Association between Glycemic Control and Lipid Profile in Adults with Type 2 Diabetes Mellitus

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Abstract
Background*: Diabetes mellitus is the most common metabolic disease. Impaired lipid metabolism resulting from uncontrolled hyperglycemia has been implicated in cardiovascular complications in diabetic patients. Also, glycosylated hemoglobin (HbA1c) has been regarded as an independent risk factor for cardiovascular disease.* ***Objective****: The aim of this study was to examine the correlation between HbA1c, fasting blood sugar (FBS) with serum lipid levels in type 2 diabetes mellitus (T2DM).* ***Subjects and Methods****: Venous blood samples were collected from 84 type 2 diabetic patients as well as 42 age and sex matched apparently healthy control. Blood samples of all participants were analyzed for HbA1c and fasting blood glucose (FBG). Serum was analyzed for lipid profile including: total cholesterol (TC), triacylglycerol (TAG); low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C). TC/HDL-C ratio as well as HDL-C/LDL-C ratio was calculated.* ***Results****: All lipid parameters were significantly altered in T2DM patients as compared to normal control. Moreover, Patients with uncontrol diabetes (UCD) had significantly higher levels of FBG and lipid parameters than those with WCD. No significant difference in lipid parameters was found between both genders, except for TC/HDL-C ratio and HDL-C/LDL-C ratio of PCD females.*
Keywords: *Type 2 diabetes mellitus-lipid profile-fasting blood glucose-Glycosylated hemoglobin-glycemic control.*

Introduction

Diabetes mellitus (DM) is a common metabolic disorder characterized by absolute or relative deficiencies in insulin secretion and/or insulin action associated with chronic hyperglycemia and disturbances of carbohydrate, lipid and protein metabolism [(1)]. Type 2 diabetes mellitus (T2DM) has a rising attitude globally. The worldwide spread of diabetes among general population is estimated to increase to 300 million in 2025 [(2,3)].

Glycosylated hemoglobin (HbA1c) is a stable, irreversible product of non-enzymatic glycosylation of the hemoglobin β-chain by plasma glucose. HbA1c is used as an indicator for the state of glycemic control, progression of the disease and development of complications in diabetic patients [(4,5)].

Impaired lipid metabolism resulting from uncontrolled hyperglycemia has been implicated in increasing cardiovascular risks, and so the mortality and morbidity among diabetic patients [(6)]. The term diabetic dyslipidemia comprises a triad of raised TAG reduced HDL-C and excess of small, dense LDL-C particles in diabetic patients [(7)]. Dyslipidemia is a risk factor for coronary artery disease, a leading cause of mortality in patients with diabetes mellitus. It has been proposed that the composition of lipid particles in diabetic dyslipidemia is more atherogenic than other types of dyslipidemia [(8)].

Frequent and accurate measurements of lipids profile and glycosylated hemoglobin are necessary in T2DM.The aim of this study was to find out the relationship between glycemic control as reflected by HbA1c and serum lipid profile in T2DM patients.

Subjects and methods

Subjects

This study comprises eighty four adult patients with T2DM (treated with hypoglycemic drugs) as well as forty two ages and sex matched apparently healthy adults serve as a control group. They were recruited from the Governmental and NGO's Hospital at Cairo, Egypt. Diabetic patients met the criteria of **American Diabetes Association (9)**. Subjects of the control group were confirmed by fasting blood glucose to be non-diabetic. The study was conducted after obtaining a permission from Ethical Committee of the GOTHI (**G**eneral **O**rganization for **T**eaching **H**ospitals and **I**nstitutions), and informed consent were taken from all subjects before commencing the study.

The inclusion criteria include type 2 diabetic adults (both sexes) in the age group of 35–45 years, without complications.

Exclusion criteria

- Subjects received any medication other than insulin or complained from any acute or chronic illness other than diabetes mellitus.
- Subjects have anemia therapy, acute and chronic inflammation and blood transfusion that could affect ferritin levels.

Diabetic patients were categorized according to their HbA1c values into two sub-groups: Well controlled diabetic (WCD) with HbA1c value ≤7.0 % (and uncontrolled diabetic (UCD) with HbA1c value >7.0% according to **Rohlfing *et al*** **(10)**

Biochemical analysis:

After an overnight fast, venous blood samples were taken into vacationer tubes, FBG was determined according to **Barham D, and Trinder (11)**. The method of **Abraham *et al*. (12)** was used for blood HbA1c determination. Serum was separated by centrifugation and used for determination of lipid profile including: TC (**Allain, 13**), TAG (**Fossati and Prencipe, 14),** and HDL-C **(Finley, 15)**. LDL- C was calculated according to the equation of Friedewald et al. **(16)**.

Statistical Analyses

Data were analyzed by SPSS statistical package version 17. Excel computer program was used to tabulate the results. Independent t-test was used to declare the significant difference between each two groups at P<0.05 (Stanford and Charles, **17**). Results were expressed as means ± SE.

