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Dyslipidemia and Endocrine Disorder

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Abstract

Dyslipidemia is one of the most common risk factors for the most prevalent and fatal non-communicable diseases (NCDs); cardiovascular disease (CVD), cancer, chronic respiratory disease and diabetes and other. According to world health organization (WHO) report effective management of dyslipidemia can reduce incidence and mortality rate by NCDs up to 30%. Dyslipidemia negatively affects every vital organ; liver, kidney, heart, brain, lung and others in number of ways. In short dyslipidemia is defined as disorder of lipoprotein metabolism and it could be either hypolipoproteinemia or hyperlipoproteinemia. Endocrine disorder, poor feeding habit, physical inactivity and other factors are responsible for existence of dyslipidemia. Lipocrinology which studies about interrelationship between lipid metabolism and endocrine function in normal and abnormal condition is getting essential. Currently number of studies explain that dyslipidemia induce endocrine dysfunction and the reverse is also possible. In addition, biochemical assessment of dyslipidemia is used to monitor clinical course and progress of endocrinological diseases. Similarly, biochemical analysis of hormones helps to assess the outcome of antidyslipidemic drugs and prognoses the condition dyslipidemia. Most commonly dyslipidemia coexist with type 2 diabetes, obesity and metabolic syndrome. Abnormal distribution and accumulation fat in the body leads to deranged different hormones and factors secretion like adipokine, thereby contributing to chronic inflammation and lipotoxicity. Therefore, detailed and up-to-date review about lipid metabolism disorder and endocrine function are so essential in medicine and health science to have good service to community.

Keywords: dyslipidemia, endocrine, hormone, lipocrinology

1. Introduction

Different scientific journal define dyslipidemia in different ways but the idea is the same. Dyslipidemia defined as unhealthy levels of one or more kinds of the following lipid particles in the blood; high-density lipoprotein (HDL), low-density lipoprotein (LDL), intermediate density lipoprotein (IDL), very low-density lipoprotein (VLDL), triglycerides, cholesterol and others. In other words, dyslipidemia could be explained as disorder of lipoprotein metabolism and the condition could be either hyperlipoproteinemia or hypolipoproteinemia [1]. Higher plasma level of atherogenic and immunogenic lipid particles such as LDL, triacylglycerol, cholesterol and small density lipoprotein and lower plasma level of HDL are indicators of dyslipidemia [2].

Lipids are water-insoluble heterogeneous organic molecules and can be extracted from tissues by nonpolar solvents. As a result of its nature body lipids are generally found compartmentalized, and could exist as membrane-associated lipids or droplets of triacylglycerol in adipocytes, or transported in plasma in association with protein. Its chemical nature makes lipids as a major source of energy for the body and hydrophobic barrier. In addition, lipids act as a precursor for synthesis important biomolecules like fat-soluble vitamins, prostaglandins and steroid hormones and others [3].

An endocrine gland secretes hormone into the blood and traveled to target cells or tissues located elsewhere in the body where they have specific receptor. Accordingly target cell and tissue produce unique response. Hormones are responsible to regulate most biological activity in the body essential for survival and reproduction [4]. Every physiological activity; sleeping, drinking, feeding, growth, aging and others needs the involvement of hormones [5].

Hormones like leptin, insulin and adiponectin influence lipid metabolism and plasma lipid profile level which is associated with obesity. Leptin and adiponectin regulate lipid metabolism and increase fatty acid oxidation in the peripheral tissue by activating adenosine monophosphate (AMP) dependent kinase pathway. In addition, adiponectin increase insulin sensitivity to tissue thereby it decreases triacylglycerol and downregulate its plasma level [6]. Currently number of studies explain that dyslipidemia induce endocrine dysfunction and the reverse is also possible. In addition, biochemical assessment of dyslipidemia is used to monitor clinical course and progress of endocrinological diseases. Similarly, biochemical analysis of hormones helps to assess the outcome of antidyslipidemic drugs and prognoses the condition dyslipidemia [7].

1.1 Dyslipidemia among non-communicable disease

Lipids are one of the most important macromolecules; used by our body as energy source, structural components of cell membrane, precursor for synthesis of steroid hormones and fat-soluble vitamins etc. There are also essential fatty acids like linolic and linolenic which are necessary for normal biological activity and human body cannot synthesis them. Knowing lipid biochemistry and its metabolic disorder (dyslipidemia) is necessary in understanding the biomedical areas of non-communicable disease like hypertension, diabetes, cancer, cardiovascular disease, obesity, nutritional value of unsaturated fatty acids and others [8].

