

SERUM TRIGLYCERIDES AND TOTAL CHOLESTEROL LEVELS AND ITS RELATION WITH TYPE 2 DIABETES MELLITUS

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Abstract

Diabetes mellitus is one of the most widespread endocrine disorder in female and its complications are increasing all over the world, leading to life threatening medical problems like cardiovascular diseases, stroke and end stage renal diseases. A relation between hyperlipidemia and diabetes mellitus has been identified. The study was carried out to observe the serum triglycerides and total cholesterol levels its relation with type 2 diabetes mellitus in adult female subjects. This cross sectional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka, during the period of January 2011 to December 2011. A total number of sixty female subjects were selected with age ranging from 30 to 50 years. Among them 30 female subjects with diabetes were included from out-patient department of Endocrinology, Dhaka Medical College Hospital, Dhaka as study group (B) and 30 apparently healthy female were taken as control group (A) for comparison. Estimation of fasting serum triglycerides (TG) and total cholesterol (TC) levels were done by enzymatic method in the Department of Physiology, Dhaka Medical College Dhaka in both groups. Fasting serum insulin level was measured by ELISA method in the Department of Laboratory of National Institute of ENT, Dhaka and fasting blood glucose was estimated by glucose oxidase method in Department of Dhaka Medical College in both groups. Data were analyzed by Unpaired Student's- test and Pearson's correlation co-efficient (r) test as applicable. The value of fasting serum TG and TC level were significantly higher in study subjects than those of control. In study subjects fasting serum TG and fasting serum TC levels showed positive correlation with fasting blood glucose and serum insulin level.

Conclusion: Present study revealed that fasting serum triglyceride (TG) and fasting serum cholesterol (TC) levels have positive relationship with fasting serum insulin and fasting blood glucose levels.

Key words: Fasting serum insulin, fasting blood glucose, fasting serum triglyceride and fasting serum cholesterol levels, diabetes mellitus.

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Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion and / or insulin action.¹ Diabetes

mellitus (DM) is one of the common non-communicable diseases and it is one of the most challenging health problems in the 21st century.² There are two general types of diabetes mellitus, one is type 1 or insulin dependent DM (IDDM) and other is type 2 or non-insulin

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dependent DM. Among them, type 2 diabetes mellitus is more common and about 90 to 95% of all cases of diabetes mellitus.³ Type 2 diabetes mellitus and its prevalence has increased continuously over past decades. Rapid economic growth, increased life expectancy and altered life style have significantly increased the prevalence of type 2 diabetes mellitus. The chronic hyperglycemia of diabetes is associated with long term dysfunction, damage and failure of various organs especially the eyes, kidney, nerves, heart and blood vessels⁴. According to American Diabetes Association, diagnostic criteria of diabetes mellitus are fasting blood glucose ≥ 7.0 mmol/l or 2 hours after 75 gm glucose ≥ 11.1 mmol/l or random blood glucose ≥ 11.1 mmol/l or HbA1c $\geq 6.5\%$.⁵ According to International Diabetic Federation (IDF), about 24.4 million diabetic people in the USA, 65.1 million in India and 5.1 million in Bangladesh. This number is gradually increasing day by day will rise to 592 million by the year 2035 representing about 8.8% of the world population. By the year 2035, the number of diabetic people will be about 29.7 million in USA, 109.2 million in India and 16.8 million in Bangladesh.⁶ In each year about 5% of all death are caused by diabetes mellitus globally⁷. Hyperlipidemia is the most important risk factor for premature cerebrovascular disease, stroke and peripheral vascular disease⁸. Hyperlipidemia stands for abnormal elevation of various lipids and lipoprotein in the blood thus leading to atherosclerosis of arteries, especially in the aorta, coronaries, carotids and cerebral arteries. Hypercholesterolemia and hypertriglyceridemia both of which constitute major risk factor for cardiovascular diseases⁹.

