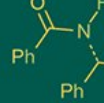


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Evaluation of HbA1c and lipid profile as early metabolic indicators in healthy individuals with and without a family history of type 2 diabetes mellitus

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Abstract

Introduction: Diabetes is characterized by chronic hyperglycaemia and disturbances of carbohydrate, lipid and protein metabolism. We aimed to research association between serum lipid profile and blood glucose, hypothesizing that early detection and treatment of lipid abnormalities can minimize the risk for atherogenic cardiovascular disorder in patients with type 2 diabetes mellitus.

Materials and Methods: This is a cross-sectional observational study conducted at the Department of Biochemistry, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, from May 2017 to April 2018. Apparently healthy first-degree relatives of T2DM patients aged 18-60 years were included as cases (n = 45). Age- and gender-matched healthy adults with no family history of diabetes were recruited as controls (n = 45). Participants with chronic illnesses, pregnancy, or regular physical activity were excluded.

Results: Results of serum lipid profile showed that the mean values for TC, TG, HDL and LDL in female patients were 227.6±57.7 mg/dl, 221.6±101.1 mg/dl, 31.5±6.7 mg/dl and 136.5±43.7 mg/dl, respectively. The mean values for TC, TG, HDL and LDL in male patients were 219.1±34.7 mg/dl, 250.0±100.7 mg/dl, 30.2±7.4 mg/dl and 125.7±21.4 mg/dl, respectively. Significantly higher mean serum levels of TC, TG and LDL and significantly lower mean serum levels of HDL were noted in patients with diabetes (p<0.001). FBG showed significant positive correlation with TC (p<0.05) and TG (p<0.05). Significant correlations were observed between serum levels of TC, TG, LDL and HbA1c (p<0.05).

Discussion: Fasting blood glucose (FBG), total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), triglyceride (TG) and glycated haemoglobin (HbA1c) levels were evaluated. Test of significance was calculated by unpaired student's t test between cases and controls. Correlation studies (Pearson's correlation) were performed between the variables of blood glucose and serum lipid profile. From our study it is evident that lipid profile is abnormal in diabetes mellitus. Realizing that most of the diabetics have a high probability of developing cardiovascular and cerebrovascular disease, it is essential that an individual who is diabetic should take care of dyslipidaemia. Our study definitely shows that there is hyperlipidaemia which may be harmful to diabetics.

Conclusion: The study revealed that lipid abnormalities were prevalent in the course of diabetes, which included hypercholesterolemia, hypertriglyceridemia, elevated LDL and decreased HDL. This study proposes the predominance of hyperlipidaemia over increased prevalence of diabetic dyslipidaemia.

Keywords: Cardiovascular disease, type 2 diabetes mellitus, Lipid profile, cross-sectional study

Introduction

Diabetes mellitus is a frequent metabolic disease in which there is a deficiency of insulin secretion and/or insulin action, which leads to chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism [1]. There have been a few studies that have tried to correlate the blood glucose with the serum lipid profile parameters. Research findings show that mainly body fat is responsible for increase in prevalence of this disease among the body composition components. It was first described as a multifactorial metabolic abnormality with insulin resistance and compensatory hyperinsulinaemia, type 2 diabetes mellitus (T2DM), essential hypertension and hypercholesterolaemia as early as 1988 [2]. Today, however, the World Health Organization (WHO) and International Diabetes Federation (IDF) use the term "Metabolic Syndrome" to describe this clustering of conditions [3]. The term diabetic dyslipidaemia comprises a triad of raised triglycerides, reduced high density lipoprotein (HDL) and excess of small, dense low-density lipoprotein (LDL) particles. The lipid abnormalities are prevalent in diabetes mellitus because insulin resistance or deficiency affects key enzymes and pathways in lipid metabolism [4].

