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Relationship between Low Density Lipoprotein and High Density Lipoprotein in Diabetes Mellitus

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ABSTRACT
Diabetes mellitus is a group of metabolic diseases characterized by abnormally high level of glucose in the blood. A lipoprotein is a biochemical assembly whose purpose is to transport hydrophobic lipid molecules in water as in blood or extracellular fluid. Fasting venous blood samples were collected from 60 diabetic patients (30 males and 30 females, aged 30 – 50 years) and 60 non-diabetic persons (30 males and 30 females, aged 30-50 years) into fluoride and plain tubes. The fluoride samples were estimated for fasting blood glucose (FBG) with glucose oxidase method while the serum samples were assayed for total cholestorol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL) and triglyceride (TG) spectrophotometrically. Total serum cholesterol increased from a control value of 4.8±0.9 mmol/L to 8.6± 3.7 mmol/L, LDL increased from 1.38±1.02mmol/L to 4.7±2.9 mmol/L, HDL increased from 0.7±0.3mmol/L to 2.1±1.4mmol/L and triglyceride from 0.79±0.31mmol/L to 1.8± 0.99mml/L. The ratio of LDL-to HDL concentration was 2.2:1; HDL: TC ratio 1:2.5; LDL: TC ratio1:1. All these are statistically significant (P<0.05) and unacceptable in the management and control of diabetes.
Key words: *Cholesterol, HDL, LDL, ratio, relationship.*

INTRODUCTION
Diabetes is a chronic disease associated with abnormally high levels of glucose in the blood caused either by impaired insulin secretion or impaired insulin action or both. It is a progressive non-communicable disease and the presence of glucose in urine gives rise to the symptoms of diabetes noticed in the suffers (Kerner and Bruckel, 2014). The two main types of diabetes are insulin dependent (Type 1) and non –insulin dependent (Type11) diabetes. In type I, there is no insulin or not enough of it while in type II, there is generally enough insulin but the cells upon which it should act are not normally sensitive to its action. Diabetes mellitus (Type I) is known for its high concentration of sugar in blood which is difficult to sustain since glucose is lost in urine and because of the loss in urine there is increase in the production of glucose in the liver from amino acids in order to maintain the level of glucose in the body (American Diabetes Association, 2010). If the glucose level is not achieved from amino acid or protein other sources are explored like the muscle which leads to loss of weight, wasting and muscular weakness. There is also increased mobilization of fat since more fat is used to supply the energy of the body (Shoback and Gardner, 2011). This may lead to lipid abnormalities. Blood lipids are lipids in the blood, either free or bound to other molecules. They are mostly transported in a protein capsule and the density of the lipids and type of protein determines the fate of the particle and its influences on metabolism. The concentration of lipids depends on intake and excretion from the intestine and uptake and secretion from cells. The majority of lipids found in the human body from ingesting food are cholesterol and triglyceride (Schmidt et al., 2016). Cholesterol is an unsaturated alcohol of the steroid family. It is essential for the normal function of all animal cells and is a functional element of their cell

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members. A variety of factors can affect blood cholesterol level and they include diet, weight, age, gender, exercise, heredity, medical condition and medications (Hongbao and Kuan, 2006). Cholesterol is transported in the blood by combinations of lipids and proteins called lipoproteins (Harris, 2010). The two major forms of cholesterol are high density lipoprotein (HDL) which removes fats and cholesterol from the serum and transfer them back to the liver for reuse or excretion. The other form is low density lipoprotein (LDL) which is the left over cholesterol after it has provided substances to the cells to create hormones and to strengthen cell membranes. Triglyceride or triacylglycerol is a type of primary fat which provides energy to the appropriate tissues in the body. It is formed in the liver and found in the blood. Other groups of lipoproteins are the chylomicrons and very low density lipoprotein (Robert et al., 2003). Low density lipoproteins have a low density or low amount of proteins and more fat. LDL caries the majority of the cholesterol that is in circulation and consists of a spectrum of particles varying in size and density. A single LDL particle is about 220-275 angstroms in diameter, transports 3,000 to 6,000 fat molecules/ particle and varies in size according to the number and mix of fat molecules contained within. They easily enter the arterial wall and bind more avidly to intra –arterial proteoglycans, which traps them in the arterial wall and are therefore referred to as 'bad cholesterol' (Gofman et al., 2014). High density lipoprotein has high protein-to-lipid ratio which accounts for the high density and is enriched in cholesterol and phospholipids. HDL plays a primary role in the removal of excess cholesterol from cells and returning it to the liver where it is metabolized to bile acids and salts that are eventually eliminated through the intestine (Ginsberg, 2012).

