

Risk factors and management of Hyperlipidemia (Review)

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Abstract

Hyperlipidemia involves abnormally elevated levels of any or all lipids and/or lipoproteins in the blood. Hyperlipidemia may basically be classified as either familial hyperlipidemia or acquired hyperlipidemia. There are two types of hyperlipidemia; modifiable and non-modifiable risk factors. Management of hyperlipidemia requires multi-team intervention include medical, nutritional and lifestyle modifications. Searching on the internet using the Google search engine was the main source of data as well as books. This review will try to draw a picture about hyperlipidemia; its risk factors and management. Adiposopathy is raised by non healthy diet and a low active lifestyle in environmentally and genetically predisposed people. Management strategies depend on the specific lipid abnormality. Many countries or regions have developed their own dyslipidaemia guidelines. Prevention and treatment of dyslipidaemia consists assessment, establishment of treatment goal, increase activity level, dietary modification, medical therapy, follow up, re-assess and modifying the procedure as necessary.

Key Words: Hyperlipidemia, Management, Risk factors,

Introduction

Hyperlipidemia, or hyperlipoproteinemia, is defined as abnormally elevated levels of one or more of lipids and/or lipoproteins in the blood. The terms hyperlipidemia and hyperlipoproteinemia are used interchangeably. Hyperlipoproteinemia happens when there large amounts of lipids (fats) in the blood stream. Lipoproteins is the boats which carry lipids within the blood. Hyperlipidemia is the most prevalent episode of dyslipidaemia (which includes any hypo and hyper lipid levels).⁽¹⁻²⁾ Hyperlipidemia is a group of heterogeneous disorders characterized by an elevation of lipids in the blood stream. These lipids include triglycerides, phospholipids, cholesterol, and cholesterol esters.⁽¹⁻⁴⁾ The small intestine absorbs fat from diet and transfers it into chylomicrons, which are sent to peripheral tissues via the bloodstream. The lipoprotein lipase enzyme breaks down chylomicrons, and fatty acids are transferred into adipose tissues and muscle. Liver takes the chylomicron remnants and subsequently starts the process of very-low-density lipoproteins (VLDLs) synthesis. High Density Lipoprotein HDL is produced in the liver. HDL transports cholesterol from the body to

the liver. For this reason, HDL is called “good cholesterol” lipoprotein.^(1-3,5) HDL also work as anti-inflammatory, antioxidant, and antithrombotic effects. HDL is cardioprotective molecules. Hyperlipidemia is fundamentally classified as either primary (familial) caused by specific genetic abnormalities, or secondary (acquired) which causing by another underlying disorder. Hyperlipidemia sometimes is idiopathic, which is resulted without known cause. Furthermore, numerous research have confirmed a strong association between elevated Lp(a) and heart disease. Hyperlipidemia is also classified according to types of elevated lipids, such as hypercholesterolemia, hypertriglyceridemia.⁽²⁻⁶⁾ secondary hyperlipidemia often mimics familial forms of hyperlipidemia and can have similar effects. They may cause an increased risk of premature atherosclerosis or, when happen with sever hypertriglyceridemia, may cause pancreatitis and other consequences of the chylomicronemia syndrome.⁽⁷⁾ Diabetes mellitus, some rare endocrine disorders, nephrotic syndrome, renal failure, use of medications such as beta blockers, estrogens, thiazide diuretics, and hypothyroidism, alcohol consumption, and metabolic disorders are the

most common causes of acquired hyperlipidemia. Management of the underlying causes, when possible or changing of the offending medications usually improve the hyperlipidemia. ^(6,8) Hypertriglyceridemia refers to an elevation of triglycerides. A certain amount of triglycerides is needed in the blood stream to work as an energy source. Triglycerides themselves do not directly lead to the fatty deposits that accumulate in atherosclerosis, but the cholesterol particles inside triglyceride-rich particles called very low density lipoproteins (VLDLs) may cause the formation of plaques. Postprandial hyperlipidemia is another form of acquired cause of hyperlipidemia, which is a normal elevation following consumption of food. ^(8, 9) in a study search the mean total cholesterol level in thirty countries ranged from 158 mg/dl in China to 246 mg/dl in Luxemburg among men. The same study revealed that the mean total cholesterol ranged from 162 mg/dl in China to 246 mg/dl in United Kingdom (UK) among the women. ⁽¹⁰⁾ Elevations of cholesterol and low density lipoprotein cholesterol have received the most attention. ^(8, 10, 11,12) A study in America found that an estimated 53% of United States adults have lipid abnormalities: 27% have high LDL-C, 23% have low HDL-C, and 30% have high TG. ⁽¹¹⁾ In Saudi Arabia, the prevalence of dyslipidaemia among adults ranges from 20% to 44%. ⁽¹³⁾ In Iran, a study which was conducted in the city of Tehran among almost

half of Tehranian adults, mean cholesterol level was 210 mg/dl. ⁽¹⁴⁾ In Beijing, the prevalence of hypercholesterolemia, hypertriglyceridemia, mixed hyperlipidemia, lower indices of high-density lipoprotein cholesterol, and high indicators of (LDL-C) are 10.1%, 17.7%, 5.1%, 11.0%, and 8.8% respectively. ⁽¹⁵⁾ Globally, dyslipidaemia affects about 1 in every 3 female and 1 in every 8 male. ^(11,13,15)

Research have concluded that health care cost for dyslipidaemia increase yearly. In the United States 12 to 18 billion dollar is used in dyslipidaemia management yearly. While in Kingdom Saudi Arabia dyslipidaemia consequence diseases yearly at a cost of \$1.14 billion, dyslipidaemia also has an impact on the workforce and reduces the private country output. ^(3,11,14,16) Globally, high cholesterol level is estimated to cause 2.6 million deaths (4.5% of total) and 29.7 million disability adjusted life years. High total cholesterol is a major cause of disease burden in both the developed and developing nations. All these reasons have made dyslipidaemia an important issue to review and worthwhile topic to study. The paper is aiming to review the risk factors, and management of hyperlipidemia. Table one shows serum lipid profile values. Table two classifies different types of primary hyperlipidemia. Table three shows cholesterol level worldwide according to World Health Organisation report. Table four shows lipoprotein (a) levels.