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Microvascular and macro-vascular complications such as, cardiovascular disease (CVD), retinopathy, nephropathy, and neuropathy, occur due to chronic uncontrolled hyperglycaemia in diabetics. The lipid particle composition of diabetic dyslipidaemia has been suggested to be more atherogenic than other forms of dyslipidaemia. The relationship between atherosclerosis and dyslipidaemia is well known. The hyperglycaemia associated with diabetes, obesity and insulin changes greatly accelerate the progression to atherosclerosis [5]. In a recent study, it was noted that there were significant trends for increased risk of coronary heart disease, stroke and all-cause mortality with increasing baseline HbA1c in over 11,000 individuals in the Atherosclerosis Risk in Communities Study. In HbA1c categories <6.5% and $\geq 6.5\%$, there was a significant association between fasting blood glucose levels and coronary heart disease, stroke or death, from any cause [6]. In earlier studies it was tried to correlate blood glucose with serum lipid profile parameters and it is evident that the HbA1c levels are lower in the people having low risk of micro-vascular complications. In the present study, we aimed to research association between serum lipid profile and blood glucose, hypothesizing that early detection and treatment of lipid abnormalities can minimize the risk for atherogenic cardiovascular disorder and cerebrovascular accident in patients with type 2 diabetes mellitus.

Materials and Methods

This is a cross-sectional observational study conducted in the Department of Biochemistry, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, from May 2017 to April 2018. The study was approved by the Institutional Ethics Committee of Sree Balaji Medical College and Hospital [approval number to be confirmed by corresponding author]. All participants provided written informed consent prior to enrolment.

Inclusion Criteria

- Either gender, aged 18 to 60 years.
- First-degree relatives of Type 2 Diabetes Mellitus patients (case group).

- Age- and gender-matched apparently healthy adults with no family history of diabetes (control group, n = 45).

Exclusion Criteria

Morbid obesity, chronic alcoholism, chronic smoking, pregnancy, lactating women, kyphosis, scoliosis, use of medications preventing sub-maximal exercise, or regular engagement in physical activity, yoga, or biofeedback.

Sample Size

The sample size of N = 90 (45 per group) was calculated based on the expected effect size for group differences in body composition and oxidative stress parameters, with $\alpha = 0.05$ and power = 80%.

Procedure

One day prior to recording, participants were instructed to obtain adequate sleep and abstain from caffeinated beverages, exercise, alcohol, and nicotine for 24 hours.

Study subjects were asked to complete a generalized questionnaire that contains demographic information including past and present medical history, and to return after fasting for more than 8 hours for anthropometry and blood withdrawal. At the screening visit, blood samples were examined for levels of glucose and lipid profile. After overnight fasting, participants reported to the Department of Cardiology in the morning. Anthropometric and basal characteristics (height, weight, body mass index [BMI], waist-hip ratio [WHR], body fat percentage, and visceral fat) were recorded after participants had emptied their bladders.

A fasting venous blood sample (5 mL) was collected from the median cubital vein using sodium fluoride tubes for biochemical analysis. Fasting blood glucose (FBS), HbA1c and lipid profile was measured using a semi-automated analyser. Observations were analysed using an independent samples t-test with IBM SPSS Statistics, version 25.

Results

Table 1: Baseline and anthropometric parameters of controls and cases

Parameter	Controls (Without FH of T2DM) Mean $\pm$ SD	Cases (With FH of T2DM) Mean $\pm$ SD	p value
Age (years)	37.76 $\pm$ 1.64	37.63 $\pm$ 1.55	0.400
Height (cm)	163.11 $\pm$ 7.19	161.25 $\pm$ 9.26	0.072
Weight (kg)	58.68 $\pm$ 8.19	71.28 $\pm$ 9.69	<0.001*
BMI (kg/m ²)	19.28 $\pm$ 1.95	21.66 $\pm$ 3.06	<0.001*
WHR	0.66 $\pm$ 0.05	0.76 $\pm$ 0.01	0.004*

FH = Family History; T2DM = Type 2 Diabetes Mellitus; BMI = Body Mass Index; WHR = Waist-Hip Ratio. *statistically significant ($p < 0.05$).

Table 1 shows the baseline and anthropometric parameters of controls and cases. There was no significant difference in age ($p = 0.400$) or height ($p = 0.072$) between groups,

confirming adequate matching. Between controls and cases, significant differences were observed in weight ($p < 0.001$), BMI ($p < 0.001$), and WHR ($p = 0.004$).

