful in treatment of high fat deposition in various organs. *Echinochloa crus galli* plant has pharmacological importance in regarding hyperlipidemia and its information about hypolipidemic activity was written in some Ayurvedic books. Current study is under taken to evaluate weather the *Echinochloa crus galli* possess antihyperlipidemic or hypolipidemic activity. So the purpose of present study is to evaluate effect of *Echinochloa crus galli* on hyperlipidemia..

INTRODUCTION

Hyperlipidemia is a condition excess of fatty substances called lipids, largely cholesterol and triglycerides, in the blood. It is also called hyperlipoproteinemia because these fatty substances travel in the blood attached to proteins. This is the only way that these fatty substances can remain dissolved while in circulation.

The most recent cholesterol management guidelines (the third report of the adult treatment panel APT III), which are issued by the national cholesterol education program (NCEP) in may 2001, redefine the levels at which blood cholesterol should be treated [1]. These new evidence-based recommendations are departure from the NCEP's previous guidelines (ATP II) in several ways.

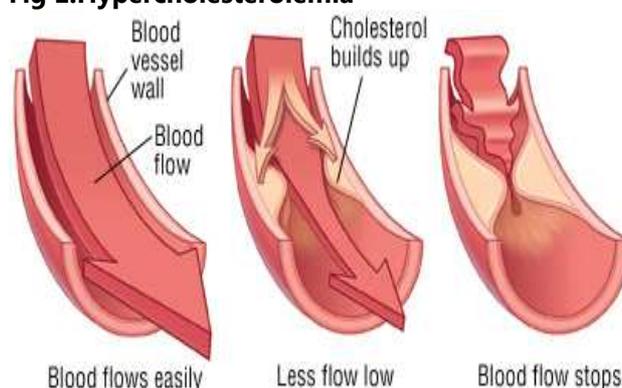
American heart association defined hyperlipidemia is a high level of fats in the blood. These fats, called lipids include cholesterol and triglycerides. There are different types of hyperlipidemia depending on which lipid levels are high in the blood [2].

HYPERLIPIDEMIA IN GENERAL CAN BE DIVIDED INTO TWO SUBCATEGORIES

1. Hypercholesterolemia, in which there is a high level of cholesterol

2. Hypertriglyceridemia, in which there is a high level of triglycerides, the most common form of fat

Fig 1. Hypercholesterolemia



DESCRIPTION OF HYPERLIPIDEMIA

The fat-protein complexes in the blood are called lipoproteins. The best-known lipoproteins are LDL (low-density lipoprotein) and HDL (high-density lipoprotein). Excess LDL cholesterol contributes to the blockage of arteries, which eventually leads to heart attack. Population studies have clearly shown that the

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higher the level of LDL cholesterol, the greater the risk of heart disease. This is true in men and women, in different racial and ethnic groups, and in all adult age groups. Hence, LDL cholesterol has been labeled the bad cholesterol. In contrast the lower the level of HDL cholesterol, the greater the risk of coronary heart disease. As a result, HDL cholesterol is commonly referred to as the good cholesterol. Low HDL cholesterol levels are typically accompanied by an increase in blood triglyceride levels. Studies have shown that high triglyceride levels are associated with an increased risk of coronary heart disease. Although hyperlipidemia does not cause to feel bad, it can significantly increase the risk of developing coronary heart disease, also called coronary artery disease or coronary disease. People with coronary disease develop thickened or hardened arteries in the heart muscle. This can cause chest pain, a heart attack, or both. Because of these risks, treatment is often recommended for people with hyperlipidemia. High lipid levels can speed up a process called atherosclerosis, or hardening of the arteries. Arteries are normally smooth and unobstructed on the inside, but as age goes, a sticky substance called plaque forms in the walls of your arteries. Plaque is made of lipids and other materials circulating in your blood. As more plaque builds up, your arteries can narrow and stiffen. Eventually, enough plaque may build up to reduce blood flow through your arteries. Hyperlipidemia has been implicated in atherosclerosis, which is the primary cause of heart disease and stroke [3]. Atherosclerosis increases your risk of heart disease, stroke, and other vascular diseases. Fortunately, may be able to reduce high lipid levels and therefore prevent or slow the progression of

atherosclerosis. Lifestyle changes like exercising and eating a healthy diet can also lower your lipid levels and are often the first step in treatment.

CLASSIFICATION OF HYPERLIPIDEMIA

Hyperlipidemia may be classified as either familial (also called primary) caused by specific genetic abnormalities, or acquired (also called secondary) when resulting from another underlying disorder that leads to alterations in plasma lipid and lipoprotein metabolism. Also, hyperlipidemia may be idiopathic, that is without known cause.

