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Relation between dyslipidemia and obesity: A concise review

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Abstract

Dyslipidemia is a pathological condition in which lipid levels are deranged and it is a major health problem leading to dreadful complications if untreated. Presently its prevalence is high in developed countries especially in women. Concept of dyslipidemia does not exist in classical test but resemble sign and symptoms are described under the description of *Samin-e-mufrit* and Unani Physician recommended various drugs for its management. Therefore, it was determine to correlate between dyslipidemia and obesity, whereas Unani physicians well described etiology, pathophysiology, clinical features and there management with the help of package treatment i.e., Dietotherapy, Regimes and Pharmacotherapy.

Keywords: Dyslipidemia, obesity, samin-e-mufrit, unani medicine

Introduction

Dyslipidemia is one of the common metabolic disorders ^[1]. Dyslipidemia is elevation of plasma cholesterol, triglycerides (TGs), or both, or a low high-density lipoprotein level that contributes to the development of atherosclerosis ^[2]. Raised cholesterol increases the risks of heart disease and stroke. Globally, a third of ischaemic heart disease is attributable to high cholesterol ^[3].

Dyslipidemia also defined in another terms when HDL-C levels below the 10th percentile and HDL-C levels greater than the 90th percentile for age and gender ^[4]. Dyslipidemia is one of the major risk factors for cardiovascular disease ^[5]. Dyslipidemia may be affecting either primary form or secondary form ^[6].

A primary dyslipidemia (e. g., familial hypercholesterolemia) typically refers to a genetic defect in the lipid metabolism that causes abnormal lipid levels ^[7]. A secondary dyslipidemia may be due to a variety of reasons like environmental factors (Diet rich in saturated fat or a sedentary lifestyle), diseases (Type 2 diabetes, hypothyroidism, obstructive jaundice, etc.), and medications (Thiazide diuretics, progestins, anabolic steroids, etc.) ^[11].

Nowadays, major evolution has been made in understanding the genetic basis of dyslipidemias and in studying the safety and efficacy of lipid-lowering drugs for coronary heart disease (CHD) prevention has been reported ^[8].

Cholesterol, triglycerides, and high-density lipoproteins are important constituents of the lipid fraction of the human body ^[9]. About 70% of plasma or serum cholesterol is in the esterified form, and this form of cholesterol is found in the core of lipoprotein particles along with triglycerides and fat soluble vitamins where as phospholipids and apolipoproteins form the surface of lipoprotein particles. The type of fatty acids attached to triglycerides, phospholipids, and cholesteryl esters are mainly determined by dietary intake ^[10].

Plasma lipoproteins can be divided into seven classes based on size, lipid composition, and apolipoproteins i.e. chylomicrons, chylomicron remnants, VLDL, IDL, LDL, HDL, and Lp (a) ^[11].

In above, LDLs acquires about two-third of cholesterol for peripheral tissues and get deposited there, and considered the main agent in elevated serum cholesterol levels; hence labelled as "bad" or lethally (L) dangerous (D) lipoprotein (L) due to its involvement for atherosclerosis formation ^[12]. In other hand, HDLs carry less total lipid and more carrier proteins, because HDLs carry cholesterol from the tissues to the liver for catabolism and

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excretion, higher level of this so-called “good” cholesterol form are considered protective against cardiovascular diseases. However, HDL cholesterol is good for health [13].

Lipoproteins are the primary source of transport for cholesterol among tissues and when, deviations from a proper balance of transport of cholesterol, either increases in LDL levels or decreases in HDL cholesterol flux, may result in accumulation of cholesterol in extrahepatic tissues which promote the risk factor for atherosclerosis [14].

South Asians around the globe have the highest rates of coronary artery disease and these rates are 50% to 300% higher than other populations, with a higher risk at younger ages [15].

If dyslipidaemia is left over and untreated for long time, it may affect the all system of the body and leads to various complications such as coronary heart disease, atherosclerosis, diabetes, chronic kidney disease, palpitation, stroke, myocardial infarction etc [16].

