

Effect of Fasting Blood Glucose (FBG) on Lipid Metabolism and Gender Differences in the Pattern of Dyslipidemia in Adults with Type 2 Diabetes in Northern India

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ABSTRACT The present study aims to explore the effect of hyperglycemia on lipid profile components of type 2 diabetes patients and to evaluate the gender differences in the lipid abnormalities in type 2 diabetes. A total of 680 diabetic patients (340 males and 340 females) with fasting blood glucose level (fasting glucose <126 mg/dl and with fasting blood glucose ≥ 126 mg/dl) were analyzed for serum triglycerides, total cholesterol, LDL, HDL and VLDL. The patients who had one or more parameters (TG, HDL or LDL) outside the targets recommended by American Diabetes Association (ADA) were considered to have dyslipidemia. The subjects with fasting blood glucose (FBG) ≥ 126 mg/dl had more deranged levels of lipid profile components and there was a positive significant correlation of FBG with TG ($r=0.3$), TC ($r=0.3$), HDL ($r=0.2$), LDL ($r=0.2$) and VLDL ($r=0.2$). The prevalence of dyslipidemia in males and females were 97.6 percent and 89.9 percent, respectively. Combined dyslipidemia with high LDL and high TG was the most common pattern among males and isolated high LDL among females, contributing to 43.8 percent and 18.2 percent of patients with dyslipidemia, respectively. Dyslipidemia is the commonest complication of diabetes mellitus and the patients with high FBG had more deranged lipid values indicating that poor glycemic control is associated with abnormal lipid profile.

ABBREVIATIONS FBG: Fasting Blood Glucose. TG: Triglycerides. LDL: Low Density Lipoproteins. HDL: High Density Lipoproteins

INTRODUCTION

Diabetes mellitus is a hereditary, chronic and endocrine metabolic disorder which has become a major cause of deaths worldwide (Faghilimnai et al. 2006). Type 2 diabetes accounts for approximately ninety percent of all affected individuals and is the most common form of diabetes caused by defects in insulin secretion and insulin resistance (Burtis et al. 2004; American Diabetes Association 2009). There are certain ethnic and racial groups of Africa and Asia that have a greater risk of developing diabetes (Manu et al. 2007). India is facing a grave problem in having the largest number of people with diabetes due to fast industrialization and modern lifestyle (Fall 2001; Flegal et al. 2002; Pinkney 2002) which is estimated to reach 80 million by the

year 2030 (Rao et al. 2010; Shaw 2010). It has been found that 65.1 million people were affected by type 2 diabetes in 2013 which would increase to 109 million by 2035 (IDF 2013). The pivotal factor that contributes to diabetes is increased blood sugar which affects body biochemistry and leads to complications. There are also studies that revealed that increased serum levels of glucose can influence enzymes such as serum glutamate oxaloacetate transaminase (SGOT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and creatinine kinase (CK) and change the normal serum levels of such enzymes that cause disturbances in body normal physiology and biochemistry (Chen et al. 1970; Maxwell et al. 1986; UK Prospective Diabetes Study 1997). The lipid abnormalities in either of the lipoproteins is induced due to uncontrolled hyperglycemia in Type 2 diabetes patients (Khan et al. 2007; Devkar et al. 2016). Dyslipidemia is the increase in the levels of cholesterol, triglyceride or a low HDL beyond the recommended optimal targets that leads to the development of atherosclerosis. But in Type 1,

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Type 2 and gestational diabetes there is a difference in the pattern of lipid abnormalities (Nesto 2005). It has also been reported in earlier studies that hypertriglyceridemia is a risk factor for development of CAD in patients with Type 2 diabetes (Ahmad et al. 2005; Mooradian 2007). Atherosclerotic cardiovascular disease is the most common problem induced due to dyslipidemia (Marjani 2005; Wang et al. 2006). Thus, there is a need to evaluate lipid profiles in Type 2 diabetes mellitus population and determine the major lipid risk factors for coronary artery disease. The main aim of this study was to determine the effect of increased blood glucose on lipid profile and to evaluate correlation between fasting blood glucose (FBG) with serum lipid levels in patients with Type 2 diabetes and to further find out the gender differences in the lipid abnormalities in Type 2 diabetes patients.