Table (1): Serum lipid profile values.

Serum lipids	Normal values	Desirable/ low risk level	Boder line risk level	High risk Level
VLDL-cholesterol	10-30 mg/dl	<30 mg/dl		
LDL-cholesterol	80-150 mg/dl	<130 mg/dl	130-160 mg/dl	>160 mg/dl
HDL-cholesterol	35-60 mg/dl	>60 mg/dl	35-60 mg/dl	<35 mg/dl
Total cholesterol	150-200 mg/dl	<200 mg/dl	200-240 mg/dl	>240 mg/dl
Serum triglycerides	50-150 mg/dl	<200 mg/dl	200-499 mg/dl	>500 mg/dl

Table (2) Types of primary hyperlipidemia

Class	Increased lipoprotein	Synonym
Type I	↑ chylomicrons	Familial chylomicronemia
Type IIa	↑ LDL	Familial hypercholesterolemia
Type IIb	↑ LDL and VLDL	Familial combined hyperlipidemia
Type III	↑ IDL	Familial dysbetalipoproteinemia
Type IV	↑ VLDL	Familial hypertriglyceridemia
Type V	↑ VLDL and chylomicrons	Familial mixed hyperlipidemia

Table (3): Raised total cholesterol (≥ 5.0 mmol/L) Data by WHO region(6)

WHO region	Year	Age Group	Raised total cholesterol (≥ 5.0 mmol/L) (age-standardized estimate) ^f			Raised total cholesterol (≥ 5.0 mmol/L) (crude estimate) ^f		
			Both sexes	Male	Female	Both sexes	Male	Female
Africa	2008	25+ years	23.1 [18.5-28.3]	21.2 [15.6-27.9]	24.8 [17.8-32.8]	22.0 [17.7-26.7]	20.6 [15.3-27.1]	23.4 [17.0-30.0]
Americas	2008	25+ years	47.7 [42.5-52.7]	46.4 [40.1-52.7]	48.5 [40.8-55.7]	47.9 [42.7-53.0]	46.5 [40.2-52.8]	49.3 [41.5-55.5]
South-East Asia	2008	25+ years	30.3 [24.4-36.6]	28.4 [21.4-36.2]	32.0 [23.0-41.4]	29.5 [23.8-35.5]	28.0 [21.2-35.6]	30.9 [22.3-40.0]
Europe	2008	25+ years	53.7 [48.1-58.8]	54.1 [47.4-61.1]	52.7 [44.5-60.6]	55.8 [50.1-60.9]	55.0 [48.2-61.9]	56.5 [47.9-63.0]
Eastern Mediterranean	2008	25+ years	38.4 [33.4-43.6]	36.2 [29.9-43.1]	40.4 [33.0-48.5]	36.8 [32.1-41.8]	35.4 [29.4-42.0]	38.2 [31.3-44.0]
Western Pacific	2008	25+ years	36.7 [30.2-43.4]	34.9 [27.4-43.7]	38.2 [28.5-48.8]	36.9 [30.4-43.8]	35.2 [27.6-44.1]	38.7 [28.9-48.0]
(WHO) Global	2008	25+ years	38.9 [35.7-42.2]	37.3 [33.3-41.5]	40.2 [35.3-45.2]	38.6 [35.4-41.9]	37.0 [33.1-41.2]	40.2 [35.3-44.0]

Table (4): Lipoprotein (a) levels

Desirable	< 14 mg/dL (< 35 nmol/L)
Borderline risk:	14 - 30 mg/dL (35 - 75 nmol/L)
High risk	31 - 50 mg/dL (75 - 125 nmol/L)
Very high risk:	> 50 mg/dL (> 125 nmol/L)

Material and Method

Searching on the internet using the Google search engine was the main source of data. The keywords include risk factor, management of dyslipidaemia. The search has generated about 88 sources, of which 37 sources have actually used. These 37 articles were considered relevant because they answered the

aim and objective of the review. All included articles were written in English. The inclusive criteria included studies of epidemiology, risk factors, pathogenesis, diagnosis, prevention, and management. The study period has extended from first October 2016 to end of March 2017.

Discussion

Risk factors

Overproduction and defective clearance of the cholesterol, TG and LDL is the result of the mutations of single or multiple genes. This is called non modifiable Risk Factors. it is also known as primary causes. ^(9,11)

The primary disorders are the common dyslipidemia causes to the children, although it may not affect in the most cases of adult dyslipidemia.