FAMILIAL (PRIMARY)

Familial hyperlipidemias are classified according to the Fredrickson classification, which is based on the pattern of lipoproteins on electrophoresis or ultracentrifugation. It was later adopted by the World Health Organization (WHO). It does not directly account for HDL, and it 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 [2].

ACCORDING TO “FREDRICKSON” CLASSIFICATION, THERE ARE FIVE TYPES OF HYPERLIPIDAEMIA

- 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 raised uric acid
- Type V - Raised triglycerides

Hyperlipo-proteinemia		Synonyms	Defect	Increased lipoprotein	Main symptoms	Serum appearance
Type I	A	Buerger-Gruetz syndrome, or Familial hyperchylomicronemia	Decreased lipoprotein lipase (LPL)	Chylomicrons	Abdominal pain (from pancreatitis), lipemia retinalis, eruptive skin xanthomas, hepatosplenomegaly	Creamy top layer
	B		Altered ApoC2			
	C	LPL inhibitor in blood				
Type II	A	Familial Hypercholesterolemia	LDL receptor deficiency	LDL	Xanthelasma, arcus senilis, tendon xanthomas	Clear
	B					

		Familial Combined Hyperlipidemia	Decreased LDL receptor and increased ApoB	LDL and VLDL		Clear
Type III		Familial Dysbetalipoproteinemia	Defect in Apo E 2 synthesis	IDL	Tubo-Eruptive Xanthomas & Palmar Xanthomas	Turbid
Type IV		Familial Hypertriglyceridemia	Increased VLDL production and Decreased elimination	VLDL		Turbid
Type V			Increased VLDL production and Decreased LPL	VLDL and Chylomicrons		Creamy top layer & turbid bottom

RELATIVE PREVALENCE OF FAMILIAL FORMS OF HYPERLIPOPROTEINEMIA

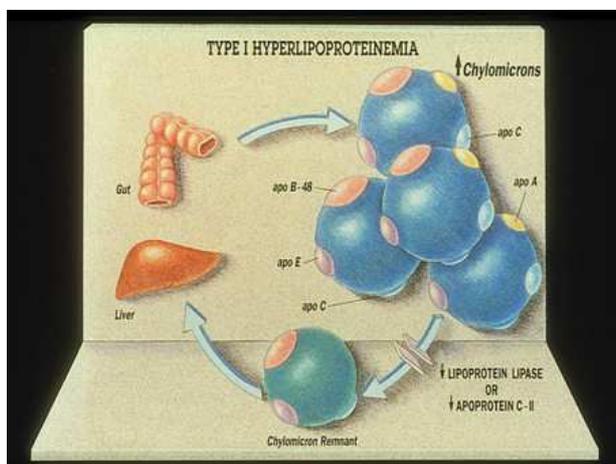
HYPERLIPOPROTEINEMIA TYPE I

Type I hyperlipoproteinemia exists in several forms:

- Lipoprotein lipase deficiency (Type Ia), due to a deficiency of lipoprotein lipase (LPL) or altered apolipoprotein C2, resulting in elevated chylomicrons, the particles that transfer fatty acids from the digestive tract to the liver.
- Familial apoprotein CII deficiency (Type Ib), a condition caused by a lack of lipoprotein lipase activator.
- Chylomicronemia due to circulating inhibitor of lipoprotein lipase (Type Ic)

Type I hyperlipoproteinemia usually presents in childhood with eruptive xanthomata and abdominal colic. Complications include retinal vein occlusion, acute pancreatitis, steatosis and organomegaly, and lipaemia retinalis.

Fig 2. Type 1 hyperlipoproteinemia



HYPERLIPOPROTEINEMIA TYPE II

Hyperlipoproteinemia type II, by far the most common form, is further classified into type IIa and type IIb, depending mainly on whether there is elevation in the triglyceride level in addition to LDL cholesterol.

TYPE II a

This may be sporadic (due to dietary factors), polygenic, or truly familial as a result of a mutation either in the LDL receptor gene on chromosome 19 (0.2% of the population) or the ApoB gene (0.2%). The familial form is characterized by tendon xanthoma, xanthelasma and premature cardiovascular disease. The incidence of this disease is about 1 in 500 for heterozygotes, and 1 in 1,000,000 for homozygotes.