Hyperlipidemia account for an estimated 54% of all strokes and 50% of all ischemic heart diseases¹⁰. A study in the USA found approximately one in every six adult has hyperlipidemia or high cholesterol in their blood. People with high cholesterol have twice the risk for heart disease than people with lower level of cholesterol but they are unaware of this condition because there are no symptoms¹¹.

Hyperlipidemia is very common in type 2 diabetes mellitus. Prevalence of hyperlipidemia

in type 2 DM is 64-75%. The risk of cardiovascular disease and cardiovascular mortality is significantly increased in patient with type 2 diabetes mellitus relative to healthy individual. Lipid abnormalities observed in type 2 DM are not only quantitative, but also qualitative and kinetic in nature. A number of factors may contribute to the change in lipid metabolism in type 2 DM, including insulin resistance and/ or relative insulin deficiency, adipocytokines (Adiponectin) and hyperglycemia¹².

Insulin resistance represents the earliest detectable abnormality in of type 2 diabetes mellitus and is one of the major underlying mechanisms of hyperlipidemia and cardiovascular diseases.¹³ Insulin is the most potent anabolic hormone which is secreted by beta cells of pancreatic islets of Langerhans. Insulin has important role in lipoprotein metabolism and the effects of insulin on lipoprotein metabolism are: insulin inhibits hormone-sensitive lipase, inhibits hepatic triglyceride rich VLDL production, activates lipoprotein lipase and increases low density lipoprotein (LDL) receptor protein expression on the plasma membrane^{14,15}.

A number of studies have shown the relationship between hyperlipidemia and insulin resistances in type-2 diabetes mellitus and they suggested that insulin resistance or insulin deficiency affects key enzymes and pathways in lipid metabolism. In particular, the following processes are affected: Apo protein production, regulation of lipoprotein lipase, action of cholesteryl ester transfer protein and hepatic and peripheral actions of insulin.¹⁶

Again some researcher suggested that lower level of adiponectin (secreted from adipose tissue) are associated with insulin resistance play an important role in development of hyperlipidemia in type 2 diabetes mellitus. Lower level of adiponectin are positively associated with triglyceride and total cholesterol levels¹⁷.

A study was done in Western Europe and they found that at least one-third of the population with type 2 diabetes mellitus have hyperlipidemia and patient with hyperlipidemia

also show evidence of diabetes mellitus. Thus type 2 diabetes mellitus and hyperlipidemia are common intertwined condition that shares a significant overlapping risk factors and complications. They suggest that higher triglycerides has a link for development of central obesity and insulin resistance and both are important factors for development of cardiovascular diseases^{18,19}.

Some studies have been done on this regard in abroad but no published data has yet been available on this aspect in our country. Therefore, the present study has been designed to observe the serum TG and TC levels and its relation with type 2 diabetes mellitus in adult female. Better understanding of these metabolic changes with hyperglycemia will help in the detection of women at risk for future cardiovascular diseases and renal diseases. Treatment and preventive measure can reduce the risk of developing cardiovascular diseases and thus reduce burden on our health budget

Methods

This cross sectional study was conducted in the department of Physiology, Dhaka Medical College, Dhaka, during the period of January 2011 to December 2011. Thirty females of 30-50 years age range with type 2 diabetes mellitus were included in this study as study (B) group. They were selected from the out-patient department of Endocrinology of Dhaka Medical College Hospital, Dhaka. Age matched thirty apparently healthy females were taken as control (A) group for comparison. Subjects having history of heart, liver, kidney diseases, endocrine disorders and women taking hormone replacement therapy, steroid, alcohol user, and smoker were excluded from the study. After selection of subjects, the objectives, nature, purpose and benefit of the study were explained to the subjects in detail. Written informed consent was taken from the participants. They were encouraged for voluntary participation. They were also allowed to withdraw themselves from the study whenever they feel like. Ethical permission was taken from ethical committee of Dhaka Medical College. Detailed medical history, menstrual history and family history