According to the world health organization 2015 report non-communicable disease (NCDs) are responsible for up to 70% of deaths and these are hypertension, cardiovascular diseases, cancer, diabetes and chronic respiratory diseases. Majority of NCDs cases and deaths are observed in low- and middle-income countries. The report shows that tobacco, insufficient physical activity, harmful use of alcohol, unhealthy diet, raised blood pressure, overweight and obesity, raised cholesterol, cancer-associated infections and others are the major risk factors for NCDs [9, 10].

Number of studies showed that dyslipidemia used as a biomarker and risk factor for different NCDs and it is highly associated with one or more hormone disfunction. For example, deficiency or defect in insulin action among diabetes induce dyslipidemia and it is one of the major risk factors for cardiovascular disease. Dyslipidemia is the common finding among different types of diabetes. Across suctional study done by Hrishow et al. found that 73% male and 71% female of diabetic patients were dyslipidemic [11]. Another similar study done by Bekele S. et al. in Ethiopia revealed that 65.6% of diabetic patients were dyslipidemic. Plasma level of LDL, total cholesterol and triacyclglycerols were higher while HDL was lower among diabetic patients [12]. Similarly, number of recent studies showed that dyslipidemia has significant association with cancer and progress of the disease.

Lipids are major constituents of cell and disorder in lipid metabolism can affect the normal integration of cell which may leads to cancerous. On the other side treatment for cancer patients specially chemotherapy induce dyslipidemia. In addition, oxidative modification of lipoprotein induces different inflammatory pathways and this enhance cell proliferation and migration and inhibit normal cell apoptosis [13]. Review done by Cedó L. et al. indicated that higher total serum cholesterol level is linked with higher risk of colorectum, colon, prostate and testicular cancer and lower risk of stomach, liver and hematopoietic and lymphoid tissues cancer. There was positive association between serum triglycerides and esophageal, colorectal, lung, renal, thyroid cancer [14]. Effective management of cholesterol may help to control the risk of cancer cases. Study by Macleod LC et al. stated that elevated LDL and impaired fasting glucose are highly associated with prostate cancer and management on them help to get better treatment outcome at the end [15].

Number of studies explained that dyslipidemia is a common risk factor for different types of cardiovascular disease. A 6 year follow up prospective cohort study done by Hedayatnia M et al. explained that serum LDL-C, TC, and TG levels were positively associated with the risk of total CVD events and the primary target of lipid-lowering therapy with statin is to reduce risk of CVD [16, 17]. Events of dyslipidemia occurred among patients with different infectious disease like HIV and TB increase risk of atherosclerosis and finally leads CVD. The infectious disease itself and the drugs given for that are responsible to induce dyslipidemia [18, 19].

1.2 Effect of dyslipidemia on vital organs

Survival of living organism like humans relies on wellbeing of vital internal organs; brain, liver, heart, lung and others. An organ which exists in most multicellular organisms is a collection of tissues joined in a structural unit to serve a common function. Normal and functional liver is responsible for healthy metabolism of lipids. Study done by Unger LW *et al* showed that liver health is a major determinant of dyslipidemia patterns and prevalence. All etiology that induces advanced chronic liver disease significantly decrease total cholesterol levels when compared to normal [20]. Dyslipidemia can cause fatty liver disease and the reverse also possible. A multicenter retrospective cross-sectional study done for 5 years by Méndez-Sánchez N *et al* showed that dyslipidemia was the very common risk factor which is directly associated with advanced liver disease and cirrhosis [21].

Brain is one of very important vital organ for normal function of all other body organ and organ system. Studies indicated that dyslipidemia can affect the integrity and function of brain and significantly associated with number brain disorder like Alzheimer's Disease. A one year follow up study done on 36 subjects with Alzheimer's Disease by Bowman GL. *et al* confirmed that dyslipidemia was highly prevalent and more than 75% of them showed blood brain barrier (BBB) impairment. According to this study triglyceride and HDL cholesterol which have a role in maintaining BBB integrity were significantly higher among subjects with BBB impairment [22]. A Meta-Meta-Analysis done by Vazquez OS *et al* conclude that LDL-C cholesterol levels significantly increase the risk for development of Alzheimer's disease. Hypercholesterolemia affect the normal function of vascular system and have neurotoxic effect thereby induce dementia and cognitive loss in Alzheimer's Disease patients. In addition, coronary heart disease and carotid artery atherosclerosis raised as a result of hypercholesterolemia and that can lead to cognitive disorder by causing cerebral embolism or hypoperfusion which are associated with Alzheimer's Disease incidence and prevalence [23]. Studies also showed that there is significant association between high total cholesterol and LDL-cholesterol with different types of stroke as a result people with hypercholesterolemia have advised to take potent lipid