Results

The present study was done on 84 type 2 diabetic patients (40 male and 44 female, age range: 35-45 years with mean age of 40±5.4. Age and sex matched healthy subjects (20 male and 22 female) were used as normal control. When cases were grouped according to glycemic control (HbA1c values), WCD (HbA1c ≤ 7%), included 38 patients (18 male and 20 female) and UCD (HbA1c <7%) included 46 patients (22 male and 24 female),

Alteration of biochemical parameters of studied subjects was shown in table (1).There were significant differences between FBG, HbA1c and lipid parameters of diabetic patients as compared to healthy control with percentages of 189.54%, 80.07%, 68.02%, 98%.86 and 96.83% for FBG, HbA1c, TC, TAG and LDL-C respectively. However, the difference between HDL-C levels of diabetic and control was non-significant. Additionally, TC/HDL-C ratio and LDL-C/HDL-C ratio were significantly higher in diabetic patients than non-diabetic ones ($p < 0.05$).

Table (1) FBG; HbA1c and lipid profile of control and type 2 diabetic patients (Mean±SE).

Parameters	Normal control (n=42)	Diabetic patients (n=84)	% Change
FBG (mg/dl)	87.35 ±11.32	252.92±31.46 [a]	189.54
Blood HbA1c %	5.42 ±0.58	9.76 ±0.66 [a]	80.07
TC (mg/dl)	164.19±21.31	275.87±28.53 [a]	68.02
TAG (mg/dl)	78.33 ±5.86	155.77±25.21 [a]	98.86
HDL-C (mg/dl)	44.90 ±3.40	41.32 ±4.45 [a]	-3.58
LDL-C (mg/dl)	104.47±21.24	205.63±37.46 [a]	96.83
TC/HDL-C ratio	3.65± 0.74	7.10±1.12 [a]	94.52
LDL-C/HDL-C ratio	2.26±0.38	5.38±1.03 [a]	138.05

a: significant difference between diabetic patients and healthy control $p < 0.05$; FBG: Fasting blood glucose; HbAIc: Glycated hemoglobin, TC: Total cholesterol, TAG: Triacylglycerol; HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol**.**

On comparing to control group, blood FBG and % blood HbA1c as well as mean values of all lipid parameters of PCD & WCD diabetic patients were significantly higher ($p <0.05$) (table, 2).

Table (2): FBG; blood HbA1c and lipid profile of control and type 2 diabetic patients categorized by glycemic control (Mean±SD).

Parameters	Normal control (n=42)	Diabetic Patients	
		HbA1c levels	
		WCD (n=38)	PCD (n=46)
FBG (mg/dl)	86.57 ±12.81	172.12±25.90 [b,c]	329.18±62.47 [b]
Blood HbA1c%	5.35 ±0.76	6.64 ±0.81 [b,c]	10.99 ±1.09 [b]
TC (mg/dl)	162.36±32.52	210.41±39.51 [b,c]	351.94±41.76 [b]
TAG (mg/dl)	78.35 ±11.27	120.63±9.68 [b,c]	191.39±30.39 [b]
HDL-C (mg/dl)	44.75 ± 7.58	39.83 ±5.15 [b,c]	36.19 ±6.57 [b]
LDL-C (mg/dl)	102.79±18.36	149.78±31.58 [b,c]	269.52±46.96 [b]
TC/HDL-C ratio	3.58±0.61	5.13±0.92 [b,c]	9.58±1.82 [b]
LDL-C/HDL-C ratio	2.18±0.38	3.77±0.55 [b,c]	7.32±0.65 [b]

b: significant differences between well controlled or uncontrolled and normal control c: significant differences between well controlled and uncontrolled diabetic patients. WCD: Well controlled diabetic patients; UCD: Uncontrolled diabetic patients; FBG: Fasting blood glucose; HbAIc: Glycated hemoglobin; TC: Total cholesterol. TAG: Triacylglycerol. HDL-C: High density lipoprotein cholesterol. LDL-C: Low density lipoprotein cholesterol

The effect of gender on the biochemical parameters was presented in table (3), the differences between PCD & WCD diabetic males and females for all measured parameters were significant. However, no significant differences were detected in blood levels of FBG and HbA1c %, as well as in serum lipid parameters between males and females of both glycemic status. On contrast, TC/HDL-C ratio was significantly higher ($p < 0.05$) in WCD females and in UCD males as compared with their corresponding opposite sexes. HDL-C were higher in females than males for the two glycemic status, but the differences were non-significant. Moreover, LDL-C/HDL-C ratio of UCD females was significantly higher than males ($p < 0.05$).