1. Non modifiable risk factors

((Age, Gender and Genetic))

Although unhealthy lifestyle choices are the main cause of hyperlipidemia, patient can also inherit it. Once a man reaches age 45 and a women reaches age 55, the risk naturally goes up due to age-related changes in the body. ^(13,15,17) With age, the heart muscle doesn't work as well as it once did. This can increase pressure on arteries. ^(18,19) For women it happens later, after they go through

menopause and their cholesterol levels tend to rise. Post-menopausal female have elevated levels of total cholesterol, LDL-C, and apolipoprotein B as compared with pre-menopausal women. Total HDL decreases in postmenopausal women. Although there is nothing people can do about age or genetic makeup, this does not mean the condition cannot be controlled. ^(10, 12, 20)

Chronic Diseases

Chronic diseases that make the cardiovascular system work harder can also cause high cholesterol levels. If the test positive for high cholesterol and the cause is not obvious, the physician may look for an underlying disease. This includes kidney problems and liver disease, conditions that affect your thyroid, a malfunction of the pituitary gland, and diabetes. ^(16,17,20) In many cases, when these conditions are controlled, cholesterol levels improve. High blood sugar contributes to higher LDL cholesterol and lower HDL cholesterol. ⁽¹⁷⁾ High blood sugar also damages the lining of the arteries. Other cholestatic liver diseases and primary biliary cirrhosis increase the risk of dislipidemia. ^(16,20)

II. Modifiable risk factors

Medications

Drugs like thiazides, retinoids, estrogens and glucocorticoids, among others also increase the risk of dislipidemia. ^(10, 12, 20,21)

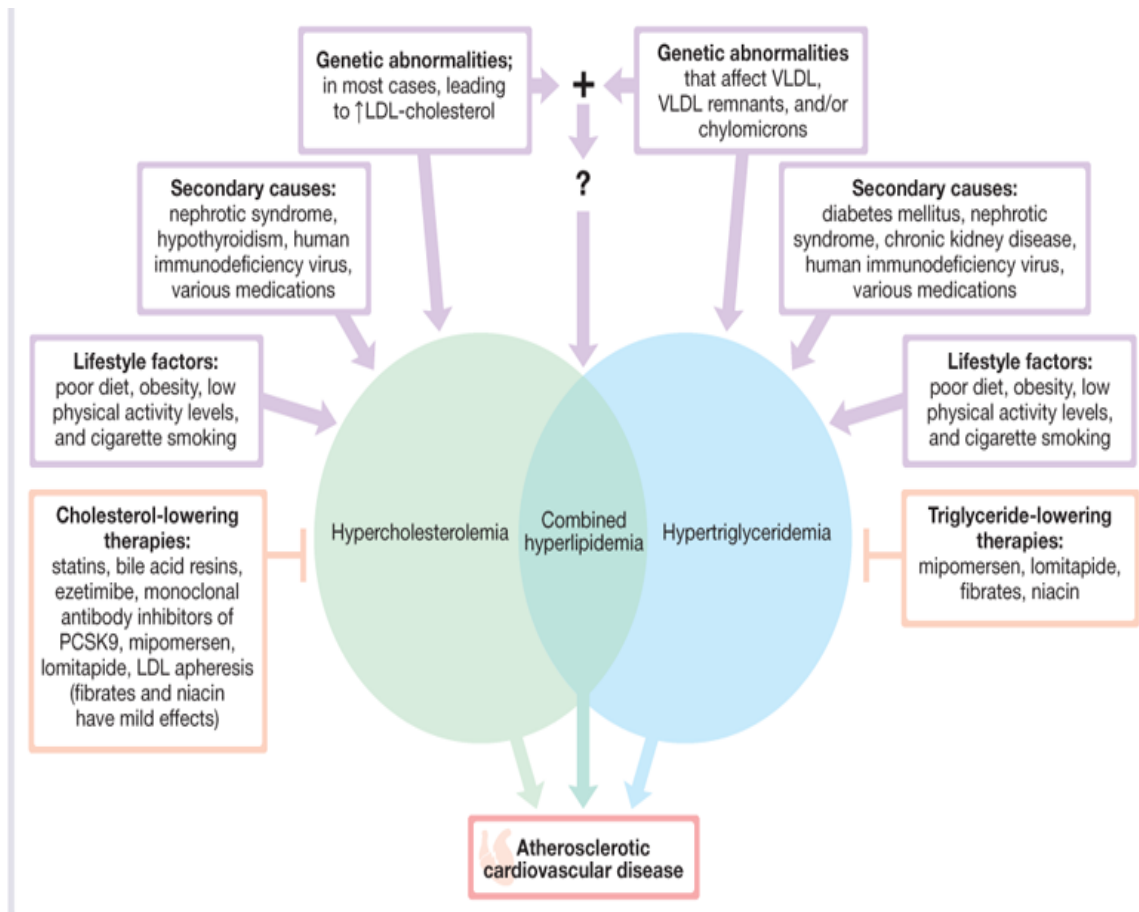
Nutrition

Unhealthy diet raises the risk for hyperlipidemia in two ways. First is what the diet is made up of. Eating high amounts fat and cholesterol contribute to higher lipid levels in the blood. In addition, consuming more calories leads to the excess calories being stored in the body as fat. ^(11,17,19) According to the National Cholesterol Education Program (NCEP), losing weight and eating healthy lowers the bad cholesterol that gets stored in the body and raises the good kind of cholesterol that tends to be excreted from the body. ^(19,21)

Physical inactivity

Being active also tends to lower the bad cholesterol numbers and raise the good. Physical inactivity can lead to weight gain. This is why physical inactivity is also considered a risk factor for hyperlipidemia. ⁽²¹⁻²³⁾ Cigarette smoking damages the walls of the blood vessels, making them likely to accumulate fatty deposits. Smoking may also lower your level of HDL. ^(12, 13) The risk increases if the patient is a man with a waist circumference of at least (102 cm) or a woman with a waist circumference of at least (89 cm). ⁽²¹⁾ Figure one elaborate the interaction between causes.

