Dyslipidemia
Dyslipidemia

Dyslipidemia, Which include both abnormally high levels of specific lipoproteins e.g. LDL-C, VLDL and abnormally low levels of other lipoproteins e.g. HDL-C.
Aetiology

Primary dyslipidemia
Genetic disorders

Secondary dyslipidemia
Diabetes
Hypothyroidism
Chronic renal failure
Nephrotic syndrome
Obesity
Alcohol
Drugs
Primary dyslipidemia

Up to 60% of them are of genetic or familial disorders including the followings:

✓ Familial hypercholesterolaemia
✓ Familial combined hyperlipidaemia
✓ Familial type III hyperlipoproteinaemia
✓ Familial lipoprotein lipase deficiency
✓ Familial apolipoprotein C-II deficiency
✓ Lipoprotein(a)
**Familial hypercholesterolaemia**

✓ Heterozygous familial hypercholesterolaemia

• The most common mutation affects the LDL receptor gene.

• LDL receptor are responsible for catabolism of LDL this cause increase LDL level.

• In patients with heterozygous FH, CVD presents about 20 years earlier than in the general population, with some individuals, particularly men, dying from atherosclerotic heart disease often before the age of 40 years.
• The adult heterozygote typically exhibits the signs of cholesterol deposition such as corneal arcus, tendon xanthoma and xanthelasma.

✓ Homozygous FH

• It associated with an absence of LDL receptors and almost absolute inability to clear LDL-C.
• Sudden death from acute coronary insufficiency before the age of 20 years was normal.
• Patient have cutaneous and tendon xanthoma.
Familial combined hyperlipidaemia

• it is associated with excessive synthesis of VLDL-C. In addition to increases in triglyceride and LDL-C levels, patients also typically have raised levels of apoB.

• It is associated with an increased risk of atherosclerosis before the age of 60 years.
Familial type III hyperlipoproteinaemia

• It is characterised by the accumulation of chylomicron and VLDL that fail to get cleared at a normal rate by hepatic receptors.

• Triglycerides and TC are both elevated and accompanied by corneal arcus, xanthelasma, eruptive xanthomas and palmar striae

• The disorder predisposes to premature atherosclerosis.
Familial lipoprotein lipase deficiency

• It is characterised by marked hypertriglyceridaemia and chylomicronaemia, and usually presents in childhood.

• The affected patient presents with recurrent episodes of abdominal pain, eruptive xanthomas and enlarged spleen.

• The major complication is acute pancreatitis.
Familial apolipoprotein C-II deficiency
✓ In the heterozygous state
• It is associated with reduced levels of apoC-II, the activator of lipoprotein lipase.
✓ In the rare homozygous state
• There is an absence of apolipoprotein C-II and despite normal levels of lipoprotein lipase, it cannot be activated.
• It may develop acute pancreatitis.
Lipoprotein(a)

- Lp(a) is a low-density lipoprotein-like particle synthesised by the liver.
- Early-onset CVD is associated with raised concentrations of Lp(a), and these appear to play a role in both atherogenesis and thrombosis.
Secondary dyslipidemia

Dyslipidaemias that occur secondary to a number of disorders, diet or as a side effect of drug therapy and it is account for up to 40% of all dyslipidaemias.
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Treatment

- The serum concentrations of cholesterol, HDL and triglycerides should be measured to determine the lipid profile of a patient.
- Serum concentration TG increase after the ingestion of a meal and, therefore, patients must fast for 12–15 h before measurement and Patients must be seated for at least 5 min prior to drawing a blood sample.
Lifestyle

Before a decision is made to start treatment with a lipid lowering agent, other risk factors should be considered such as smoking, obesity, high alcohol intake and lack of exercise.

- **Weight reduction**

  ✓ An overweight individual is at increased risk of atherosclerotic disease and typically has elevated levels of plasma TG and a low HDL-C.
Weight reductive will improve the lipid profile and reduce overall cardiovascular risk.

- **Diet**

Diet modification is rarely successful alone in bringing about a significant improvement in the lipid profile.

Lipid lowering diet should contain less total fat, less saturated fat and cholesterol, more polyunsaturated, fish and antioxidants (antioxidants occur naturally in fruit and vegetables).
• Exercise

✓ Aerobic exercise (walking, swimming, cycling) have desirable effect on serum lipids (decrease LDL and raise HDL).

• Salt

✓ Salt intake should be reduced.
Drug therapy

Statins

• Available statins are simvastatin, pravastatin, fluvastatin, atrovastatin, lovastatin and rosvastatin.