Rational of Study

Low density lipoprotein and high density lipoprotein are the major factors involved in maintaining the cholesterol balance of the body (Pengfei et al., 2015). High density lipoprotein is labeled 'good cholesterol' because of its role in removing fats and cholesterol from the system while low density lipoprotein is referred to as 'bad cholesterol' since it is the leftover cholesterol in the arterial wall. LDL particles, by virtue of their small size infiltrate tissues by passive diffusion and cause damage as in atheroma formation within arterial walls. In diabetes mellitus, there is increased appetite due to heavy loss of material from the body. Consequently, there is increased mobilization of fat to supply energy which leads to increased blood fat (shoback and Gardner, 2011). Lipid abnormalities are dangerous because they are associated with an increased risk for blood vessel disease, atherosclerosis, coronary heart disease, heart attacks and strokes (Baynes and Mark, 2014). Low density lipoprotein are derived from very low density lipoprotein (VLDL) and intermediate-density lipoprotein (IDL) and further enhanced in cholesterol. It carries the majority of the cholesterol that is in the circulation. The lipids carried include all fat molecules with cholesterol, phospholipid, and triglycerides dominant. (Uttra et al., 2011, Voet et al., 2013). High density lipoprotein particles have anti- oxidant, anti-inflammatory and anti-apoptotic properties which contribute to their ability to inhibit atherosclerosis (Gofman et al., 2010). Thus it was the aim of this study to determine the relationship between low density lipoprotein and high density lipoprotein in diabetes mellitus.

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MATERIALS AND METHODS

Fasting venous blood sample were collected into plain and fluoride bottles from 60 diabetic patients (30 males and 30 females, aged 30 -50 years) and 60 healthy individuals (30 males and 30 females, aged 30-50 years) as controls. Plain bottle blood samples were allowed to stand at room temperature for 1 hour, centrifuged at 3,000 revolutions per minutes for 5 minutes (Heraeuslo Centrifuge) and serum samples transferred to plain specimen containers. The fluoride samples were analyzed for fasting blood glucose (FBG) using glucose oxides method while the serum samples were assayed for total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL) and triglyceride (TG) with Randox Kits (Randox Laboratories Ltd, Diamond Road, crumlin, Country Autrim, BT294QY united Kingdom) and measured spectrophotometerically.

RESULTS

Table 1: Mean Values for Controls and Diabetic Patients

	FBG (mmol/L)	TC (mmoL/l)	LDL (mmol/L)	HDL (mmol/L)	TG (mmol/L)
Controls	4.8±0.9 (2.1-5.4)	3.75±1.65 (0.36-2.4)	1.38±1.02 (0.4-1.0)	0.7±0.3 (0.47-1.09)	0.79±0.31 (3.9-5.7)
Subjects	8.6±3.7 (4.9-123)	5.25±3.05 (2.2-83)	4.7±2.9 (1.8-7.6)	2.1±1.4 (0.7-3.5)	1.8±0.99 (0.81-2.8)

P<0.05

Table 2: Mean Values for Male Diabetic Patients

No.	FBG (mmol/L)	TC (mmoL/l)	LDL (mmol/L)	HDL (mmol/L)	TG (mmol/L)
Controls	4.8±0.9 (3.9-5.7)	3.75±1.65 (2.1-5.4)	1.4±1.0 (0.4-2.4)	0.7±0.3 (0.4-1.0)	0.79±0.31 (0.47-1.09)
Subjects	8.2±3.2 (5.0-11.4)	5.0±32.8 (2.2-7.8)	4.75±2.85 (1.9-7.6)	2.1±1.4 (0.7-3.5)	1.8±0.99 (0.81-2.8)

P<0.05

Table 3: Mean Values for Female Diabetic Patients

	FBG mmol/L	TC (mmoL/l)	LDL (mmol/L)	HDL (mmol/L)	TG (mmol/L)
Controls	4.8±0.9 (3.9-5.7)	3.75±1.65 (2.1-5.4)	1.4±1.0 (0.4-2.4)	0.7±0.3 (0.4-1.0)	0.79±0.31 (0.47-1.09)
Subjects	8.6±3.7 (4.9-12.3)	5.25±3.05 (2.2-8.3)	4.6±2.7 (1.9-7.3)	2.03±1.28 (0.75-3.3)	1.77±0.92 (0.85-2.7)