Figure (1): Causes of Hyperlipidemia(15,17)



Global Risk Assessment

Identify risk factors is the first step in dyslipidaemia prevention. ^(10, 19, 22) It is recommended more frequent assessments for all people with a family history of premature coronary artery diseases mainly definite myocardial infarction or sudden death before age 55 years in father or other man first-degree relative, or before age 65 years in mother or other woman first-degree relative. Moreover, it is essential to have yearly screening for all adult diabetic patients for dyslipidaemia. In the

absence of coronary artery diseases; screening for dyslipidaemia may be carried out at least every 1 to 2 years. ^(15,23) Screening is used with children older than 2 years every 3 to 5 years if they have coronary artery diseases risk factors, are overweight or obese, have insulin resistance syndrome. On the other hand, screening should apply for adolescents every 5 years or more frequently if they have the previously mentioned risk factors, ⁽²⁴⁾

Pathogenesis, Symptoms, and Diagnosis

Fatty acid synthesis initiates with acetyl-CoA and throughout addition of two-carbon atoms. Fatty acid synthesis occurs in the cells cytoplasm, while Fatty acid oxidation occurs in the mitochondria. The main sites of fatty acid synthesis are the liver and adipose tissue. Hyperlipemia happens when adipose lipolysis (HSL-dependent and ATGL-) and consequent hepatic VLDL synthesis (substrate-dependent and MTP-) exceeds the rate of

clearance of plasma VLDL (LPL- and VLDL receptor-dependent). Hyperlipidemia is promoted by a sedentary lifestyle and unhealthy diet in environmentally and genetically predisposed people. Impaired adiposenseness of subcutaneous, peripheral lipids tissue during positive caloric balance, may increase lipids deposited in non-adipose tissue organs such as muscle, liver, and pancreas causing lipotoxicity. ^(13,25,26) Adiposopathic endocrine is directly pathogenic to the cardiovascular system and other body.

Adiposopathy is indirectly promote other atherosclerotic risk factors such as high blood pressure, type 2 diabetes mellitus. ^(22,27) Thus, adipose tissue is a rich, nonembryonic root of mesenchymal cells whose relative ease in accessibility and capacity for differentiating into blood vessel cells and heart which have medical applications to cardiovascular diseases regenerative medications, cell replacement therapies, tissue engineering, and represents a potential therapeutic modality to repair post-infarcted heart or tissue ischemic. ^(22,23) Many

patients are asymptomatic for many years before to the appearance of physical findings of hyperlipidemia. Physical signs include tuberous xanthomas in the Achilles tendon, hands, feet, elbows, and/or knees and corneal arcus of the eye. Symptoms of dyslipidemia can include dyspnea, paresthesias, , and confusion. Dyslipidemia does not have symptoms at all, but it can cause other symptomatic vascular disease, like coronary artery disease. ^(10, 24,25) Figure two shows diagnostic criteria for dyslipidaemia.

Figure (2): Diagnostic criteria for dyslipidaemia(2,6)

Point	Criteria
1	Total cholesterol levels > 290mg/dL (7.5 mmol/L) or LDL-C > 190 mg/dL (4.9 mmol/L) in adults. Total cholesterol levels > 260 mg/dL (6.7 mmol/L) or LDL-C > 155 mg/dL (4.0 mmol/L)
2	Tendon xanthomas in the patient or tendon xanthomas in a first or second degree relative.
3	DNA-based evidence of an LDL-receptor mutation, familial defective apo B-100, or a PCSK9 mutation.
4	Family history of myocardial infarction before age 50 years in a second degree relative or before age 60 years in a first degree relative.
5	Family history of elevated total cholesterol > 290 mg/dL (7.5 mmol/L) in an adult first or second-degree relative. Family history of elevated total cholesterol > 260 mg/dL (6.7 mmol/L) in a child, brother, or sister 16 years or younger.
DIAGNOSIS	
Definite familial hypercholesterolemia = 1+2 or 3	
Possible familial hypercholesterolemia = 1+4 or 5	

Management of Dyslipidaemia

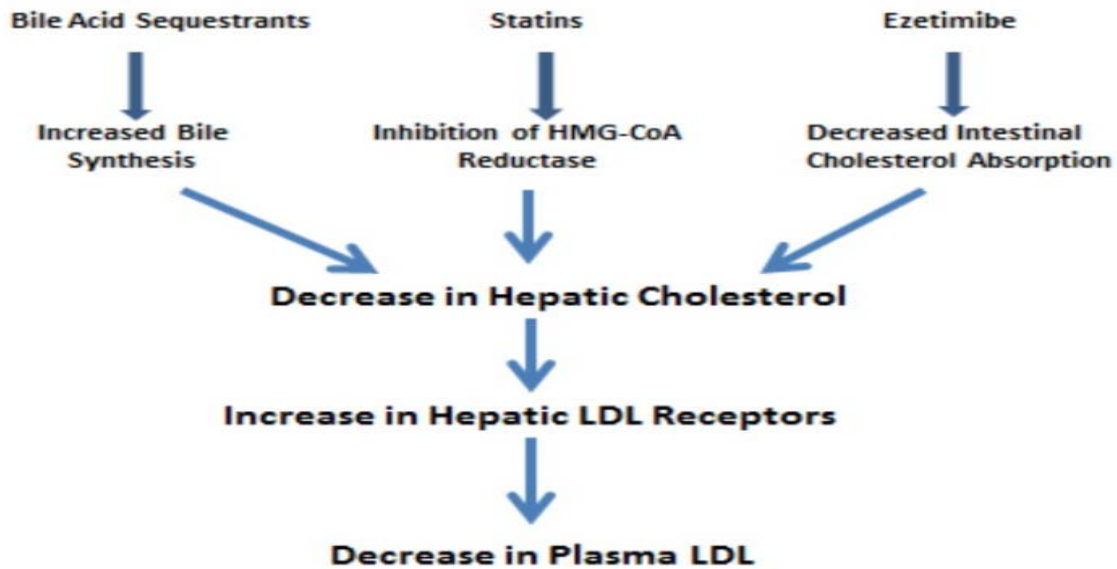
The main goal for dyslipidaemia management is prevention of atherosclerotic coronary disease, including stroke, acute coronary syndromes, transient ischemic attack, or peripheral arterial disorders. ⁽²⁶⁾ Treatment strategies depend on the specific lipid abnormality, although different lipid abnormalities often happen at the same time. ^(13,25,28) A single lipid abnormality may require different interventions; in others, a single management option may be adequate for different lipid abnormalities. Management should always include smoking cessation and treatment of diabetes, and hypertension. ^(10, 24,25,29-31) Management strategies of high LDL cholesterol include lifestyle modification (exercise and diet), medications, dietary supplements, experimental therapies, and procedural interventions. ^(10, 14,25) These options