TYPE II b

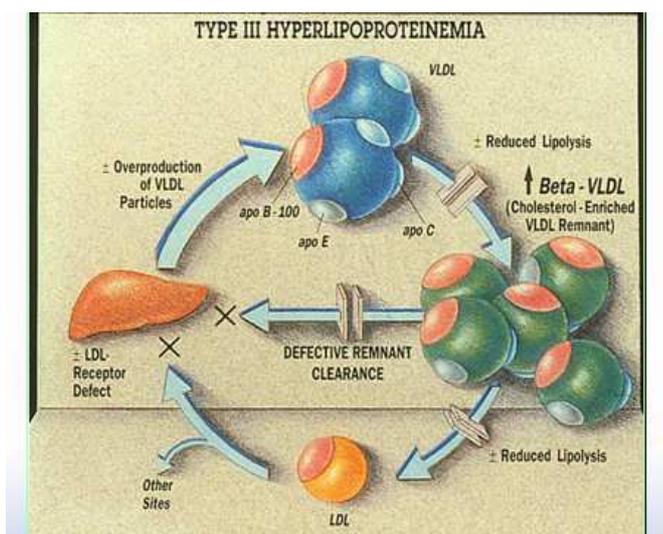
The high VLDL levels are due to overproduction of substrates, including triglycerides, acetyl CoA, and an increase in B-100 synthesis. They may also be caused by the decreased clearance of LDL. Prevalence in the population is 10%.

- Familial combined hyperlipoproteinemia (FCH)
- Lysosomal acid lipase deficiency, often called (Cholesteryl ester storage disease)
- Secondary combined hyperlipoproteinemia (usually in the context of metabolic syndrome, for which it is a diagnostic criterion)

HYPERLIPOPROTEINEMIA TYPE III

This form is due to high chylomicrons and IDL (intermediate density lipoprotein). Also known as broad beta disease or dysbetalipoproteinemia, the most common cause for this form is the presence of ApoE E2/E2 genotype. It is due to cholesterol-rich VLDL (β -VLDL). Its prevalence has been estimated to be approximately 1 in 10,000.

Fig 3. Hyperlipoproteinemia type III



HYPERLIPOPROTEINEMIA TYPE IV

Familial hypertriglyceridemia is an autosomal dominant condition occurring in approximately 1% of the population.

HYPERLIPOPROTEINEMIA TYPE V

Hyperlipoproteinemia type V is very similar to type I, but with high VLDL in addition to chylomicrons. It is also associated with glucose intolerance and hyperuricemia

UNCLASSIFIED FAMILIAL FORMS

Non-classified forms are extremely rare:

- Hyperalphalipoproteinemia
- Polygenic hypercholesterolemia

ACQUIRED (SECONDARY)

Acquired hyperlipidemias (also called secondary dyslipoproteinemias) may mimic primary forms of hyperlipidemia and can have similar consequences. They may result in increased risk of premature atherosclerosis or, when associated with marked hypertriglyceridemia, may lead to pancreatitis and other complications of the chylomicronemia syndrome. The most common causes of acquired hyperlipidemia are:

- Diabetes Mellitus
- Use of drugs such as diuretics, beta blockers, and estrogens

Other conditions leading to acquired hyperlipidemia include:

- Hypothyroidism
- Renal Failure
- Nephrotic Syndrome

- Alcohol
- Some rare endocrine disorders and metabolic disorders

According to "Greenspan's Basic & Clinical Endocrinology" by Dr. David Gardner, acquired hyperlipidemia is high fat and cholesterol in the blood due to other conditions or medications. Diabetes, low thyroid hormone levels, kidney disease and some other metabolic disorders cause hyperlipidemia. Some drugs can also cause hyperlipidemia, including alcohol, diuretics, estrogens and beta-blockers.

PRIMARY TYPE I

Type I hyperlipidemia is quite uncommon according to "Harrison's Principles of Internal Medicine" by Anthony S Fauci. It is also called familial hyperchylomicronemia and Buerger-Gruetz syndrome. This disorder causes high chylomicrons, the proteins that carry fat from the intestine to the liver. It can cause abdominal pain, pancreatitis, fat deposits in the skin and eyes and a large liver and spleen. Treatment involves eating a healthy diet.

PRIMARY TYPE II

Type II hyperlipidemia is divided into type IIa and type IIb. Type IIa is also known as familial hypercholesterolemia and type IIb is also known as familial combined hyperlipidemia. Type IIa results in high LDL or "bad" cholesterol levels. Type IIa also raises levels of LDL, as well as a similar lipoprotein, VLDL, which results in elevated fat levels in the blood. These conditions cause fat deposits under the skin and around the eyes, and are treated medically and with dietary control.

PRIMARY TYPE III

Type III hyperlipidemia is an uncommon disorder also known as familial dysbetalipoproteinemia, remnant removal disease or broad-beta disease. It results in high levels of LDL and carries a very significant risk of heart disease. It is treated with medicine and diet.

PRIMARY TYPE IV

Type IV is also known as familial hyperlipidemia. Cholesterol levels tend to be normal and fat is elevated in the blood as VLDL levels are elevated. It is also treated with medicines and proper diet.

PRIMARY TYPE V

Type V is another rare type that is characterized by elevated chylomicrons and VLDL. It is also known as endogenous hypertriglyceridemia. The LDL level is

typically low. High fat levels in the blood can cause pancreatitis.