of the subjects were taken and recorded in a pre-designed data collection form. The subjects were advised to attend the laboratory in the department of Physiology of Dhaka Medical College, Dhaka between 8AM to 10AM in fasting state. Then with all aseptic precautions 5 ml of venous blood was drawn from antecubital vein by disposable plastic syringe. Blood was allowed to clot and then centrifuged at rate of 3000 rpm and supernatant clear serum was separated. Serum was taken in eppendorf tube and was preserved in refrigerator. Fasting serum insulin level was assessed by Enzyme Linked Immunosorbent Assay (ELISA) method in the laboratory of National Institute of ENT, Dhaka and fasting blood glucose level was estimated by glucose oxidase method in the laboratory of Physiology of Dhaka Medical College, Dhaka. Fasting serum TG and fasting TC level were estimated by enzymatic method in the laboratory of Physiology of Dhaka Medical College, Dhaka. Statistical analysis was done by Unpaired Student's t- test. Correlation was analyzed by Pearson's correlation co-efficient (r) test. P value <0.05 was taken as of significance.

Results

In this study the mean (\pm SD) of serum TG level was 99.93. \pm 32.37 mg/dl in group A and 238.77 \pm 85.05 mg/dl in group B. The level of serum TG was significantly higher in group B than that of control and the result was statistically significant (p<0.001). The mean (\pm SD) of serum TC was 130.20 \pm .41.33 mg/dl in group A and 226. \pm 35.24 mg/dl in group B. The level of TC was significantly higher in group B than that of control and the result was statistically significant (p<0.001) (Table-I).

The mean (\pm SD) of fasting serum insulin level was 5.76 \pm 3.27 mm/Hg in group A and 20.58 \pm 6.57 uIU/ml in group B. The level of serum insulin was significantly higher in group B than that of control and the result was statistically significant (p<0.001). The mean (\pm SD) of fasting blood glucose level was 5.08 \pm 1.25 uIU/ml in group A and 9.91. \pm 3.32 uIU/ml in group B. The level of blood glucose was

significantly higher in group B than that of control and the result was statistically significant ($p < 0.001$) Table-II.

Table I

Fasting serum triglyceride (TG) and Fasting serum total cholesterol (TC) in both groups

Groups	n	TG (mg/dl) (Mean±SD)	TC (mg/dl) (Mean±SD)
A	30	99.93±32.37	130.20±41.33
B	30	238.77±85.05	226.±35.24

Statistical analysis

Groups	TG (p value)	TC (p value)
A vs B	0.001***	0.001***

Unpaired Student's 't' test was performed to compare between groups. The test of significance was calculated and p values < 0.05 was accepted as level of significance.

- Group A : Healthy adult female
n = Number of subjects
- Group B : subjects with hyperlipidemia
*/**/** = Significant

Table II

Fasting serum insulin (FSI) and Fasting blood glucose (FBG) in both groups

Groups	n	FSI(uIU/ml) (Mean±SD)	FBG(mmol/L) (Mean±SD)
A	30	5.76.±3.27	5.08±1.25
B	30	20.58±6.57	9.91±.3.32

Statistical analysis

Groups	FSI (p value)	FBG (p value)
A vs B	0.001***	0.001***

Unpaired Student's 't' test was performed to compare between groups. The test of significance was calculated and p values < 0.05 was accepted as level of significance.

- Group A : Healthy adult female
n = Number of subjects
- Group B : Diabetic adult female
ns = Not significant
*/**/** = Significant

Serum fasting TG level showed positive correlation ($r = 0.858$) with fasting serum insulin level in study group and result was statistically significant. Again serum TG level showed positive correlation ($r = 0.983$) with fasting blood glucose level in study group and result was also statistically significant. Table- III and Figure-1, 2.

Table-III

Correlation of fasting serum triglycerides level with FSI and FBG in study group (B)

Parameters	Group B (n=30)	
	r	p
Fasting serum insulin (FSI)	+ 0.858	0.001
Fasting blood glucose (FBG)	+0.983	0.001

Pearson's correlation coefficient (r) test was performed to compare relationship between parameters. The test of significance was calculated and p value < 0.05 was accepted as level of significance.