MATERIAL AND METHODS

Subjects

A total of 680 diabetic patients (340 males and 340 females) ranging in age from 35-60 years residing in Malwa region of Punjab were included in the study as subjects after obtaining their informed consent. The initial screening was based on clinical records available in the hospitals and after confirming the status based on the records and tests, patients were informed about the study. The study protocol was reviewed and approved by the Institutional Ethical Committee of Punjabi University, Patiala. Inclusion criteria was Type 2 diabetes mellitus for more than 3 years and the patients who had major complications related to diabetes were excluded from the study.

Blood Collection and Assays

Blood samples were obtained from patients after at least 8 hours of fasting. Serum was separated from the clots after complete coagulation by centrifugation (15 min at 2000 g). Fasting blood samples were analyzed for fasting blood sugar, serum triglycerides and total cholesterol by using automated chemistry analyzer (MED-O-SOURCE). Serum glucose was measured by glucose oxidase-peroxidase (GOD-POD) method. Serum total cholesterol was determined by an enzymatic (CHOD-PAP) method and triglycer-

ides were determined by an enzymatic (GPO-PAP) method. HDL-C was determined by precipitation method and LDL-C and VLDL-C were estimated by the formula (Friedwald et al. 1972).

$$\text{LDL-C} = \text{TC} - \text{HDL-C} - (\text{TG}/5)$$

$$\text{VLDL} = \text{TG}/5$$

The definitions given by American Diabetes Association (2013) and NCEP Adult Treatment Panel III (2002) were used to label patients as Type 2 diabetics and to classify lipoprotein concentrations into different cardiovascular disease risk categories, respectively.

Chemicals

The diagnostic kits for the estimation of fasting blood sugar, total cholesterol, triglycerides and HDL-C were procured from Med-o-source. The reagents were stored at 2-8°C till use and all procedures were performed at room temperature.

Statistical Analysis

Statistical analysis was performed using SPSS software (version 16). The values of all the parameters were given in mg/dl and they were expressed as mean±SD. The statistical significance of the differences between the males and females were evaluated by the student's t-test. Pearson's correlation test was performed to examine various correlations and chi square analysis was performed to find out the significant differences in the proportions.

RESULTS

The baseline characteristics of the participants have been presented in Table 1. The males were slightly older than the females and the duration of the disease was almost similar in both the sexes.

Table 1: Baseline characteristics of the study participants

Variables	Males (N=340)	Females (N=340)	t-value
Age (years)	52.7± 7.1	50.5±10.4	1.8
Duration of disease (years)	6.8± 2.8	6.0± 1.5	1.2

The fasting blood glucose (FBG) was also higher in males as compared to females ($p<0.05$).

The lipid profile analysis showed that the males had higher levels of total cholesterol, TG, LDL, HDL and VLDL (Table 2) than females which is evident from statistically significant differences ($p < 0.05$).

The overall prevalence of dyslipidemia among males and females was 97.6 percent and 89.9 percent, respectively. The most common pattern among males was combined two parameter dyslipidemia with high levels of LDL and TG (43.8%), followed by isolated single parameter dyslipidemia of high levels of LDL (17.7%). Among the females, there was high prevalence of isolated single parameter dyslipidemia with

high levels of LDL (18.2%), followed by combined two parameter dyslipidemia having high levels of LDL and TG (16.7%) and mixed dyslipidemia (14.1%) (Table 3).

It was found that hypercholesterolemia, hypertriglyceridemia and high levels of LDL were more prevalent in the males as compared to females but low levels of HDL were more in females (Table 4).

Chi-square analysis for the gender wise distribution of dyslipidemia showed that there were statistically significant differences for hypercholesterolemia, hypertriglyceridemia and low HDL levels ($p < 0.0001$). The subjects who had

Table 2: Lipid profile in type 2 diabetes patients

Variables	Males	Females	t-value
Fasting blood sugar(FBS) (mg/dl)	251.6±111.4	194.6±110.5	3.2*
Total Cholesterol (TC) (mg/dl)	239.7± 78.7	204.8± 68.6	3.0*
LDL (mg/dl)	144.7± 70.8	122.5± 63.2	2.1*
HDL (mg/dl)	53.4± 13.3	50.4± 11.7	1.3
VLDL (mg/dl)	41.6± 12.9	31.8± 7.4	3.1*
Triglyceride (TG)(mg/dl)	207.9±114.8	159.0± 86.9	3.1*