• Statins are selectively inhibit 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA reductase), the rate-limiting enzyme in cholesterol biosynthesis, thus it use in treatment of sever hypercholesterolemia.

• The overall effect is a reduction in TC, LDL-C, VLDL-C and triglycerides with an increase in HDL-C.

• Statins are first-line lipid-lowering agent in most guidelines.
Adverse effects of statins

• The commonest side effects include gastrointestinal symptoms, altered liver function tests and muscle aches.

• Less common are elevation of liver transaminase levels, hepatitis, rash, headache, insomnia, nightmares.

• Myopathy leading to myoglobinuria secondary to rhabdomyolysis is also a rare but serious potential adverse effect of all the statins that can occur at any dose.
The risk of myopathy is increased:

✓ when there are underlying muscle disorders, a family history of muscle disorders, renal impairment, untreated hypothyroidism, alcohol abuse, or the recipient is aged over 65 years or female.

✓ where statins are co-prescribed with other lipid-lowering drugs, for example, fibrates, nicotinic acid

✓ when there is a past history of myopathy with another lipid-lowering drug or statin

✓ where there is co-prescription of simvastatin or atorvastatin with drugs that inhibit CYP3A4.
• Statin are plaque stabilize, inhibit of thrombus formation, reduced serum viscosity and anti-inflammatory and antioxidant activity.

• Statin should be taken once daily in the evening.
Fibrates

• Members of this group include bezafibrate, ciprofibrate, fenofibrate and gemfibrozil.
• Fibrates reduce triglyceride and, to a lesser extent, LDL-C levels while increasing HDL-C.
• In the patient with elevated triglycerides and gout, only fenofibrate has been reported to have a sustained uricosuric effect on chronic administration.
• Fibrates should not be used first line to reduce lipid levels in either primary or secondary prevention.
• Fibrates can be used first line in patients with isolated severe hypertriglyceridaemia.
• In individuals with mixed hyperlipidaemia, fibrates may be considered when a statin or other agent is contraindicated or not tolerated.
Adverse effects

• The side effects of fibrates are mild.
• Gastro-intestinal symptoms such as nausea, diarrhoea and abdominal pain that resolve after a few days of treatment.
• Myositis has been described, and is associated with muscle pain, unusual tiredness or weakness.
Bile acid binding agents

- The three members of this group in current use are colestyramine, colestipol and colesevelam.
- Each of the bile acid binding agents reduce TC and increase triglyceride levels.
Adverse effects

• With all three agents, side effects are more likely to occur with high doses and in patients aged over 60 years.

• Bloating, flatulence, heartburn and constipation are common complaints.

• Constipation is the major subjective side effect, and although usually mild and transient, it may be severe.
• Colestyramine, colestipol and colesevelam are known to interact with many drugs primarily by interfering with absorption like fat soluble vitamins, folic acid, warfarin, thyroxin, thiazide diuretic and propranolol. This interaction can be minimized by administering these drugs 1 hr (at least 4hrs for colesevelam) before or at least 4hr after the bile acid binding agent.
Cholesterol absorption inhibitors

Ezetimibe

• It reduces cholesterol re-absorption from the gastro-intestinal tract.

• It can reduce LDL-C and TG and increase HDL_C.

• Ezetimibe should be prescribed either with a statin, a fibrate or a nicotinic acid derivative.
Nicotinic acid and derivatives

• Nicotinic acid lowers serum LDL-C, TC, VLDL-C, and increases levels of HDL-C.
• It clearly has a range of beneficial effects on the lipid profile and is licensed for use in combination with a statin, or by itself if the patient is statin intolerant or a statin is inappropriate.
Adverse effects

• The commonest side effect of nicotinic acid is flushing.
• Less common side effects of nicotinic acid include postural hypotension, diarrhoea, exacerbation of peptic ulcers, hepatic dysfunction, gout and increased blood glucose levels.
Acipimox

• It is structurally related to nicotinic acid, has similar beneficial effects on the lipid profile and a better side effect profile but appears to be less potent.
Fish oils

• Fish oil preparations rich in omega-3 fatty acids which lower serum triglyceride levels by decreasing VLDL-C synthesis.

• It can be used as an alternative to a fibrate or in combination with a statin.
Soluble fibre

• Preparations containing soluble fibre, such as ispaghula husk, have been shown to reduce lipid levels.
• They bind bile acids in the gut and increase the conversion of cholesterol to bile acids in the liver.
• They are much less effective than statins in reducing TC and LDL-C.