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RESEARCH ARTICLE

Lipoprotein State in Families Who Have History of Type 2 Diabetes

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ABSTRACT

This study aims to determine the correlation between genetic predisposition to dyslipidemia and the risk of type-II diabetes. The lipoprotein state was tested in students of the University whose families have a history of type-II diabetes in comparison to normal subjects. The study was conducted in the laboratory of the Faculty of Science and Health at Koya University. The study included 60 male students (average weight 66.3±3.1 Kg and average age21±1.6 years) and 60 female students (average weight54±2.8 Kg and average age 21±1.2 years). They were divided into control groups of normal males and females and groups of males and females with a family history of type-II diabetes. Fasting blood serum was drawn from each group. The results showed a significant increase of LDL and triglyceride in females and males with a family history of type-II diabetes compared with the control group.HDL showed a significant decrease in normal subjects with a family history of type-II diabetes compared to the control group. HDL may influence β-cell function through its abilities to produce cholesterol efflux, antioxidation, anti-inflammation, and antiapoptosis. Ectopic accumulation of triglycerides in tissues other than adipose may impair insulin signaling as well as insulin secretion. These results give evidence supporting the probability of a causal relationship between low HDL cholesterol/high triglyceride levels and an increase of LDL levels and the risk of type-II diabetes.

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INTRODUCTION

Diabetes mellitus is a complex, progressive disease, which is accompanied by multiple complications. It has been recognized as the sole independent risk factor for the development of cardiovascular disease (Jay *et al*., 2006). Cardiovascular complications include stroke, myocardial infarction and atherosclerosis which are considered to be important causes of health-related deaths in diabetic patients.

A lipoprotein is a biochemical assembly that contains both proteins and lipids water-bound to the proteins. Many enzymes, transporters, structural proteins, antigens, adhesins, and toxins are lipoproteins. Examples include the high-density (HDL) and low-density (LDL) lipoproteins, which enable fats to be carried in the blood stream, the transmembrane proteins of the mitochondrion and the chloroplast, and bacterial lipoproteins (Madan *et al*., 2003).

Lipid abnormalities in type-2 diabetes are characterized by high triglyceride concentrations, low high density lipoprotein cholesterol concentrations and normal total and low density lipoprotein-cholesterol concentrations (Valabhji and ElkelesL, 2003). Premature atherosclerosis and other vascular disorders are serious complications of diabetes mellitus due to increased peroxidation of LDL leading to foam cell formation, fatty streaks and plaque formation in the arterial wall, and hyper-reactivity of blood platelets leading to increased platelet adhesion and aggregation. Altered platelet morphology and function have been reported in patients with metabolic syndrome, stroke and diabetes mellitus (Ferreiro *et al*., 2010).

Researchers are still figuring out exactly how diabetes changes cholesterol levels at the microscopic cellular level. They do know that high levels of insulin in the blood tend to adversely affect the number of cholesterol particles in the blood. High insulin levels act to raise the amount of LDL cholesterol (the "bad cholesterol") that tends to form plaques in arteries, and lower the number of HDL cholesterol particles ("good cholesterol") that help to clear out dangerous plaques before they break off to cause a heart attack or stroke. Diabetes also tends to cause higher levels of triglycerides, another type of fat circulating in the blood (McCulloch and David, 2007), (McCulloch and David, 2008).

Similarly, high cholesterol can also be a predictor of diabetes; elevated cholesterol levels are often seen in people with insulin resistance, even before they have developed full-blown diabetes. When LDL levels start to climb, experts recommend paying close attention to blood sugar control and starting a diet and exercise regimen to help stave off diabetes and cardiovascular disease. This is especially important if you have a family history of heart disease.

For people with Type 1 diabetes, controlling blood sugar can make a big difference. Good blood sugar control is related to near-normal cholesterol levels, similar to those seen in people without diabetes. But people with poorly controlled Type 1 diabetes have increased triglyceride levels and lower HDL levels, which contribute to the development of clogged arteries (Nesto, 2008).

People with Type 2 diabetes, regardless of blood sugar control, tend to have increased triglycerides, decreased HDL, and sometimes increased LDL. This cholesterol profile tends to persist even if blood sugar levels are under control--pointing to an even higher likelihood of developing plaques. In fact, plaques formed in the arteries of people with Type 2 diabetes tend to be more fatty and less fibrous than in people with Type 1 diabetes, leading to an even higher risk of a plaque dislodging to cause a heart attack or stroke.

The American Diabetes Association recommends checking cholesterol levels at least once a year--more often if they are high and not controlled by medication. For people with diabetes and no known coronary heart disease, it is recommended that LDL levels in the blood be below 100 milligrams per deciliter (mg/dL), that HDL levels are above 50 mg/dL, and triglycerides below 150 mg/dL. The recommended blood sugar, or glucose, level is less than 7% (<7%) in the HA1C test.