* represents statistically significant at $p < 0.05$

** represents statistically significant at $p < 0.01$

Table 3: Pattern of dyslipidemia in type 2 diabetes patients

	Males	Females
<i>Mixed Dyslipidemia</i> (LDL $\geq$ 100,TG $\geq$ 150 and HDL $<$ 40{males}/50{females})	4.40% 15 (4.4)	14.10% 48 (14.1)
<i>Combined Two Parameter Dyslipidemia</i> a. (LDL $\geq$ 100,TG $\geq$ 150 and HDL $\geq$ 4 0/50) b. (LDL $<$ 100,TG $\geq$ 150 and HDL $<$ 4 0/50) c. LDL $\geq$ 100,TG $<$ 150 and HDL $<$ 40 /50)	53.50% 149 (43.8)	43.50% 57(16.7)
<i>Isolated Single Parameter Dyslipidemia</i> a. LDL $\geq$ 100 TG $<$ 150,HDL $>$ 40/50) b. LDL $<$ 100,TG $\geq$ 150 and HDL $>$ 40 /50) c. LDL $<$ 100,TG $<$ 150 and HDL $<$ 40/50)	11 (3.2) 39.70% 60 (17.7)	43 (12.7) 32.30% 62 (18.2)
	56 (16.5) 19 (5.5)	28 (8.5) 19 (5.6)
<i>Total</i>	97.60%	89.90%

Table 4: Distribution of dyslipidemia in type 2 diabetes patients

Variables	Normal		Abnormal		χ^2	p-value
	Males	Females	Males	Females		
TC $<200 \geq 200$	127 (37.4%)	182 (53.5%)	213 (62.6%)	158 (46.5%)	17.3**	<0.0001
TG $<150 \geq 150$	108 (31.9%)	163 (47.9%)	232 (68.1%)	177 (52.1%)	17.9**	<0.0001
LDL $<100 \geq 100$	90 (26.4%)	125 (36.6%)	250 (73.6%)	215 (63.4%)	7.9**	0.005
HDL Males $>40 \leq 40$ Females $>50 \leq 50$	273 (80.3%)	182 (53.5%)	67 (19.7%)	158 (46.5%)	53.8**	<0.0001

* represents statistically significant at $p < 0.05$

** represents statistically significant at $p < 0.001$

high levels of FBG in both males and females had high levels of TC, TG, LDL and low levels of HDL. There were statistically significant differences found in TC, TG and HDL levels in males and females with high levels of FBG (Tables 5 and 6).

The Pearson correlation analysis (Table 7) revealed that there was positive correlation of FBG with all the lipid parameters ($p < 0.05$) in both the groups and the gender wise distribution showed a positive correlation of FBG with HDL in males ($p < 0.05$) and FBG with TG, LDL and VLDL in females ($p < 0.05$).

DISCUSSION

Lipid abnormalities (increased levels triglycerides, LDL and low levels of HDL) are an important cause of atherogenesis and are known as atherogenic dyslipidemia (Ahmad et al. 2008). Dyslipidemia as a metabolic abnormality is frequently associated with diabetes mellitus and lipid profile and diabetes in the previous studies have been shown to be the important predictors for metabolic disturbances including dyslipidemia, cardiovascular diseases, hyperinsulinemia, etc. (Goldberg 2001). Thus, the present study

Table 5: Association between Fasting Blood Sugar (FBS) in males with type 2 diabetes

		Fasting Blood Sugar (mg/dl)			χ^2	p-value
		<100 (N=6)	100-125 (N=14)	>126 (N=320)		
TC	<200	3	9	113	7.2*	0.02
	≥ 200	1	5	207		
TG	<150	0	10	100	3.6**	0.001
	≥ 150	6	4	220		
LDL	<100	4	2	80	0.9	0.62
	≥ 100	2	12	240		
HDL	>40	4	8	260	9.3**	0.009
	≤ 40	2	6	60		

* represents statistically significant at $p < 0.05$

**represents statistically significant at $p < 0.001$

Table 6: Association between Fasting Blood Sugar (FBS) in females with type 2 diabetes

		Fasting Blood Sugar (mg/dl)			χ^2	p-value
		<100 (N=22)	100-125 (N=61)	>126 (N=257)		
TC	<200	16	25	137	9.6*	0.008
	≥ 200	6	36	120		
TG	<150	10	38	113	7.2*	0.02
	≥ 150	12	23	144		
LDL	<100	9	25	90	4.7	0.09
	≥ 100	13	36	167		
HDL	>50	2	57	123	59.8**	< 0.0001
	≤ 50	20	4	134		

* represents statistically significant at $p < 0.05$

**represents statistically significant at $p < 0.001$

Table 7: Correlation of Fasting Blood Sugar (FBS) with the components of lipid profile of the diabetic patients

	Total Cholesterol	Triglycerides	HDL	LDL	VLDL
Males	0.2	0.1	0.3*	0.1	0.08
Females	0.4*	0.4*	-0.02	0.3*	0.4*
Pooled Sample	0.3*	0.3*	0.2*	0.2*	0.2*

* represents statistically significant at $p < 0.05$

explored the effect of hyperglycemia on lipid profile components of Type 2 diabetes patients and the gender differences in the lipid abnormalities in Type 2 diabetes patients.