Hyperlipidemias may also be classified directly into which types of lipids are elevated, that is hypercholesterolemia, hypertriglyceridemia or both in combined hyperlipidemia. Elevated levels of Lipoprotein (a) may also be classified as a form of hyperlipidemia.

SIGNS AND SYMPTOMS OF HYPERLIPIDEMIA

Hyperlipidemia usually has no noticeable symptoms and tends to be discovered during routine examination or evaluation for atherosclerotic cardiovascular disease [4-5].

1. Xanthoma
2. Xanthelasma of eyelid
3. Chest Pain
4. Abdominal Pain
5. Enlarged Spleen
6. Liver Enlarged
7. High cholesterol or triglyceride levels
8. Heart attacks
9. Higher rate of obesity and glucose intolerance
10. Pimple like lesions across body
11. Atheromatous plaques in the arteries
12. Arcus senilis
13. Xanthomata

CAUSES OF HYPERLIPIDEMIA

1. Lifestyle habits or treatable medical conditions. Lifestyle contributors include obesity, not exercising, and smoking
2. Diabetes(type 2)
3. Kidney disease
4. Pregnancy
5. An under active thyroid gland
6. Environmental and genetic factors
7. Alcohol
8. Monoclonal Gammopathy
9. Nephrotic Syndrome
10. Obstructive Jaundice
11. Hypothyroidism
12. Cushing's Syndrome
13. Anorexia Nervosa
14. Medications-
 - Thiazide Diuretics
 - Ciclosporin
 - Glucocorticoids
 - Beta Blockers
 - Retinoic Acid
15. High dietary simple carbohydrates
16. Estrogen therapy

17. Lipoprotein lipase mutations [6].

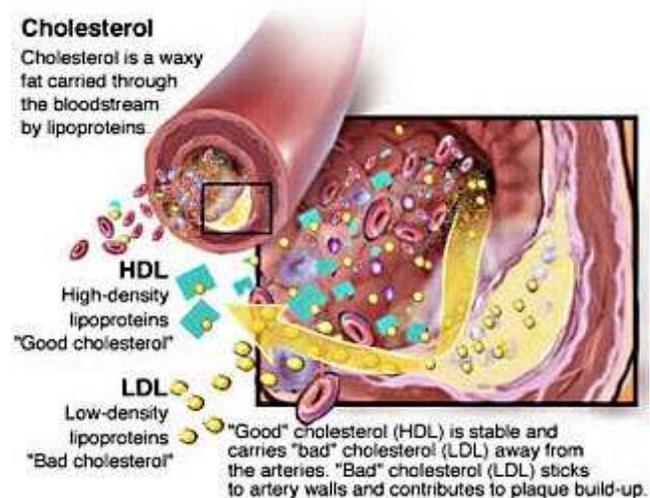
PATHOPHYSIOLOGY OF HYPERLIPIDEMIA

- Decreased clearance of triglyceride-rich lipoproteins due to inhibition of lipoprotein lipase and triglyceride lipase.
- Other factors such as peripheral insulin resistance, carnitine deficiency, and hyperthyroidism may contribute to lipid abnormalities.
- In nephrotic syndrome, decreased effective plasma albumin circulation results in increased lipoprotein synthesis to maintain plasma oncotic pressure [7].

PATHOPHYSIOLOGY OF HYPERCHOLESTEROLEMIA

LDL cholesterol normally circulates in the body for 2.5 days, and subsequently binds to the LDL receptor on the liver cells, undergoes endocytosis, and is digested. LDL is removed, and synthesis of cholesterol by the liver is suppressed in the HMG-CoA reductase pathway [7]. In FH, LDL receptor function is reduced or absent, and LDL circulates for an average duration of 4.5 days, resulting in significantly increased level of LDL cholesterol in the blood with normal levels of other lipoproteins [8]. In mutations of ApoB, reduced binding of LDL particles to the receptor causes the increased level of LDL cholesterol. It is not known how the mutation causes LDL receptor dysfunction in mutations of PCSK9 and ARH [9].

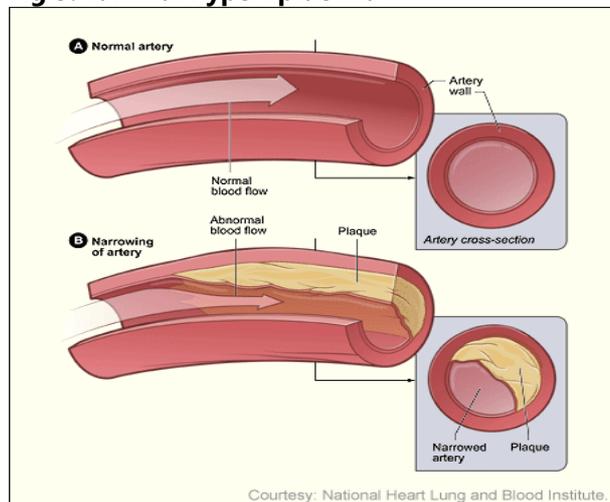
Fig 4. Low Density And High Density Lipoproteins