are also effective for managing of other lipid abnormalities. Dietary modifications include low intake of saturated lipids and cholesterol; high intake of dietary fiber, and maintaining ideal body weight. ^(6, 21,29) Referral to a dietitian is often useful, especially for old people. Exercise helps maintain ideal body weight and lowers LDL cholesterol in some people. Dietary modifications and physical activity should be applied whenever feasible but using medications for certain groups of patients after discussion of the risks and benefits of therapy. ^(10, 24,25) American Heart Assosiation recommends management with a statin for four groups of patients, comprised of those with any of the clinical coronary artery diseases, LDL cholesterol ≥ 190 mg/dL, age 40 to 75, with diabetes and LDL cholesterol 70 to 189 mg/dL, age 40 to 75, LDL cholesterol 70 to 189 mg/dL, and estimated 10 years risk of coronary artery diseases ≥ 7.5%. ^(10, 24,25,32)

Management of children is controversial; dietary modification may be difficult to apply, and no research conclude that low lipid levels for children effectively minimise risk of heart disease during adulthood. Moreover, the effectiveness and safety of long-term use of lipid-lowering medication are questionable. ^(1, 14,15) Children with homozygous familial high cholesterol level need medications, and diet, to prevent premature death. ⁽³¹⁾ Dietary recommendations is used for children with LDL cholesterol more than 110 mg/dL. Drug therapy is used with children older than 8 years and with either poor response to dietary treatment, LDL cholesterol \geq 190 mg/dL, with no family predisposition of premature coronary artery disease. ^(10, 24,33) there is no guidelines specifically target management of elevation in TGs in children. The overall strategy is to apply lifestyle modifications, such as increase physical activity, weight loss, and avoidance consumption of high alcohol dietary sugar and. Intake of two to four servings per week of fish high in omega-3 fatty acids may be effective, however; supplements may be useful because diet only usually does not meet the requirements. ^(10, 24,25,29,34) In diabetic patients, glucose levels should be strictly controlled. Patients with elevated TGs may require beginning medication therapy at diagnosis to more quickly reduce the risk of acute pancreatitis. ⁽³¹⁾ Fibrates reduce TGs by about 50%. ⁽³²⁾ Statins is useful in patients with TGs < 500 mg/dL if high LDL cholesterol are also diagnosed; statins may reduce both LDL and TGs through reduction of VLDL. Fibrates are the drug of choice, if only TGs are elevated. ⁽³¹⁾ High doses of eicosapentaenoic acid and docosahexaenoic acid can be effective in reducing hyperlipidemia. ^(10, 24,35) Prescription omega-3 fatty acid preparations are indicated for triglyceride levels > 500 mg/dL. ^(33,35) Management for TG and LDL cholesterol reduction often elevates HDL cholesterol, and the 3 goals can usually be achieved at the same time. No guidelines specifically target management of low HDL cholesterol in children. Management includes lifestyle modification such as weight loss and an increase in activity level. Medications may be successful in increasing HDL levels when

lifestyle modifications alone are in useful, ^(17, 28,36) Niacin (nicotinic acid) is the most effective MEDICATION for increasing HDL. Niacin also reduces LDL cholesterol; and decreases TGs in doses of 1500 to 2000 mg/day. ^(10, 24,35) In patients with below-average HDL cholesterol levels and, average LDL cholesterol statin combined with niacin management may be useful in preventing cardiovascular diseases. niacin does not appear to have added benefit in patients treated with statins to lower LDL to < 70 mg/dL, ^(32, 35) Fibrates may decrease cardiovascular risk in patients with TGs > 200 mg/dL and HDL cholesterol < 40 mg/dL. Few research guide the management of high Lp(a). Niacin is the only management that directly minimise Lp(a); niacin can decrease Lp(a) by \leq 20% at higher doses. Lowering LDL aggressively is the usual approach in patients with high Lp(a). ^(14, 16 -19) Management of diabetic dyslipidemia should always consists of lifestyle modification as well as statins to decrease LDL. ^(30, 34,35) To minimise the risk of pancreatitis, fibrates can be applied to minimise TGs when levels are higher than 500 mg/dL. Metformin decreases TGs, for this reason, it is used over other oral antihyperglycemic medication during treating diabetes. Some TZDs also lower TGs. Some thiazolidinediones (TZDs) rise both LDL cholesterol and HDL cholesterol. ⁽³⁴⁻³⁶⁾ These antihyperglycemic medication should not be involved over lipid-lowering agents to manage lipid abnormalities in diabetic patients. ^(10, 24,25) Dyslipidemia Treatment of patients with liver disease, renal disease, hypothyroidism, or a combination of these disease s involves treating the underlying disorders firstly and lipid abnormalities secondarily. Abnormal lipid levels in patients with low- ^(22, 29) No studies support specific monitoring periods, however measuring lipid profile every 2 to 3 months after starting or changing treatment and once or twice yearly after lipid levels are normalised is helpful strategy. ⁽³⁶⁾ Figure three shows statins, ezetimibe and bile acids resins affects on dyslipidaemia.