The results of the present study revealed that subjects with higher fasting blood glucose had higher prevalence of elevated serum lipids and there were significant differences in the TG levels in males and HDL levels in females. Other studies have also reported that in hyperglycemic patients, the lipid profile levels were elevated (Uttra et al. 2011; Sarfraz et al. 2016). It has been concluded that chronic hyperglycemia in diabetes causes glycation of apolipoproteins and interferes with the normal pathways of lipoprotein metabolism and leads to dyslipidemia (Carmena 2008).

There was a positive significant correlation of FBG with TG, TC, HDL, LDL and VLDL indicating that poor glycemic control is associated with abnormal lipid profile which are in conformity with the results of earlier studies which showed a positive correlation of FBG with TC, TG, and VLDL (Khan et al. 2007; Sheikhpour et al. 2013; Dixit et al. 2014; Khadke et al. 2015). Thus, it clearly suggests a correlation between hyperglycemia and dyslipidemia.

The researchers' study revealed high percentages of hypercholesterolemia (62.6% among males and 46.5% among females), hypertriglyceridemia (68.1% in males and 52.1% in females) and high levels of LDL (73.6% among males and 63.4% in females). Coronary artery disease is the most common mortality in hyperglycemic patients and is associated with increased level of LDL. In the present study 73.6 percent of males and 63.4 percent of females had high levels of LDL which are in concordance with the results reported by other studies (Bays 2003; Rajput et al. 2015; Borle et al. 2016).

But an interesting observation was made in the present study that high proportion of females had low HDL as compared to males. It has been observed that HDL cholesterol levels were lower in diabetic women than men. In fact it has also been postulated that the inverse association between CHD and HDL levels is stronger in women than men (Walden et al. 1984). A study reported that for each milligram-per-decilitre increase in HDL, there was ~two percent decrease in CHD risk in men and a three percent decrease in women (Gordon et al. 1989). The results of the present study showed that the males had poor

lipid as well as glycemic control as compared to females and this difference was statistically significant. The results were in contrast to the studies in which the females had higher levels of lipid profile parameters as compared to males (Juutilainen et al. 2004; Habib 2013; Dixit et al. 2014; Ozder 2014).

The prevalence of dyslipidemia in males and females in the researchers' study was 97.6 percent and 89.9 percent, respectively. Similar results of high prevalence of dyslipidemia in Type 2 diabetes patients have been reported in a study in which 99.1 percent of diabetic males and 89.1 percent of diabetic females had dyslipidemia (Udawat et al. 2001) and another study showed the prevalence of dyslipidemia to be 85.5 percent among diabetic males and 97.8 percent among diabetic females (Parikh et al. 2010). A recent study by Kaithala et al. (2016) showed the prevalence of dyslipidemia of 97.2 percent in diabetic patients.

The most common pattern of dyslipidemia among males and females was combined dyslipidemia with high LDL and high TG (43.8%) and isolated high LDL (18.2%) respectively. The second most common pattern among males was isolated high LDL (17.7%) while in females it was high LDL and TG (16.7%). These results were in conformity to the results shown by earlier studies (Parikh et al. 2010; Pandya et al. 2012) but contrasting results have been reported in some studies (Cook et al. 2000; Borle et al. 2016).

CONCLUSION

Dyslipidemia is the commonest complication of diabetes mellitus and it predisposes them to premature atherosclerosis and macro vascular complications. One or another lipid level is found to be abnormal in most of the diabetic patients, this indicates the influence of Type 2 diabetes on abnormal lipid profile of patients due to hyperglycemia and its associated danger of elevated CVD risk.

RECOMMENDATIONS

The diabetes patients must be educated on the risks and the complications they face as a result of their condition and the necessary steps that could be taken manage it and prevent further complications associated with diabetes.

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