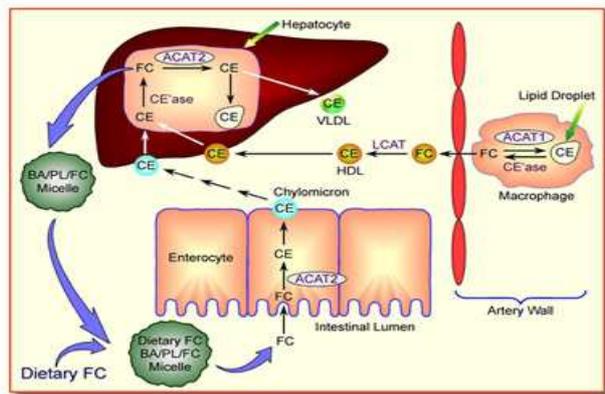
Although atherosclerosis occurs to a certain degree in all people, FH patients may develop accelerated atherosclerosis due to the excess level of LDL. The degree of atherosclerosis approximately depends of the number of LDL receptors still expressed and the

functionality of these receptors. In many heterozygous forms of FH, the receptor function is only mildly impaired, and LDL levels will remain relatively low. In the more serious homozygous forms, the receptor is not expressed at all [9].

Fig 5. Familial hyperlipidemia



Courtesy: National Heart Lung and Blood Institute.



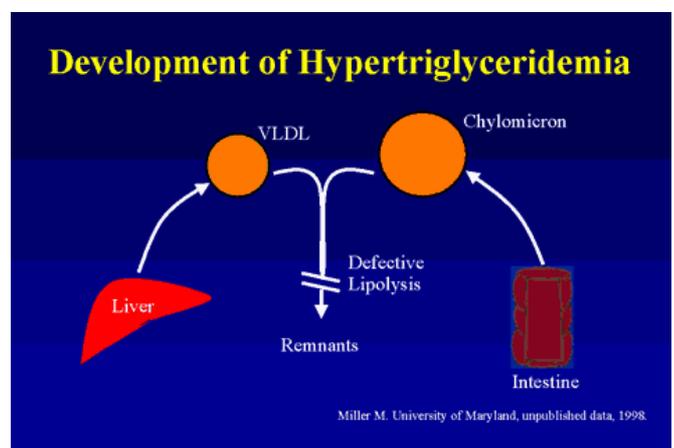
Some studies of FH cohorts suggest that additional risk factors are generally at play when an FH patient develops atherosclerosis [10-11]. In addition to the classic risk factors such as smoking, high blood pressure, and diabetes, genetic studies have shown that a common abnormality in the prothrombin gene (G20210A) increases the risk of cardiovascular events in patients with FH [12]. Several studies found that a high level of lipoprotein(a) was an additional risk factor for ischemic heart disease [13]. The risk was also found to be higher in patients with a specific genotype of the angiotensin-converting enzyme (ACE) [14-15].

PATHOPHYSIOLOGY OF HYPERTRIGLYCERIDEMIA

Hypertriglyceridemia may be the result of two processes.

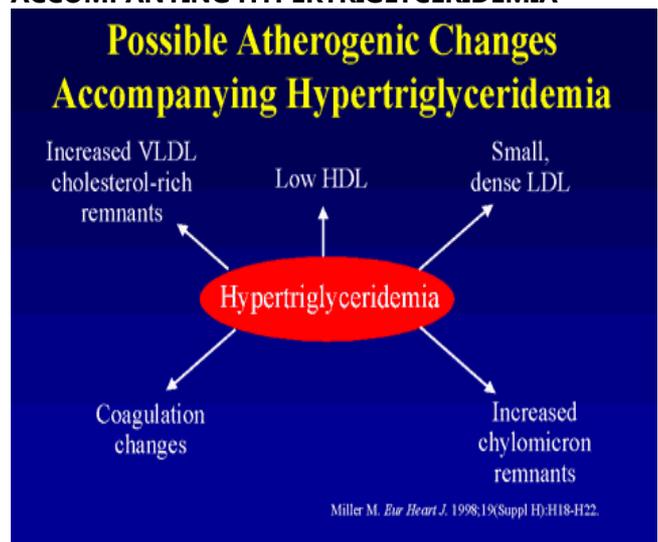
- One process is the overproduction of VLDL by the liver in response to an increase in free fatty acids flowing to this organ.
- The other process is a defect in the lysis of VLDL triglycerides and chylomicrons by lipoprotein lipase. When lipoprotein lipase activity is deficient, triglycerides cannot be converted, hydrolyzed, or broken down, and the metabolism of chylomicron and VLDL remnants may be delayed, as in type III hyperlipoproteinemia (dysbetalipoproteinemia) [16-17].