lowering drugs mainly statin to reduce risk of stroke. But there is an evidence that low level of total cholesterol can induce hemorrhagic stroke. Cohort study for one year on Patients with Transient Ischemic Attack done by Sirimarco G. *et al* showed that atherogenic dyslipidemia was significantly associated with intracranial artery stenosis and higher risk of early recurrent stroke. In general disorder in lipid metabolism have a complex relationship with cerebrovascular disease [24, 25].

Bones which are found in different shapes and sizes have many roles in wellbeing life and its health has intimate association with normal metabolism of lipids. Evidence indicated that highly increased adipocyte can be independent risk factor for osteoporosis and disorder of bone metabolism [26, 27]. Oxidation products of lipids as a result of hyperlipidemia can be accumulated in the subendothelial spaces of vasculature and bone and these affect the normal developments of bone negatively. Study done on mice by Pirih F *et al* explain as dyslipidemia is one risk factor for thyroid dysfunction and impairs regeneration and mechanical strength of bone [28]. Another study done on rabbit to study the effect of hyperlipidemia on quality and quantity of bone and wound healing condition showed that hyperlipidemia negatively affect bone implant stability and pre-implant stability [29].

1.3 Dyslipidemia induce endocrine dysfunction

Disorder in lipid metabolism is a multifactorial problem; genetic and environmental risk factors are very important modulators. Number of studies explain that dyslipidemia has significant association with age, sex and educational status and others. Dyslipidemia affect the normal health in number of ways and the mechanism is complex. Diabetes, cardiovascular disease, hypertension and other noncommunicable disease have direct or indirect relation with dyslipidemia. And most of non-communicable disease have endocrine bases; as a result, deep analysis of endocrine disorder and dyslipidemia is very crucial. For example, in cancers of the breast, prostate, testes, cervices, pancreas, thyroid and others patients have abnormal lipid profile and all the cases have hormonal problems. A cross sectional study done by Altahir WHM *et al* showed that triacylglycerol was significantly higher while cholesterol was lower among hyperthyroidism patients [30]. Also, other cross-sectional study done by Khan MAH *et al* indicate as there is strong association between dyslipidemia and hypothyroidism [31].

There is clear evidence as chronic elevation of triacylglycerol in the blood cause islet alpha- and beta-cells dysfunction. In the general obese population; fasting level of insulin and glucagon have positive correlation with lipid parameters. Level of glucagon is clear informative of glucose tolerance and the mechanism how elevated fatty acids affect islet-cells is through inactivation of G-protein coupled receptor called Free fatty acid receptor 1 (FFAR1) [32]. Cholesterol can modulate different metabolic pathways like signal transduction and gene expression in numbers of ways. Many studies showed that cholesterol level in the blood affect the secretion and function of insulin from beta-cell of pancreas. Animal model study done by Hao M *et al* found that elevated level of cholesterol can significantly reduce insulin secretion and the condition can be restored with management of blood cholesterol. The suggested mechanism for this is through manipulation of neuronal nitric oxide synthase dimerization [33].

Steroid hormones like sex hormones are synthesized from cholesterol, so the normal concentration of cholesterol is responsible for normal sexual development of an individual. Production, secretion and degradation of factors that are involved in function of sex hormones like Sex hormone-binding globulin (SHBG) are regulated with lipid panels of individual. Study done by Park G *et al* indicated that dyslipidemia negatively affect the level SHBG and these can disturb the normal developments children at pubertal stage [34].