P<0.05

DISCUSSION

Diabetes mellitus is a carbohydrate metabolic disorder characterized by impaired ability of the body to produce or respond to insulin. Lipid metabolism is the synthesis and degradation of lipids in cells, involving the breakdown or storage of fats for energy. These fats are obtained from consuming food and absorbing them or they are synthesized by an

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animal's liver. The majority of lipids found in the human body from ingesting food are triglyceride (triacylglycerol) and cholesterol (Howard, 2014). Other types of lipids found in the body are fatty acids and membrane lipids. A lipoprotein is a biochemical assembly whose purpose is to transport lipid molecules in water as in blood or extracellular fluid. They have a single-layer phospholipid and cholesterol outer shell with the hydrophilic portions oriented outward toward the surrounding water and lipophilic portions of each molecule oriented inwards toward the lipid molecules within the particles. This study investigated the relationship between LDL and HDL in diabetic persons. We observed a general increase in lipid profile concentrations which were statistically significant ($P<0.05$). However, the lipid profile parameters had distorted ratios in diabetes mellitus when compared with values of healthy individuals. Total cholesterol concentration increased by 28.6% and higher in females (28%) than in males (25%). Excess cholesterol is eliminated from the body via the liver which secretes cholesterol in bile or converts it to bile salts. The liver removes LDL and other lipoproteins from the circulation by receptor –mediated endocytosis (Gofman et al., 2013). Cholesterol is important to overall health but when concentrations are very high, it can be harmful by contributing to narrowed or blocked arteries and eventually may cause blockage of blood flow.

LDL increased more than HDL. The function of LDL is to deliver cholesterol to cells, where it is used in membranes or for the synthesis of steroid hormones. LDL binds to a specific LDL receptor and is internalized in an endocytic vesicle (Hongboo and Kuan, 2010). Small dense LDL particles are more pro-atherogenic than large LDL particles (Pelley, 2012). Small dense LDL particles have a decreased affinity for the LDL receptor which results in prolonged retention time in the circulation. We observed a 70.6% increase in the concentration of LDL in diabetics and a 1:1.1 ratio of LDL –to –TC as against 1:2.7 in normal individuals. In nondiabetics, LDL –to-TG ratio was 1.7:1 and 2.6:1 in diabetics. This is a dangerous trend since LDL transports cholesterol from the liver to extra hepatic tissues including arteries. Elevated level of serum LDL- cholesterol is a major risk factor of atherosclerosis and coronary heart disease (Basciano et al., 2013). A consistent rise in serum LDL-cholesterol concentration causes deposition of cholesterol ester in connective tissues of arterial wall which results in hardening and narrowing of arteries. The percentage increase in the concentration of LDL was the same in both males and females. High density lipoprotein (HDL) contains the highest protein-to-lipid ratio and the resulting high density gives it the name high density lipoprotein. It is enriched in cholesterol and phospholipids. In diabetes mellitus, there was an increased ratio of LDL-to-HDL concentration (2.2:1). This is a 13.6% upward deviation from normal. It is due to the ability of diabetes to counter the normal concentrations of blood lipids and if not managed or reversed may result in conditions such as atherosclerosis, stroke, coronary heart disease, e.t.c. The increase in the concentration of HDL was more in males than in females. HDL-to-TC ratio was 1:2.5 in diabetics as against 1:5 in healthy subjects. There should be a negative correlation between the incidence of coronary heart disease and plasma or serum HDL-cholesterol concentration. HDL is involved in the reverse transport of cholesterol, scavenges blood vessels from atherosclerosis and reduces the risk of coronary heart disease. There was a 50% increase in triglyceride in diabetics.

Triglycerides are a type of primary fat which provides energy to the appropriate tissues in the body. Excess TG is stored in fat cells to use as energy when needed. When the body requires a source of energy, the liver breaks down glucose and signals the fat cells to release fatty acids it stored as triglyceride (triacylglycerol) which is metabolized into energy. High level of TG in the blood worsens other lipid particles and contributes to plaque formation (Robert et al., 2012).Management of diabetes mellitus will be greatly enhanced if periodic LDL and HDL assessment is undertaken.

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