According to the WHO, globally, a third of ischemic heart disease is attributable to high cholesterol. Overall, raised cholesterol is estimated to cause 2.6 million deaths (4.5% of total) and 29.7 million disability adjusted life years (DALYs) [17]. [Cardiovascular disease (CVD) is the leading cause of death in India and its contribution to mortality is rising; deaths due to CVDs were double between 1985–2015. Cardiovascular mortality in Asian Indian population is likely to climb up 103% in men and 90% in women by the year of 2015 [18].

Dyslipidemia has been closely linked to the pathophysiology of CVD and is a key independent modifiable risk factor for cardiovascular disease, while Asian Indians are known to have a unique pattern of dyslipidemia with lower HDL cholesterol, increased triglyceride levels and higher proportion of small dense LDL cholesterol [19].

Dyslipidemia plays a crucial role in the development of cardiovascular disease, which has become the leading cause of death in most developed countries as well as in developing countries [20]. In developed countries it arises due to change in their lifestyle pattern [21].

Recent studies have reported that high cholesterol is present in 25–30% of urban and 15–20% rural subjects. The most common dyslipidemia in India are borderline high LDL cholesterol, low HDL cholesterol and high triglycerides [22]. Reddy Ks *et al.*, reported that as per WHO Bulletin, in India, CVD is projected to be the largest cause of death and disability by 2020, with 2.6 million Indians predicted to die due to coronary heart disease, which constitutes 54.1% of all CVD deaths. Nearly half of these deaths are likely to occur among young and middle-aged individuals [23].

Therefore, the change in lifestyle behaviours and proper management of dyslipidaemia is important strategies for preventing cardiovascular disease [24]. Current classification schemes and treatment levels for hyperlipidemia are based on the National Cholesterol Education Panel’s (NCEP) Adult Treatment Program-3 (ATP-III) guidelines [25].

Elevated serum total cholesterol and low-density lipoprotein cholesterol (LDL-C) levels are among the primary causal risk factors for cardiovascular disease [26].

Peoples who are prone for dyslipidemia they are using lipid-lowering agents and long term used leads to various complications [27].

Therefore, the appropriate diagnosis and management of lipoprotein disorders is of critical importance in the practice

of medicine [28]. There is no such explanation of dyslipidaemia in classical Unani literature, but the concept of *Dasumat Fid Dam* (presence of fatty and oily substance mixing in blood which found in urooque) and *Samin-e-Mufrit* exists since Hippocratic Period [29]. The renowned Unani physicians considered *Dasumat Fid Dam* and *Samin-e-Mufrit* as consequence of each other. It is evidence base from the Unani literature that the aetiological factors (asbab), clinical features (alamat), complications (Awarijat), principle of treatment and treatment (Usool-e-Ilaj waj Ilaj) mentioned by eminent scholars and the description of obesity gives a clue by that they were aware regarding concept of dyslipidemia [30].

Hippocrates was the first, who gave detailed explanation of *Samin-e-Mufrit* including its complications [31]. Later on renowned Unani physicians like *Galen*, *Zakaria Rhazi*, *Ali Ibn Abbas Majoosi*, *Ibn-e-Sina* Ismail Jurjani have described the concept of obesity and their treatises [32, 33, 34]. Author of *Zakhira Kharzam Shahi* and *Moalaja-e-Nafeesi* specially noted that obese people are more prone to develop cardiac and cerebral complications i.e. *Khafqan* (palpitation), *Ghashi* (syncope), *Sakta* (stroke), concealed haemorrhage, coma and sudden death [35, 36].

In Unani system of medicine, mizaj of *Shaham* is considered as *Barid Ratab* [37], and its classification is also described by renowned physician in detail. It is also mentioned that those persons who possess *Barid Ratab Mizaj* are more liable to develop *Samin-e-Mufrit* [32]. *Samin-e-Mufrit* (obesity) is defined as a condition in which there is increase of ratoobat (wetness) and baroodat (coldness) in the body and qillate-harkate A’za (slow movements of organs) due to excessive accumulated fat and cold temperament i.e. the person becomes lazy and dull [31].