1.4 Endocrine disorder risk for dyslipidemia

An endocrine system secretes specific chemicals, called hormones into the blood and travel through the blood to target cells or tissues that they induce a particular response or action. Hormones involved in regulation of biological activities like growth, reproduction, metabolism of biomolecules (protein, lipids, carbohydrate, nucleic acids and others). Endocrine disorders are among the most common medical problems faced by individual in both sexes. Defect in synthesis, storage, secretion and action of hormones can seriously affects normal biological activities of individuals in number of ways. One of the most important system affected as a result of endocrine disorder is lipid metabolism and these in turn risk for developments of different non-communicable diseases. Diabetes mellitus is one common endocrinological disorder and it leads to dyslipidemia. Cross-sectional study done by Xi Y *et al* showed that all types of diabetes and postmenopausal hormonal changes are positively correlated with dyslipidemia [35]. Hormones regulate expression of lipoprotein receptors, apoproteins, enzymes and control circulating triacylglycerol and glucose. Typical hormones involved in modulating lipid metabolism are leptin, insulin, adiponectin, glucagon, catecholamines, cortisol and growth hormone and any disorder on these hormones' synthesis, storage, secretion and action leads to dyslipidemia. Body lipid synthesis and degradation are under control of the above hormonal activity [36, 37]. Number of studies confirmed that dyslipidemia is the most common disorder among diabetes especially type 2 diabetes. As a result, people with diabetes should monitor their blood lipid levels regularly and get nutrition education periodically to prevent and control dyslipidemia [38].

Higher level of growth hormone and factors like insulin like growth factor-1(IGF-1) leads to a medical problem called acromegaly. And these conditions alter the metabolism of biomolecules and activity of other hormones like insulin thereby risk for cardiovascular disease mainly by inducing dyslipidemia. Study done by Keskin H *et al* explained that LDL-C, triglyceride, IGF-1 level was significantly higher among acromegaly patients than control groups while HDL-C level was lower. In addition, growth hormone has positive correlation with LDL-C and triglyceride and negative correlation with HDL-C level [39].

One important steroid hormone called cortisol is responsible to regulates a wide range of vital biological processes including metabolism of biomolecules and immune response throughout the body. Cortisol is made in the cortex of the adrenal glands and released into the blood. Most of body cells have receptor for cortisol so that it produces different effect. Cortisol secretion regulated by close interaction of hypothalamus, pituitary gland and adrenal gland. One of the metabolic process regulated by cortisol is lipid metabolism. Study done by Djurhuus C. B. showed that cortisol is a potent stimulus of lipolysis in both femoral and abdominal adipose tissue [40]. Hypersecretion of cortisol which resulted from altered function of hypothalamus, pituitary gland and adrenal gland can leads to dyslipidemia. The mechanism by which cortisol disturb lipid metabolism is vary; initiate lipolysis, free fatty acid production and turnover, VLDL synthesis and fatty accumulation in liver and adipose tissue. Modulation of insulin sensitivity and adenosine monophosphate kinas (AMPK) activities are the key by which glucocorticoid-induced dyslipidemia will develop. In addition, defects of the glucocorticoid receptor affecting cortisol sensitivity is involved in lipid metabolism disorder and risk for cardiovascular disease [41].

Similarly, sex hormones are responsible in regulating metabolism lipids and any disorder regarding these sex hormones leads to dyslipidemia. In study done by Yeasmin N *et al* showed that serum total cholesterol and triacylglycerol level were significant higher in postmenopausal women than premenopausal women and they have negative correlation with serum estrogen as a result of this

postmenopausal women are more prone to have CVD and associated complications and recommended to monitor their lipid profile regularly [42, 43].

1.5 Assessment of lipid profile as marker for endocrine disease

Lipids are a group of fats and fat-like substances that are important constituents of cells and sources of energy. Assessments lipid panel is simply qualitative and quantitative determination of the specific lipid parameters in the blood. Lipid profile test commonly performed to evaluate cardiovascular diseases including coronary heart disease (CHD), myocardial infarction (MI), coronary insufficiency, angina, ischemic stroke, hemorrhagic stroke, transient ischemic attack, peripheral artery disease (PAD) and heart failure. Directly or indirectly all the above cases related with endocrine disorder. In addition, evaluation of TG/HDL-C and TC/HDL-C ratios are useful markers of metabolic syndrome with high predictive value in general population. Studies showed that LDL-C, total cholesterol, triglyceride and apolipoproteinB (apoB) can serves as biomarker Cushing syndrome [44]. Similarly, one or more lipid profile abnormality is common prior to type 2 diabetes [45]. In general, in most of endocrine disease dyslipidemia is common and physician who suspect his patients have hormonal problem should order lipid profile test [46].

1.6 Conclusion

Dyslipidemia is an abnormal amount of lipids commonly triglycerides, cholesterol LDL-C, HDL.C and other in the blood and it is highly prevalent among patients with noncommunicable disease. Each and every lipid profile parameter abnormality has direct or indirect relation with endocrine disorder. Even though it needs more extended research disorder in lipid metabolism induce hormonal dysfunction and the reverse also possible.

Conflict of interests

The authors declare that they have no competing interests.

Ethical statement

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