Table 2: The concentration of fasting blood glucose and HbA1c percentage in diabetic patients

Parameter	Controls (Without FH of T2DM) Mean $\pm$ SD	Cases (With FH of T2DM) Mean $\pm$ SD	p value
Glucose	186.7 $\pm$ 61.2	198.61 $\pm$ 51.3	<0.001*
HbA1c	7.46 $\pm$ 1.86	8.84 $\pm$ 1.53	<0.001*

Units expressed as mg/dl for plasma blood glucose. Units expressed as percentage (%) for HbA1c.* statistically significant ($p < 0.05$).

Table 2 presents blood glucose and HbA1c level statistically significant ($p < 0.001$) as compared to normal range for

plasma blood glucose. Statistically significant ($p<0.001$) as

compared to normal range for HbA1c

Table 3: Estimation of TC, TG, HDL and LDL in serum of diabetic patients

Parameter	Controls (Without FH of T2DM) Mean±SD	Cases (With FH of T2DM) Mean±SD	p value
TC	227.6±57.7	219.1±34.7	<0.001*
TG	221.6±101.1	250.0±100.7	<0.001*
HDL	31.5±6.7	30.2±7.4	<0.001*
LDL	136.5±43.7	125.7±21.4	<0.001*

Units expressed as mg/dl * statistically significant ($p<0.05$).

Table 3 presents Lipid profile data. All parameters differed significantly between groups: Lipid TC ($p<0.001$), TG ($p<0.001$), HDL ($p<0.001$) and LDL ($p<0.001$). Significant ($p<0.001$) as compared to normal range for related serum lipids.

Discussion

Many studies have clearly shown that the complications in patients with diabetes are primarily caused by chronic hyperglycemia, which has several mechanisms of injurious to health effects: dyslipidemia, platelet activation, altered endothelial metabolism [7, 8]. Both lipid profile and diabetes have been found to be the significant factors for metabolic disturbances such as dyslipidaemia, hypertension and cardiovascular diseases [9]. Lipids are important in the pathogenesis of diabetes mellitus. Patients with diabetes mellitus have been reported to have abnormalities in lipid metabolism and cardiovascular arteriosclerosis [10]. In the present study, significantly higher mean serum levels of total cholesterol, triglycerides and LDL cholesterol were noted in patients with diabetes, which are well known risk factors for cardiovascular diseases among patients, when compared to the normal values. In diabetes many factors may affect blood lipid levels, because of interrelationship between carbohydrates and lipid metabolism. Thus, any disturbance of carbohydrate metabolism results in disturbance of lipid metabolism and vice versa. Insulin resistance is one of the main defects in the majority of patients with T2DM. In non-diabetic individuals' insulin resistance in combination with hyperinsulinemia has a strong predictive value for future development for type 2 diabetes [11]. Several studies showed that insulin affects the liver apolipoprotein production and regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transport protein, which causes dyslipidemia in diabetes mellitus. Furthermore, insulin deficiency decreases the activity of hepatic lipase and some of the steps involved in the biosynthesis of biologically active lipoprotein. lipase [12, 13]. Decreased HDL cholesterol is also a common characteristic of plasma lipid abnormalities in people with diabetes [14, 15] and is often associated with hypertriglyceridaemia. The combination of lipid abnormalities seen in T2DM is characterized by elevated TG and low HDL cholesterol, and small dense LDL. The association between reduced HDL cholesterol levels and increased risk of heart disease is, on the other hand, well established, independently of TG levels and other risk factors [16, 17]. The mechanism that may be responsible for hypertriglyceridaemia could be due to an increase in the secretion of very low density lipoprotein (VLDL) and a decrease in the clearance of triglyceride rich lipoproteins, mainly attributed to an increase in substrates for triglyceride. Production, free fatty acids and glucose [18]. Serum total cholesterol, triglycerides, LDL cholesterol and hepatosteatosis were significantly correlated with blood

concentrations of HbA1c in the present study Results of the correlation there is a definite link between hyperglycemia and the onset of dyslipidemia, according to studies. Our results were consistent with a previous study indicating that glycaemic control is generally good or near good when the level of total cholesterol is normal or near normal, and that the deterioration of glycaemic control is usually accompanied by an increase in total cholesterol. The level is increased by control [19]. Therefore, improving glycaemic control might substantially reduce the risk of cardiovascular events in diabetic patients.