Fig 6. Hypertriglyceridemia



Miller M. University of Maryland, unpublished data, 1998.

POSSIBLE ATHEROGENIC CHANGES ACCOMPANYING HYPERTRIGLYCERIDEMIA



Miller M. Eur Heart J. 1998;19(Suppl H):H18-H22.

- Plasma triglyceride levels less than 200 mg/dL are classified as normal.
- There has been some debate about whether an elevated triglyceride level is an

independent risk factor for atherosclerosis. However, it is clearly associated with a number of metabolic or physiologic changes that are risk factors for this disease. These include:

- Low HDL
- Unusually atherogenic forms of LDL
- Elevated triglycerides often reflect an increase in triglyceride-rich remnant lipoproteins that have atherogenic potential [18-22].

PREVELANCE

Many studies have shown that there is a direct correlation between the incidence of coronary artery disease (CAD) and total low-density lipoprotein (LDL) cholesterol levels. Every year, approximately 1.5 million Americans experience an acute myocardial infarction and one-third of them do not survive. Because of adaption of the new NCEP GUIDELINES many more patients are now candidates for intensive lipid lowering therapy and these guidelines estimates that the number of Americans who qualify for dietary treatment will rise from 52 million to 65 million, and the number who candidates for drug therapy will nearly triple-from 13 million to 36 million.

THE RISK FACTORS FOR HYPERLIPIDEMIA ARE

1. High fat intake is one of the factor which leads to hypercholesterolemia
2. Type 2 diabetes mellitus
3. Hypothyroidism
4. Chronic renal failure
5. Nephritic syndrome
6. Obesity
7. Alcohol intake
8. Drugs
 - a. Number of drugs can adversely affect the serum lipid and lipoprotein concentrations.
 - b. Antihypertensive agents
 - c. Diuretics
 - d. Oral contraceptives
 - e. Corticosteroids- administration of glucocorticoids increases total cholesterol and TG by elevating LDL-C and to less extent VLDL-C
9. Metabolic syndrome [23-24]

COMPLICATIONS OF HYPERLIPIDEMIA

- Pancreatitis
- Premature coronary artery disease
- Heart attack
- Stroke
- Atherosclerosis
- myocardial infarction

DIAGNOSIS

BLOOD TESTS			
S.NO	TEST NAME	NORMAL VALUES	INDICATORS
1	Total Cholesterol	Total Cholesterol: < 200 mg/dL (desirable) (< 180 optimal)	200-239 mg/dL = Borderline High (borderline risk for coronary heart disease [CHD]) > 240 mg/dL = Hypercholesterolemia
2	Total Cholesterol for children	< 180 mg/Dl	> 180 mg/dL may lead to premature Atherosclerosis
3	Triglyceride Levels	Less than 150 mg/dL	150-199 mg/dL is Borderline High 200-499 mg/dL is High 500 mg/dL or above is Very High
4	HDL Cholesterol	≥ 60 mg/dL is desirable	In general, HDL levels < 40 mg/dL increases risk for CHD. Women with levels < 47 mg/dL

			and men < 37 mg/dL have increased risk.
5	LDL Cholesterol	< 100 mg/dL (optimal) 100-129 mg/dL (near optimal/above optimal)	130-159 mg/dL Borderline High 160-189 mg/dL High ≥190 mg/dL Very High
6	C-reactive Protein (CRP)	CRP < 1 mg/dl	CRP > 1 mg/dl (> 10 mg/dl often seen) suggests inflammation
7.	VLDL cholesterol	The VLDL normal range is between 0–40 mg/dL and the recommended optimum range is between 0–30 mg/dL	> 40 suggests can increase the risk of developing heart disease
TESTS			
TEST NAME		INDICATORS	
1	Skin assessment	Xanthelasma and xanthomas are fatty deposits under the skin surface commonly found in patients with metabolic disorders such as elevated blood lipids and genetic disorders such as familial hypercholesterolemia. A biopsy will show fatty deposits.	

PROGNOSIS

Hyperlipidemia is a condition characterized by an increased amount of fats (lipids) present in the bloodstream. The prognosis (outlook) for the condition varies according to a number of different factors.

The prognosis for persons is in direct proportion to their serum cholesterol levels. Persons with hypercholesterolemia are at high risk of dying from heart disease or stroke. Many studies have looked at the relationship between elevated cholesterol levels, increased risk for heart attack and death. In one research investigation of relatively young males who had no known heart disease, cholesterol levels were measured and participants were followed for 6 years. During this time, all heart attacks and deaths that occurred among participants were recorded. As serum cholesterol levels increased, so did the risk of experiencing a fatal heart attack. The risk of a fatal heart attack was approximately five times higher among persons having cholesterol levels of 300 mg/dL or more compared to those with cholesterol levels below 200 mg/dL.