Thus, *Samin-e-Mufrit* is conditions which arise due to accumulation of *Barid Ratab madda (Shaham)* and falls under the caption of *Amraz-e-Balghamiya* [38, 39]. Those people who are suffering from obesity may susceptible to develop condition like *tangi urooq* (narrowing of vessels) and resultant *Sakta* (stroke) and finally sudden death ensues [31, 36].

Samin-e-Mufrit can be managed through Black Box Design i.e. multidirectional therapeutic approach such as; - Change in dietary pattern, regular exercise appropriate medicament [40]. In Unani system of medicine, a large number of drugs are being used in clinical practice in the management of obesity by different Unani physicians from past. Some of the scientific studies have revealed that most of the ingredient of this formulation exhibit as hypolipidemic activity [41, 42, 43, 44].

Relation between lipids and humors

In the Unani Classical texts, there is no perception of hypercholesterolemia as such; but in many cases has been depicted it as a disorder. As far as the presence of fat (Lipids) is concerned in blood, Ibn Sina an ancient Iranian traditionalphysician has reported its existence in blood, producedfrom "*Dasoomat Al-Dam*". "*Dasoomat*" means "fatty, oily" and "*Dam*" means "blood". *Dasoomat* of blood or the oily matters could bethe lipids but as the biochemical analysis of blood wasnot available and they could not explain it as permodern parameters. According to the fundamentals concept ofUnani medicine, the blood circulating in the Urooque (vessels) is a mixture of four humours. Consequently, the clues of blood lipids should be

required between the humours. Thus to make clear this issue, it is essential to explain the production path of the akhlat [45].

Lipids and lipoprotein metabolism

Lipids

Fat (Lipid) is insoluble in plasma, and hence, cannot be transported directly through the blood. It is now recognised that lipids (fat/ cholesterol) in their various forms are transported by lipoproteins [46].

Lipoproteins

Lipoproteins are a group of heterogenous substances, metabolically active, constantly circulating through the vasculature and existing in a state of dynamic equilibrium between tissues and liver [47]. Triglyceride-fats and cholesterol esters are carried internally in a lipoprotein and shielded from water by the phospholipids monolayer and the apoproteins. Such characteristics make them soluble in the salt water-based blood pool. These lipoprotein particles have hydrophilic groups of phospholipids, cholesterol and apoproteins directed outward [48]. The functions of lipoprotein particles includes absorption of dietary fat and transportation of lipids (triglyceride and cholesterol), absorption of and transportation of fat-soluble vitamins; and transportation of cholesterol from peripheral tissues back to the liver [49].

Chylomicrons

Chylomicrons are produced in the intestinal lumen following the absorption of digested fat. These are the largest lipoproteins and are rich in triglyceride (TG) [50]. Because of their particle size, chylomicrons scatter more light and may cause the serum to take on a cloudy appearance after meals or in patients with dyslipidaemia characterised by the inability to catabolise chylomicrons and TG rich lipoproteins. Chylomicrons are transported in the blood to tissues, such as skeletal muscle, fat, and the liver [51].

Dyslipidaemia: Classification of Lipid Disorders

Dyslipidaemia is a disorder of lipoprotein metabolism, which can include overproduction or deficiency of lipoproteins or both. The disorder can manifest as an elevation of plasma cholesterol, TGs, or both, or a low high density lipoprotein level or all three together that contributes to the development of atherosclerosis [16, 28].

Classification of Dyslipidaemia Conventionally, dyslipidaemia is classified based on patterns of elevation in lipids and lipoproteins (Fredrickson phenotype classification) [7].

This classification does not consider specific dyslipidaemia where there is low HDL that may contribute to the disease despite normal cholesterol and TG levels. A more practical system classifies dyslipidaemia due to the aetiological factors (Aetiological classification); categorised as primary (genetic) and secondary (lifestyle and other) [52].