Figure (3): statins, ezetimibe and bile acids resins affects on LDL.



Treatment Goals and recommendations

In adults of both genders, a goal LDL level lower than 100 mg/dL and lower than 70 mg/dL in patients at very high risk. For diabetes mellitus patients LDL goal of lower than 100 mg/dL, and in those with risk factor(s) such as cardiovascular diseases, the recommended LDL target is lower than 70 mg/dL. (6, 20,35) Increasing HDL levels as much as possible is another target, but minimally to higher than 40 mg/dL in both male and female. However, it does not effectively increase HDL levels alone (11,25) It is also suggested that an optimal apolipoproteins “apo B” level for patients with risk of coronary artery diseases, diabetes, is lower than 90 mg/dL, while patients with established diabetes, coronary artery diseases or one or more additional risk factor(s) should have an apo B target lower than 80 mg/dL. Triglyceride level lower than 150 mg/dL in both male and female is recommended. ((10,24,25,35) It is recommended to control lipid levels follow a comprehensive strategy to and to manage associated modifiable risk factors and metabolic abnormalities such as diabetes, hypertension, obesity, and cigarette smoking. The first-line strategy to fundamental prevention in patients with lipid disorders consists of the implementation of lifestyle modification, including medical nutrition therapy and exercise. (10, 24,25) Treatment may

also involve patient education programs, as well as, pharmacotherapy to promote further risk reduction through weight loss smoking and cessation. (10, 12,13) Physical activity programs include at least 30 minutes of moderate-intensity activity 4 to 6 times weekly, with an expenditure of at least 200 kcal/day). Suggested activities include brisk walking, bike, water aerobics, riding a stationary cleaning/scrubbing, mowing the lawn, and sporting activities. (30) For adults, international guidelines recommend a low calorie diet that consisting of vegetables and fruits (≥ 5 servings/day), grains (≥ 6 servings/day, one-third of those as whole grains), lean meats and fish. Intake of cholesterol trans fats, and saturated fats, should be limited. LDL-C-lowering nutrients include plant stanols/sterols (~ 2 g/day) and soluble fiber (10-25 g/day). (30,39) Cigarette smoking is a powerful risk factor, especially for myocardial-infraction, stroke peripheral vascular and disease. Numerous researches have concluded that smoking has a substantial, negative effect on the LDL-C to HDL-C ratio and HDL levels. Smoking also found to have a negative effect on postprandial lipids, mainly triglycerides. Smoking cessation significantly increases HDL-C, with improvement observed in a short period of 30 days. (22, 28) (40-41)

Conclusion

Lipid disorders, also called dyslipidaemia, are abnormalities of lipoprotein metabolism and include elevations of total cholesterol, LDL-C, or triglycerides (TG), or deficiencies of HDL-C. These disorders can be acquired or familial. The disorder become one of the most three common disorders in the world during the last five years due to several modifiable and none modifiable risk factors. The modifiable risk factors include diet, physical activity level and smoking. While the none modifiable factors include age and gender. Adiposopathy is raised by non healthy diet and a low active lifestyle in environmentally and genetically predisposed people. Prior to the appearance of physical findings, most patients are asymptomatic for many years. Even though different lipid abnormalities often coexist; management strategies

depend on the specific lipid abnormality. Many countries or regions have developed their own dyslipidaemia guidelines. Prevention and treatment of dyslipidaemia consists of many procedures. These procedures include risk assessment, establishment of treatment goal, increase activity level, dietary modification, medical therapy, follow up, re-assess and modifying the procedure as necessary. Increase the awareness about the disorder which have to be conduct for all members of family. Future studies are needed to help uncover the mechanobiological rules that help to govern lipid profile response to nutritional loading. The limitations of this review include limited resources are available regarding the lipid profile of different countries. Different settings and age groups between different studies which make them non-comparable