For people with diabetes and known coronary heart disease, including blocked arteries or a prior heart attack, the ADA recommends LDL below 70 mg/dL. Reaching this very low LDL goal may require high doses of statin medications, but is shown to significantly reduce the risk of a heart attack. Triglyceride levels should be below 150 mg/dL and HDL above 40 mg/dL. Women with diabetes and existing coronary heart disease are recommended to have HDL levels above 50 mg/dL.

One medication, WelChol (colesevelam), has been shown to lower both glucose and cholesterol levels in people with Type 2 diabetes. Welchol acts by preventing the intestines from absorbing fat molecules from food. Although Welchol does lower LDL levels, it can actually raise triglyceride levels in the blood, and should not be used by people with high triglycerides (Pyorala *et al*., 2004; Rosenson, 2008; Third Report of the National Cholesterol Education Program, 2002).

The present study aimed to evaluate the association of the lipoprotein levels with type 2 diabetes mellitus.

MATERIALS AND METHODS

Chemical analysis

Total cholesterol concentration in serum, triglycerides concentration in serum, high-density lipoprotein cholesterol (HDL) concentration in serum, low-density lipoprotein cholesterol (LDL) concentration in serum and glucose concentration in serum were measured by enzyme colorimetric methods using a Spectrophotometer. Commercially available kits (BiolaboSA, France) were used. The samples had been collected from the students of the Faculty of Health and Science at Koya University and were tested in the laboratory of the Faculty.

The procedure

1- The study included 60 male students (average weight 66.3±3.1 Kg and average age 21±1.6) and 60 female students (average weight54±2.8 Kg and average age 21±1.2). They were divided into 4 groups as follows:

- 30 normal (control) males
- 30 normal(control) females
- 30 normal females with a family history of type 2 diabetes
- 30 normal males with a family history of type 2 diabetes

2- Fasting blood serum had been drawn from each group.

3- T–test at $P<0.001$ used for statistically significant differences

RESULTS AND DISCUSSION

Serum lipid and serum glucose values in 60 females and 60 males are presented in table 1and table 2 (see also figure 1, 2). The tables showed significant increasing ($P<0.001$) of LDL and triglyceride in females and males in normal subjects with a family history of type 2 diabetes compare to the control group. HDL showed significant decreasing in normal subjects with a family history of type 2 diabetes compare to control group in both genders. Averages of serum glucose in female and male did not change in both groups.

Table 1: Averages of female lipid profiles and glucose in blood serum of fasting normal subjectsand fasting normal subjects with a family history of type 2 diabetes.

Parameters	Normal ranges	Control (normal subjects)	normal subjects with a family history of type 2 diabetes
Total cholesterol (mg/dl)	Optimal :Less than 200 Borderline: 200 -239 High: above 240	157.61±10.2	162.10±11.5
LDL (mg/dl)	Optimal: Less than 100 Borderline : 130-159 High : 160 -189	75.11±5.7	93.58±7.10*
HDL (mg/dl)	Optimal : 60 mg /dl and aboveLow risk: less than 40 mg / dl in menless than 50 mg / dl in women	65.80±5.5	48.26 ±4.7*
VLDL (mg/dl)	Normal in male : 15.5 – 42.5 Normal in female : 7.7 – 35	16.70±2.4	20.26±3.2
Triglyceride(mg/dl)	normal :Less than 150 mildly high : 150 – 199 High : 200 – 499	83.50± 8.6	101.32±9.4*
Glucose(mg/dl)	Normal : 80 – 120	106.50±6.9	112.23±8.9

T –test at $P<0.001$, *average is significant different from the normal average; average weight in = 54±2.8 Kg and average age = 21±1.2 of both groups; number of control subjects = 30, number of normal subjects with a family history of type 2 diabetes = 30

Table 2: Averages of male lipid profiles and glucose in blood serum of fasting normal subjectsand fasting normal subjects with a family history of type 2 diabetes.

Parameters	Normal ranges	Control (normal subjects)	normal subjects with a family history of type 2 diabetes
Total cholesterol (mg/dl)	Optimal :Less than 200; Borderline: 200 -239 High: above 240	164.33±12.2	170.50±13.6
LDL (mg/dl)	Optimal: Less than 100; Borderline : 130-159; High : 160 -189	84.33±6.1	103.34±8.10 *
HDL (mg/dl)	Optimal : 60 mg /dl and aboveLow risk: less than 40 mg / dl in menless than 50 mg / dl in women	61.80±6.0	45.41±4.2 *
VLDL (mg/dl)	Normal in male : 15.5 – 42.5; Normal in female : 7.7 – 35	18.20± 3.1	21.75±3.4
Triglyceride (mg/dl)	normal : Less than 150 mildly high : 150 – 199; high : 200 – 499	91.11±7.81	108.73±8.8 *
Glucose(mg/dl)	Normal : 80 – 120	115.76±10.6	119.20±9.6