The most common metabolic abnormality in individuals with T2DM and low HDL, high LDL, hypercholesterolemia and hypertriglyceridaemia is an abnormal glucose reading. Hypertriglyceridaemia and poor glycaemic control are important biochemical abnormalities in T2DM patients. Dyslipidemia management in people with diabetes mellitus, just like in any other individual, starts with a flawless evaluation that the goal of aim is to find secondary causes which may be responsible for the abnormal lipid profile [20]. Recently, the triglyceride-to-HDL cholesterol (TG/HDL) ratio has been studied for several potential clinical applications in adults and children. It has been shown to be positively correlated with adverse cardio-metabolic risk factor profiles, metabolic syndrome and the risk of developing diabetes or its complications in previous studies [21, 22]. This can happen because the TG/HDL ratio shows a correlation with insulin resistance [23]. A number of studies have shown that the TG/ HDL ratio has a good correlation with the generally There are accepted methods to define insulin resistance and it is regarded as a surrogate marker of insulin resistance. The significant positive correlation of TG/HDL ratio with HbA1c found in this study is in line with the studies in the literature ($p<0.01$) [24]. Although obesity and T2DM commonly co-exist [25], mean BMI in our study was in the overweight range. Subjects enrolled in the study were the patients who have diagnose of their diabetes for averagely 3 years. They were under control of a dietitian since the date of diagnose. This could be the reason why patients in our group are experiencing this. The majority of the study were overweight, but not obese. The milestones of management are lifestyle changes, such as increased physical activity and dietary changes. More efforts are needed from family members, community and healthcare professionals to: Preventive based approach in the management of diabetes. This can be done by focusing more on lifestyle modification measures like exercise, increased dietary restrictions and weight control strategies especially for those with impaired fasting glucose. Monitoring of lipid profile by blood tests done in regular intervals in primary healthcare also might play an important role to detect and take care of lipid abnormalities both in diabetics and non-diabetics. The advantage of this study is that it is the first study in Istanbul, Turkey which investigated the association

between serum lipid profile and blood glucose in T2DM patients in primary healthcare. As far as we know, there is no there had been no previous study that had both blood tests and hepatic ultrasound performed on this group of subjects. Despite several important findings in the present study, relatively small sample size is considered as a limitation of it. Diabetic people who have the goal of poor glycaemic control should be to get blood glucose levels as close to normal as possible, and it is hoped that this will lead to an improvement in dyslipidaemia^[26, 27]. From our study it is evident that lipid profile is abnormal in diabetes mellitus. Realizing that most of the diabetics have a high probability of developing cardiovascular and cerebrovascular disease, it is essential that an individual who is diabetic should take care of dyslipidaemia. Our study definitely indicates the presence of hyperlipidaemia which might be hazardous for diabetics.

Conclusion

This cross-sectional observational study demonstrates that apparently healthy adults with a positive family history of T2DM exhibit significantly higher lipid in diabetes, which lead to dyslipidemia are hypercholesterolemia hypertriglyceridemia and high LDL cholesterol and elevated blood glucose, compared to individuals without such family history. This showed the increased prevalence of dyslipidemia, which seems to have an important role in the genesis of cardiovascular and cerebrovascular accidents among diabetics. Diabetes patients should be followed by serial check of blood glucose and serum lipid profile as a routine in optimum care. Any attempt to achieve lifestyle modification such as weight loss, physical exercise, smoking cessation should be prompted, and then should be followed by drug therapy with lipid lowering drugs on an evidence based necessary basis. The optimum drug therapy with appropriate antidiabetic drugs to get fair glycaemic control should go hand to hand with lipid lowering drugs and with taken dietary measures. With all the above it can properly be stated that benefits provided by primary health care can be emphasized by regular close monitoring of the patients.

Declarations

Ethics Approval: The study was approved by the Institutional Ethics Committee of Sree Balaji Medical College and Hospital, Chennai [approval reference number to be confirmed by corresponding author]. All participants provided written informed consent.

Conflict of Interest: The author declares no conflict of interest.

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Data Availability: The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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