References

1. Block, E.R., Edwards, D. Effect of plasma membrane fluidity on serotonin transport by endothelial cells. *American Journal of Physiology*; 1987;253: 672–678.
2. Brunner, L.J., Vadieli, K., Luke, D.R. Cyclosporine disposition in the hyperlipidemic rat model. *Research Community*. 1988; 59:339–348.
3. Diebold, K., Michel, G., Schweizer, J., Diebold-Dorsam, M., Fiehn, W., Kohl, B. Are psychoactive-drug-induced changes in plasma lipid and lipoprotein levels of significance for clinical remission in psychiatric disorders?. *Pharmacopsychiatry*. 1998; 31:60–67.
4. Dursun, S.M., Szemis, A., Andrews, H., Reveley, M.A. The effects of clozapine on levels of total cholesterol and related lipids in serum of patients with schizophrenia: a prospective study. *Journal of Psychiatry Neurosciences*. 1999;24:453–455.
5. Yeragani, V.K., Balon, R., Pohl, R., Ramesh, C. Imipramine treatment and increased serum cholesterol levels. *Canadian Journal of Psychiatry*. 1989;34:845
6. World Health Organization, “Quantifying Selected Major Risks to Health,” World Health Organization, Geneva, 2002.
7. D. Smith, “Epidemiology of Dyslipidemia and Economic Burden on the Healthcare System,” *American Journal of Managed Care*, Vol. 13, No. S3, 2007, pp. S68-S71.
8. J. Stamler, M. L. Daviglius, D. B. Garside, A. R. Dyer, P. Greenland, et al., “Relationship of Baseline Serum Cholesterol Levels in 3 Large Cohorts of Younger Men to Long-Term Coronary, Cardiovascular, and All-Cause Mortality and to Longevity,” *The Journal of the American Medical Association*, Vol. 284, No. 3, 2000, pp. 311-318. doi:10.1001/jama.284.3.311
9. WHO, “Country Cooperation Strategy for WHO and Saudi Arabia 2006-2011,” 2012. http://www.who.int/countryfocus/cooperation_strategy/ccs_sau_en.pdf
10. M. M. Al-Nozha, M. R. Arafah, M. A Al-Maatouq, M. Z. Khalil, N. B. Khan, K. Al-Marzouki, Y. Y. Al-Mazrou, M. Abdullah, A. Al-Khadra, S. S. Al-Harathi, M. S. Al-Shahid, A. Al-Mobeireek and M. S. Nouh, “Hyperlipidemia in Saudi Arabia Saudi,” *Medical Journal*, Vol. 29, No. 2, 2008, pp. 282-287.
11. Weinreich, M. and Frishman, W.H. (2014). Antihyperlipidemic therapies targeting PCSK9. *Cardiology in Review*, 22(3):140-146.

12. Shattat, G.F. (2014). A Review Article on Hyperlipidemia: Types, Treatments and New Drug Targets. *Biomedical and Pharmacology Journal*, 7(2):399-409.
13. D. O. Ogbeide, A. Karim, I. M. Al-Khalifa and S. Siddique, "Population Based Study of Serum Lipid Levels in Al-Kharj Health Center, Saudi Arabia," *Saudi Medical Journal*, Vol. 25, No. 12, 2004, pp. 1855-1857.
14. S. N. Al-Shehri, Z. A. Saleh, M. M. Salama and Y. M. Hassan, "Prevalence of Hyperlipidemia among Saudi School Children in Riyadh," *Annals of Saudi Medicine*, Vol. 24, No. 1, 2004, pp. 6-8.
15. B. A. Abalkhail, S. Shawky, T. M. Ghabrah and W. A. Milaat, "Hypercholesterolemia and 5-Year Risk of Development of Coronary Heart Disease among University and School Workers in Jeddah, Saudi Arabia," *American Journal of Preventive Medicine*, Vol. 31, No. 4, 2000, pp. 390-395. doi:10.1006/pmed.2000.0713.
16. R. Bonita, M. de Courten, T. Dwyer, K. Jamorzik and R. Winkelmann, "Surveillance of Risk Factors for NonCommunicable Diseases," The WHO Stepwise Approach, WHO, 2001.
17. WHO, EMRO, "STEPwise WHO," 2005. http://www.who.int/chp/steps/2005_Saudi_Arabia_STEPS_Report_EN.pdf
18. W. T. Friedewald, R. I. Levy and D. S. Frederickson, "Estimation of the Concentration of Low-Density Lipoprotein Cholesterol in Plasma, without Use of the Preparative Ultracentrifuge," *Journal of Clinical Chemistry*, Vol. 18, No. 6, 1972, pp. 499-502.
19. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III)," *The Journal of the American Medical Association*, Vol. 285, No. 19, 2001, pp. 2486-2497. doi:10.1001/jama.285.19.2486
20. H. Saadi, S. G. Carruthers, N. Nagelkerke, et al., "Prevalence of Diabetes Mellitus and Its Complications in a population-Based Sample in Al-Ain, United Arab Emirates," *Diabetes Research and Clinical Practice*, Vol. 78, No. 3, 2007, pp. 369-377.
21. Jackson, Z. Al-Mousa, M. Al-Raqua, P. Prakash and A. N. Muhanna, "Multiple Coronary Risk Factors in Healthy Older Kuwaiti Males," *European Journal of Clinical Nutrition*, Vol. 56, No. 8, 2002, pp. 709-714.
22. S. Al-Moosa, S. Allin, N. Jemai, J. Al-Lawati and E. Mossialos, "Diabetes and Urbanization in the Omani Population: An Analysis of National Survey Data," *Population Health Metrics*, Vol. 4, No. 5, 2006, p. 5-17.
23. A. Bener, M. Zirie, I. M. Janahi, O. A. Al-Hamaq and M. Musallam, "Prevalence of Diagnosed and Undiagnosed Diabetes Mellitus and Its Risk Factors in a Population Based Study of Qatar," *Diabetes Research and Clinical Practice*, Vol. 84, No. 1, 2009, pp. 99-106.
24. Y. S. Khader, A. Batiha, M. El-Khateeb, M. Al Omari and K. Ajlouni, "Prevalence of Dyslipidemia and Its Associated Factors among Jordanian Adults," *Journal of Clinical Lipidology*, Vol. 4, No. 1, 2010, pp. 53-58. doi:10.1016/j.jacl.2009.12.004 .
25. C. Pongchaiyakul, P. Hongsprabhas, V. Pisprasert and C. Pongchaiyakul, "Rural-Urban Difference in Lipid Levels and Prevalence of Dyslipidemia: A Population-Based Study in Khon Kaen Province, Thailand," *Journal of the Medical Association of Thailand*, Vol. 89, No. 11, 2006, pp. 1835-1844.
26. W. H. Zhao, J. Zhang, Y. Zhai, Y. You, Q. Q. Man, et al., "Blood Lipid Profile and Prevalence of Dyslipidemia in Chinese Adults," *Biomedical and Environmental Sciences*, Vol. 20, No. 4, 2007, pp. 329-335.
27. W. M. Kang, J. S. Zhang, X. X. Liu, M. S. Wang and M. L. Zhao, "Prevalence of Abnormality of Blood Lipid and Associated Factors in Health Examination Population in Beijing," *Chinese Medical Sciences Journal*, Vol. 24, No. 3, 2009, pp. 142-146. doi:10.1016/S1001-9294(09)60078-X
28. C. Erem, A. Hacıhasanoglu, O. Deger, et al., "Prevalence of Dyslipidemia and Associated Risk Factors among Turkish Adults: Trabzon Lipid Study," *Endocrine*, Vol. 34, No. 1-3, 2008, pp. 36-51. doi:10.1007/s12020-008-9100-z
29. F. Azizi, M. Rahmani, A. Ghanbarian, H. Emami, P. Salehi, P. Mirmiran and N. Sarbazi, "Serum Lipid Levels in an Iranian Adults Population: Tehran Lipid and Glucose Study," *European Journal of Epidemiology*, Vol. 18,