The Framingham Heart Study is an ongoing research effort. Cholesterol levels, smoking habits, heart attack rates, and deaths in the population have been recorded for over 40 years. After 30 years, more than 85% of persons with cholesterol levels of 180 mg/dL

or less were still alive; almost a third of those with cholesterol levels greater than 260 mg/dL had died [25-26].

OUTLOOK (PROGNOSIS)

Diet changes, exercise, and medications can lower cholesterol levels for those with the milder form of this disorder, and may significantly delay a heart attack. Men and women with familial hypercholesterolemia typically are at increased risk of early heart attacks. Risk of death varies among patients with familial hypercholesterolemia. Persons who inherit two copies of the defective gene have a poorer outcome. That type of familial hypercholesterolemia causes early heart attacks and is resistant to treatment.

THE FACTS

The American Heart Association reports that the lipids contained in the bloodstream include cholesterol, triglycerides, cholesterol compounds (esters) and phospholipids. Terms applied to various forms of hyperlipidemia include hypercholesterolemia, hypertriglyceridemia and hyperlipoproteinemia.

SUCCESSFUL OUTCOMES

Successful outcomes for hyperlipidemia depend upon lowering levels of LDL ("bad") cholesterol, notes the Society for Vascular Surgery.

TREATMENT FACTORS

The Society for Vascular Surgery notes that treatments for hyperlipidemia vary according to factors that include heart disease risk, lipid levels and a patient's overall health.

TREATMENT OPTIONS

Potential treatments for lipid disorders include dietary changes, weight loss, regular exercise, quitting smoking, medications and periodic lipid screenings, reports the U.S. National Library of Medicine.

UNSUCCESSFUL OUTCOMES

The U.S. National Library of Medicine cites potential outcomes of unsuccessful high cholesterol treatment that include coronary artery disease, hardening of the arteries (atherosclerosis), heart attack, stroke and death. Unsuccessful treatment for high triglycerides can result in pancreatic inflammation (pancreatitis).

**TREATMENT FOR HYPERLIPIDEMIA
HMG-COA REDUCTASE INHIBITORS (STATINS)**

Statins (or HMG-CoA reductase inhibitors) are a class of drugs used to lower cholesterol levels by inhibiting

the enzyme HMG-CoA reductase, which plays a central role in the production of cholesterol in the liver. Increased cholesterol levels have been associated with cardiovascular diseases (CVD), and statins are therefore used in the prevention of these diseases. Statins have rare but severe adverse effects, particularly muscle damage, and some doctors believe they are overprescribed [27].

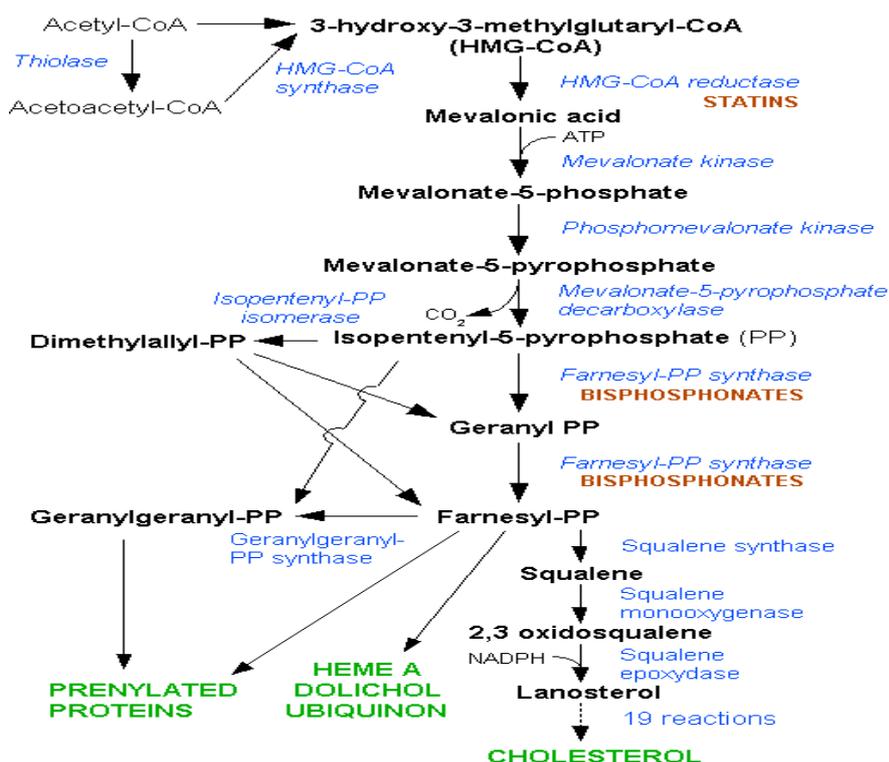
The approved statins are

- Atorvastatin
- Fluvastatin
- Lovastatin
- Pravastatin
- Rosuvastatin
- Simvastatin
- Pitavastatin

MODE OF ACTION

Statins act by competitively inhibiting HMG-CoA reductase, the first committed enzyme of the HMG-CoA reductase pathway. Because statins are similar to HMG-CoA on a molecular level they take the place of HMG-CoA in the enzyme and reduce the rate by which it is able to produce mevalonate, the next molecule in the cascade that eventually produces cholesterol, as well as a number of other compounds.