T –test at P<0.001, * average is significant different with the normal average; average weight in = 66.3±3.1 Kg and average age = 21±1.6 of both groups; number of control subjects = 30, number of normal subjects with a family history of type 2 diabetes = 30

Table 3: Averages of female lipid ratios in fasting normal subjects and fasting normal subjects with a family history of type 2 diabetes

Ratio indexes	Normal ratios	Control (normal subjects)	normal subjects with a family history of type 2 diabetes
Atherogenic Index (TC:HDL)	Normal: less than 5.0 Low risk >5.0 Moderate risk >5.0-6.0	2.4	3.4
HDL:LDL	Ideal ratio is above 0.4	0.9	0.5
TG:HDL	Normal : less than 3.0	1.3	2.1

T –test at P<0.001; average weight is 54± 2.8 Kg; average age is 21 ±1.2; number of control subjects = 30; number of normal subjects with a family history of type 2 diabetes = 30

Table 4: Averages of male lipid ratios in fasting normal subjects and fasting normal subjects with a family history of type 2 diabetes

Ratio indexes	Normal ratios	Control (normal subjects)	normal subjects with a family history of type 2 diabetes
Atherogenic Index (TC:HDL)	Normal: less than 5.0 Low risk >5.0 Moderate risk >5.0-6.0	2.7	3.8
HDL:LDL	Ideal ratio is above 0.4	0.7	0.4
TG:HDL	Normal : less than 3.0	1.5	2.4

T –test at P<0.001; average weight in = 66.3±3.1 Kg; average age = 21±1.6 of both groups; number of control subjects = 30; number of normal subjects with a family history of type 2 diabetes = 30

These findings are largely in line with previous observations from the prospective studies showing that low HDL cholesterol and high triglyceride levels, but not high LDL cholesterol levels, significantly predicted the risk of type 2 diabetes (D'Agostino *et al*., 2004; Schmidt *et al*.,2005; Wilson *et al*., 2007; Gupta *et al*., 2008; Chien *et al*., 2009; Kahn *et al*., 2009).

Thus, our results support potentially causal roles of HDL cholesterol and triglycerides in type 2 diabetes.

There are several lines of evidence supporting the probably causal relationship between low HDL cholesterol/high triglyceride levels and type 2 diabetes risks.

Recent data indicated that HDL may influence β-cell function by its abilities of cholesterol efflux, antioxidation, anti-inflammation and antiapoptosis (Kruit *et al*., 2010), and accumulation of triglycerides ectopically in other tissues than adipose may impair insulin signaling as well as insulin secretion (Szendroedi and Roden, 2009).

Findings from previous prospective studies in large populations from different ethnical groups have shown that plasma HDL cholesterol and triglyceride levels are independent predictors of future type 2 diabetes (D'Agostino *et al*., 2004; Schmidt *et al*., 2005; Wilson *et al*., 2007; Gupta *et al*., 2008; Chien *et al*., 2009; Kahn *et al*., 2009).

For instance, a previous study comprising >14,000 participants found that the risk of new-onset diabetes decreased by 28% and increased by 12% per mmol/L increase in baseline HDL cholesterol and triglyceride levels, respectively (Gupta *et al*., 2008).

The observed associations between the genetic predisposition to low HDL cholesterol or high triglycerides and elevated type 2 diabetes risk in the current study provide further evidence for the true association, because they are unlikely to be the results of confounding factors.

Moreover, importantly, data from some clinical trials have shown that bezafibrate, a drug used to treat dyslipidemia by raising HDL and lowering triglycerides, could improve insulin resistance (Tenenbaum *et al*., 2006)and lower the hazard for incident diabetes (Tenenbaum *et al*., 2004; Tenenbaum *et al*., 2005).

Taken together, these findings support that contention that dyslipidemia of low HDL cholesterol/high triglycerides plays a causal role in the development of type 2 diabetes, which suggests the potential importance of therapeutic implications of dyslipidemia, either pharmacologically or through lifestyle intervention, in preventing type 2 diabetes.

Ratios of lipid profiles in females and males are showed in table in both groups 3 and table 4 (see also figure 3, 4). Ratios of atherogenic index TC: HDL) hadn't shown change. Ratio of total cholesterol to high-density lipoprotein cholesterol (TC/HDL) is a powerful predictor of cardiovascular disease (CVD) (Richard *et al*., 2004) hadn't shown change in males and females in both groups. Ratio of HDL: LDL in males and females for both groups hadn't shown change in female diabetic patients (table 3 and figure 3) which looks at the ratio of good cholesterol (HDL) to bad cholesterol (LDL). It is used to predict the chances of developing heart disease (Boden, 2000).Ratio of TG: HDL in both genders for both groups (table 3 and figure 3) also didn't show a change.

Conclusion

Our findings support a potentially causal relationship between low HDL cholesterol or high triglyceride levels and type 2 diabetes.

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