Again, fasting serum TC level showed positive correlation ($r = 0.652$) with serum insulin level and also showed positive correlation (0.815) with fasting blood glucose level in study group and result was statistically significant. Table-IV and Figure 3, 4.

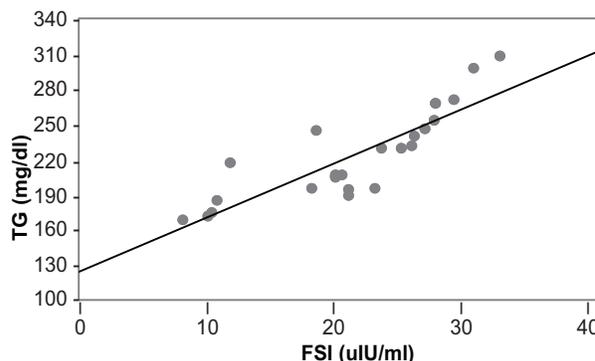


Fig.-1: Correlation of Serum TG with FSI in study group (n=30)

n = number of subjects in study group;
 $r = 0.858$; $p < 0.001$

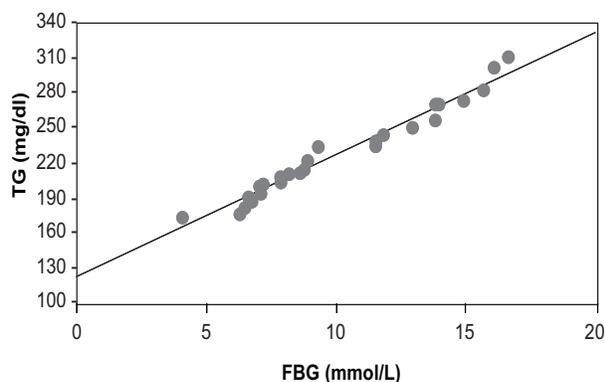


Fig.-2: Correlation of Serum TG with FBG in study group (n=30)

n = number of subjects in study group;
r= 0.983; p <0.001

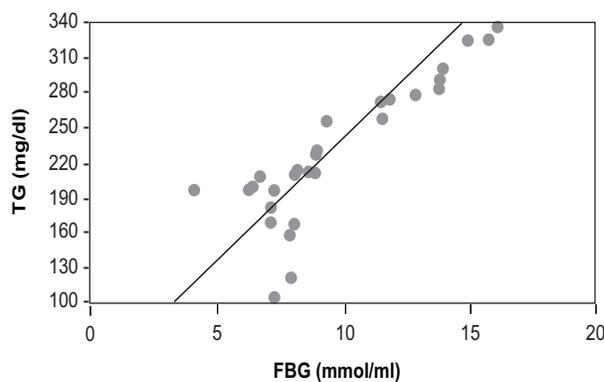


Fig.-4: Correlation of Serum TC with FBG in study group (n=30)

n = number of subjects in study group;
r= 0.815; p <0.001

Table IV

Correlation of serum total cholesterol (TC) level with FSI and FBG in study group

Parameters	Group B (n=30)	
	r	p
Fasting serum insulin	+0.652	0.001
Fasting blood glucose	+0.815	0.001

Pearson’s correlation coefficient (r) test was performed to compare relationship between parameters. The test of significance was calculated and p value <0.05 was accepted as level of Significance.