HMG-CoA (3 Hydroxy-3-Methylglutaryl-Co-A) Reductase Pathway



The HMG-CoA reductase pathway, which is blocked by statins via inhibiting the rate limiting enzyme HMG-CoA reductase. This ultimately reduces cholesterol via several mechanisms. Statins block the production of cholesterol in the liver itself. They lower LDL, the "bad" cholesterol, and triglycerides, and have a mild effect in raising HDL, the "good" cholesterol. These drugs are the first line of treatment for most people with high cholesterol. Side effects can include intestinal problems, liver damage, and in a few people, muscle tenderness [28].

FIBRIC ACID DERIVATIVES (FIBRATES)

Fibrates are cholesterol-lowering drugs that are primarily effective in lowering triglycerides and to a lesser extent in increasing HDL-cholesterol levels [29].

Fibrates prescribed commonly are

- Bezafibrate
- Ciprofibrate
- Clofibrate
- Gemfibrozil
- Fenofibrate

MODE OF ACTION

Fibrates are agonists of the PPAR- α receptor in muscle, liver, and other tissues. Activation of PPAR- α signaling results in:

- Increased β -oxidation in the liver
- Decreased hepatic triglyceride secretion
- Increased lipoprotein lipase activity, and thus increased VLDL clearance
- Increased HDL
- Increased clearance of remnant particles

Fibrates activate PPAR (peroxisome proliferator-activated receptors), especially PPAR α . The PPARs are a class of intracellular receptors that modulate carbohydrate and fat metabolism and adipose tissue differentiation. Activating PPARs induces the transcription of a number of genes that facilitate lipid metabolism. Fibrates are structurally and pharmacologically related to the thiazolidinediones, a novel class of anti-diabetic drugs that also act on PPARs (more specifically PPAR γ)

BILE ACID SEQUESTRANTS

The bile acid sequestrants are a group of medications used to bind certain components of bile in the gastrointestinal tract. They disrupt the enterohepatic circulation of bile acids by sequestering them and preventing their reabsorption from the gut. In general, they are classified as hypolipidemic agents, although

they may be used for purposes other than lowering cholesterol. They are used in the treatment of chronic diarrhea due to bile acid malabsorption. When the statins are not sufficient to lower high cholesterol, these drugs can be added. Their use is often limited by side effects, which are primarily gastrointestinal. They can include nausea, bloating, cramping, and an increase in liver enzymes.

Three drugs are members of this class; all are synthetic polymeric resins:

- Cholestyramine
- Colesevelam
- Colestipol

MODE OF ACTION

Bile acid sequestrants are polymeric compounds that serve as ion exchange resins. Bile acid sequestrants exchange anions such as chloride ions for bile acids. By doing so, they bind bile acids and sequester them from enterohepatic circulation. Since bile acid sequestrants are large polymeric structures, they are not well absorbed from the gut into the bloodstream. Thus, bile acid sequestrants, along with any bile acids bound to the drug, are excreted via the feces after passage through the gastrointestinal tract [30]

NICOTINIC ACID FOR HIGH CHOLESTEROL

MODE OF ACTION

Nicotinic acid reduces the production of triglycerides and VLDL (very low-density lipoprotein, which is converted to LDL in the blood). This leads to decreased LDL ("bad") cholesterol, increased HDL ("good") cholesterol, and lowered triglycerides. Nicotinic acid raises HDL cholesterol more than other lipid-lowering medicines. The nicotinic acid form of niacin lowers cholesterol, but other forms of niacin do not. The other forms that do not lower cholesterol include nicotinamide and inositol nicotinate (also called no-flush niacin) [31].

CONCLUSION

Hyperlipidemia has been affecting mankind since ages. Though many drugs are available to treat Hyperlipidemia, the problem of enhanced cholesterol levels in blood is still prevailing and is being a cause for many coronary disorders. Recently, certain chemicals (drugs) of natural origin have seen light in treating these cholesterol levels, reducing the risk of heart attacks. To reduce the risk due to hyperlipidemia, the various ways are to follow a healthy lifestyle and drugs that can reduce the cholesterol and triglyceride levels in blood.

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