Aetiological classification of dyslipidaemia [16, 28]

Primary hyperlipidaemia

Hypercholesterolaemia

Monogenic

- Familial hypercholesterolaemia due to decreased clearance of LDL

- Familial combined hyperlipidaemia-excess of TG and apoprotein B 100 production
- Familial monogenic hypercholesterolaemia due to over production of apoprotein B 100

Polygenic hypercholesterolaemia

- Hypertriglyceridaemia

Over production of VLDL-TG

- Familial endogenous hypertriglyceridaemia without excess of apoprotein B 100 production Familial combined hyperlipidaemia (as above)

Peripheral clearance defect of TG-rich Lipoproteins

- Familial lipoprotein: deficiency (Fredrickson Type-1)
- Familial apoprotein C-II deficiency

Primary clearance defects

- Familial endogenous hypertriglyceridaemia Familial Type V hyperlipoproteinaemia
- Familial combined hyperlipidaemia-clearance defect with excess apoprotein
- B 48 production
- Primary clearance defect combined with secondary excess production of TG.

Secondary hyperlipidaemia

A. Hypercholesterolemia

- Hypothyroidism
- Diabetes mellitus
- Cushing's syndrome
- Oral contraceptives (OCP)
- Diets rich in saturated fat
- Nephrotic syndrome
- Chronic liver disease
- Anorexia nervosa
- Acute intermittent porphyria
- Cholestasis Dysglobulinaemia

B. Hypertriglyceridaemia

- Diabetes mellitus
- Obesity
- Hypothyroidism
- Diets rich in carbohydrates
- Excessive alcohol consumption
- Chronic renal failure
- Cushing's syndrome
- Beta-blockers and diuretics
- Glucocorticoid and oestrogen use Dysglobulinaemia

C. Glycogen storage disease

- Systemic lupus erythematosus
- Bulimia
- Pregnancy
- Hypopituitarism

Clinical features

Dyslipidemia leads to various clinical features such as; Dyspnea, Giddiness, unconsciousness, obesity, atherosclerosis, high blood pressure, xanthomas.

- **Eruptive xanthomas** Red-yellow papules, especially on the buttocks (Triglyceride level above 1000 mg/dL).

- **Tendinous xanthomas** On certain tendons achilles, patella, back of the hand (High LDL concentrations) Such xanthomas usually indicate one of the underlying genetic hyperlipidemia.
- **Lipemiaretinalis** Cream-colored blood vessels in the fundus are seen (Extremely high triglyceride levels above 2000 mg/dL).
- **Xanthelasma** yellowish deposition of cholesterol underneath of skin around eyelids^[53].

Diagnosis: Clinically subjects can be diagnosed to have dyslipidaemia on the basis of the following factors (Clinical classification); Increase in cholesterol only (pure or isolated hypercholesterolaemia), Increase in TGs only (pure or isolated hypertriglyceridaemia), Increase in both cholesterol and TGs (mixed or combined hyperlipidaemias), Decrease in HDL-C (isolated low HDL-C) 5. Atherogenic dyslipidaemia (increase small dense LDL-C; increase TG, Low HDL-C and increased Lp(a)^[16, 28].

Approach to the Patient with Dyslipidaemia

After the history taking of patient the initial step is to decide which particular lipid/lipoprotein abnormalities need to be evaluated and whether they need treatment on the basis of surrogate marker abnormalities. These disorders can be divided into elevations of plasma LDL, elevations of plasma triglycerides, and decreases in plasma HDL. Frequently a patient can have multiple lipid/lipoprotein abnormalities^[11]. Some approach is based on their clinical finding which provides special clues for the patient o dyslipidaemia and associate with cardiovascular disease i.e. chest pain, breathing problem, tiredness, leg pains, muscular cramps, headache, giddiness, vertigo, confusion and unconsciousness^[16, 28, 54, 55].

Conclusion

As obesity and hypertriglyceridaemia are considered important risk factors for dyslipidaemia. Thus, it may be inferred that the Unani Medicine is effective in management of dyslipidaemia. In conventional medicine, dyslipidaemia is treated with hypolipidaemic drugs which invite unwanted results, and thus further complicate the pathogenesis. On the other hand, with the help of package treatment i.e., Dietotherapy, Regiemes and Pharmacotherapy is well described in Unani literature.

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