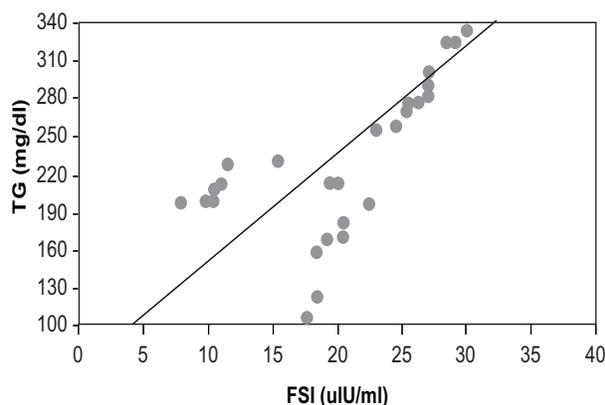


Fig.-3: Correlation of Serum TG with FSI in study group (n=30)

n = number of subjects in study group;
r= 0.652; p < 0.001

Discussion

In the present study, the values of fasting triglyceride (TG) and total cholesterol (TC) in controls were almost within normal range and also similar to reported by the several investigators from abroad ⁸⁻¹¹

In this study, triglyceride (TG) in study group was higher than that of controls and result was statistically significant. Similar types of observations were found by other workers.¹⁰⁻¹³ TC in study subjects were also higher than those of controls and result was statistically significant. Similar types of findings were reported by different researchers of different countries ^{8,11,12} On the contrary, similar observations were made by other researcher but they did not find any significant difference in TG level between the groups. It suggested that it may be due to different type of nutrition and life style in their study population.¹⁰

Again, correlation analysis showed positive correlation of serum TG level with fasting serum insulin and fasting blood glucose. In addition, serum TC level also showed positive correlation with fasting serum insulin and fasting blood glucose. The results were statistically significant. Similar observations were also reported by some investigators. ¹⁶

The exact possible mechanisms regarding these observed effects cannot be revealed directly from present study. However, several investigators of different countries proposed various

suggestions on these aspects, which might be causes of our present findings. It has been suggested that lipid metabolism in type 2 diabetes mellitus is modulated by series of factors among which insulin resistance is the most prominent feature. Insulin resistance is the pathophysiologic mechanism of diabetic hyperlipidemia. Insulin resistance in adipose tissue causes increased activity of hormone sensitive lipase resulting in increased levels of circulating fatty acids. These fatty acids are carried to the liver where they are converted to triacylglycerol and cholesterol²⁰. Again in insulin resistance state, the assembly and secretion of triglyceride rich lipoprotein is increased due to decreased Apo lipoprotein B (apoB) degradation and increased the expression of the microsomal transfer protein (MTP) in the liver and both of these factors help in overproduction of VLDL-TG and VLDL-Apo B. So TG and total TC levels are increased in blood²¹.

In addition in diabetic patient due to insulin resistance, the apoprotein CIII synthesis is also increased. This apolipoprotein has two properties that causes retention of TGS in the circulation. First, apoprotein C-III interfere with the action of lipoprotein lipase, the enzyme responsible for hydrolysis of VLDL triglyceride. Second, apolipoprotein C-III interfere the uptake of TG rich VLDL remnant by receptor on liver cells. So triglycerides level are increase in circulation.²²

Moreover, adiponectin (a hormone secreted from adipose tissue) increases the activity of lipoprotein lipase and also increases the catabolism of triglyceride rich VLDL and chylomicron particles. But in type 2 Diabetes mellitus due to insulin resistance, adiponectin production are decrease. So decreased level of adiponectin also decreased the catabolism of TG rich particles and increased the level of triglycerides²³⁻²⁵. Furthermore, insulin resistance are associated with some inflammatory cytokines namely leptin, tumor necrosis factor (TNF- α), transforming growth factor (TGF- β), IL-6, which are responsible for overproduction of TG and TC in blood. TNF- α and IL-6 increases the hepatic production of

3hydroxy-3 methyl glutaryl coenzyme A (HMG-COA) reductase, is an important for cholesterol biosynthesis. Thereby increases the synthesis of cholesterol.²⁶

Conclusion

From this study, it can be concluded that hyperlipidemia, which is characterized by higher levels of fasting serum TG and TC level present in study group, may be due to high level of serum insulin and blood glucose levels.

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