- No. 4, 2003, pp. 311-319.
doi:10.1023/A:1023606524944
30. R. W. Mahley, K. E. Palaoglu, Z. Atak, J. Dawson-Pepin, A. M. Langlois, V. Cheung, H. Onat, P. Fulks, L. L. Mahley, F. Vakar, S. Ozbayrak?, O. Gokdemir and W. Winkler, "Turkish Heart Study: Lipids, Lipoproteins, and Apolipoproteins," *The Journal of Lipid Research*, Vol. 36, No. 4, 1995, pp. 839-859.
31. V. Grabauskas, I. Miseviciene, J. Klumbiene, J. Petkeviciene, Z. Milasauskiene, A. Plieskiene and L. Margeviciene, "Prevalence of Dyslipidemias among Lithuanian Rural Population (CINDI Program)," *Medicina (Kaunas)*, Vol. 39, No. 12, 2003, pp. 1215-1222.
32. E. Polychronopoulos, D. B. Panagiotakos and A. Polystipiotti, "Diet, Lifestyle Factors and Hypercholesterolemia in Elderly Men and Women from Cyprus," *Lipids in Health and Disease*, Vol. 4, No. 17, 2005, pp. 1-7.
33. L. J. de Souza, J. T. Souto Filho, T. F. de Souza, et al., "Prevalence of Dyslipidemia and Risk Factors in Campos dos Goytacazes, in the Brazilian State of Rio de Janeiro," *Arquivos Brasileiros de Cardiologia*, Vol. 81, No. 3, 2003, pp. 249-264.
34. R. Pradeepa, R. Deepa, S. S. Rani, G. Premalatha, R. Saroja and V. Mohan, "Socioeconomic Status and Dyslipidaemia in a South Indian Population: The Chennai Urban Population Study (CUPS 11)," *National Medical Journal of India*, Vol. 16, No. 2, 2003, pp. 73-78.
35. S. Wang, L. Xu, J. B. Jonas, Q. S. You, Y. X. Wang, et al., "Prevalence and Associated Factors of Dyslipidemia in the Adult Chinese Population," *PLoS One*, Vol. 6, No. 3, 2011, p. e17326.
36. R. W. Mahley, S. Can, S. Ozbayrakci, T. P. Bersot, S. Tanir, K. E. Palaoglu and G. M. Pepin, "Modulation of High-Density Lipoproteins in a Population in Istanbul, Turkey, with Low Levels of High-Density Lipoproteins," *American Journal of Cardiology*, Vol. 96, No. 4, 2005, pp. 547-555.
37. J. Yarnell, S. Yu, E. McCrum, D. Arveiler, B. Hass, J. Dallongeville, M. Montaye, P. Amouyel, J. Ferrieres, J. B. Ruidavets, A. Evans, A. Bingham, P. Ducimetiere and PRIME Study Group, "Education, Socioeconomic and Lifestyle Factors, and Risk of Coronary Heart Disease: The Prime Study," *International Journal of Epidemiology*, Vol. 38, No. 2, 2005, pp. 268-275.
doi:10.1093/ije/dyh267
36. Z. R. Guo, X. S. Hu, M. Wu, M. H. Zhou and Z. Y. Zhou, "A Prospective Study on the Association between Dyslipidemia and Hypertension," *Chinese Journal of Epidemiology*, Vol. 30, No. 6, 2009, pp. 554-558.
39. Z. H. Liu, X. B. Xue and Z. Zhi, "Prevalence of Dyslipidemia and Associated Factors among the Hypertensive Rural Chinese Population," *Archives of Medical Research*, Vol. 38, No. 4, 2007, pp. 432-439.
40. Harikumar, K., Abdul Althaf, S., Kishore kumar, B., Ramunaik, M. and Suvarna, C.H. (2013). A Review on Hyperlipidemic. *International Journal of Novel Trends in Pharmaceutical Sciences*, 3(4): 59-75.
41. Amuamuta, A. (2014). A Review on Risk Factors/Indicators and Effects of Hyperlipidemia. *Middle-East Journal of Scientific Research*, 22(6): 886-893