Table (3): FBG; HbA1c and lipid profile of control and type 2 diabetic patients categorized by glycemic control and gender

Parameters	Male			Female		
	Normal Control (n=20)	WCD (n=18)	PCD (n=22)	Normal control (n=22)	WCD (n=20)	PCD (n=24)
FBG (mg/dl)	88.13± 11.95	170.65± 18.0 [b,c]	339.73± 25.74 [b]	86.57± 11.81	172.12± 15.90 [b,c]	329.18± 27.47 [b]
Blood HbA1c%	5.48± 0.51	6.64± 0.66 [b,c]	10.52± 1.21 [b]	5.35± 0.42	6.64± 0.59 [b,c]	10.99 ± 1.19 [b]
TC (mg/dl)	166.02± 12.10	209.62± 31.64 [b,c]	331.51± 37.27 [b]	162.36± 21.52	210.41± 27.51 [b,c]	351.94± 35.76 [b]
TAG (mg/dl)	78.30± 10.20	119.64± 20.56 [b,c]	191.43± 27.64 [b]	78.35± 9.27	120.63± 18.68 [b,c]	191.39± 23.39 [b]
HDL-C (mg/dl)	45.06± 2.55	36.19± 4.57 c [b]	37.10± 3.60 [b]	44.75± 3.58	40.16± 2.29 [b,c]	39.83± 3.15 [b,c]
LDL-C (mg/dl)	106.14± 22.05	151.83± 31.63 [b,c]	251.38± 37.20 [b]	102.79± 21.36	149.78± 22.58 [b,c]	269.52± 31.96 [b]
TC/HDL-C ratio	3.52± 0.81	7.68± 0.88 [b,c,d]	8.95± 0.95 [b ,d]	3.65± 0.86	5.18± 0.98 [b,c]	9.77± 1.02 [b]
LDL-C/HDL-C ratio	2.29± 0.42	3.78± 0.85 [b,c]	6.15± 1.15 [b,d]	2.18± 0.38	3.65± 0.78 [b,c]	7.44± 1.25 [b]

b: Significant differences between well controlled or uncontrolled and normal control c: Significant differences between well controlled and uncontrolled diabetic patients. d: Significant differences between males and females of same glycemic status WCD: Well controlled diabetic patients UCD: Uncontrolled diabetic patients FBG: Fasting blood glucose. HbAIc: Glycated hemoglobin. TC: Total cholesterol. TAG: Triacylglycerol. HDL-C: High density lipoprotein cholesterol. LDL-C: Low density lipoprotein cholesterol

Discussion

Both lipid profile and diabetes have been shown to be the important predictors for metabolic disturbances including dyslipidemia, hypertension, cardiovascular diseases (**18,19).** Patients with type 2 diabetes often exhibit an atherogenic lipid profile, which greatly increases their risk of CVD compared with people without diabetes. An early inter-vention to normalize circulating lipids has been shown to reduce cardiovascular complications and mortality (20,21).

In the present study the levels of FPG and HbA1c were significantly higher in T2DM patients as compared to healthy control ($p < 0.05$). Similar results were reported by other investigators (**22**; **23)** which may support our results.

The increased levels of HbA1c may be explained by possible lack of compliance with insulin dosage, irregular or sub-dosing of insulin, or maybe overeating and lack of a diabetic lifestyle (**24**). Higher levels of HbA1c are an indicator of poor diabetic control, which means a higher level of circulating glucose. If circulating glucose is constantly at a higher level, it can lead to more and more non-enzymatic glycosylation of tissue proteins.

This study reveals high prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL-C and low HDL-C levels which are well known risk factors for cardiovascular diseases. Insulin affects the liver apolipoprotein production. It regulates the enzymatic activity of lipoprotein lipase (LpL) and Cholesterol ester transport protein. All these factors are likely cause of dyslipidemia in Diabetes mellitus (25) Moreover, insulin deficiency reduces the activity of hepatic lipase and several steps in the production of biologically active LpL may be altered in DM (26). Similar results were obtained by **Meenu et al**. (22) and Mahato et al. (27).

Insulin impact the liver apolipoprotein production which regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transport protein. These could be the likely causes of dyslipidemia in diabetes mellitus as reported by Goldberg (25). Over and above this, insulin deficiency also reduces the activity of hepatic lipase and several other steps in the production of biologically active lipoprotein lipase may be also altered in DM (28, 29).

Glycated hemoglobin (HbA1c) is routinely used as a diagnostic tool for measuring long term glycemic control. In accordance with its function as an indicator for the mean blood glucose level. HbA1c predicts the risk for diabetic complication in diabetes patients (28). The UKPDS study has shown that in T2DM patients, the risk of diabetic complications were strongly associated with previous hyperglycemia. Glycemic control with decreased levels of HbA1c is likely to reduce the risk of complications (28).

Observation of the present study showed that TC/HDL ratio and LDL-C/HDL-C were significantly higher in diabetic patients as compared with non-diabetic ones. The same findings were reported by Mahato et al. (27).

Gimeno-Orna et al (30), showed that the main lipid predictor of vascular events was mean TC/HDL-C ratio with hazard ratio (HR) of 1.46. In the same study, the predictive power of the TC/HDL ratio was found to be higher than that of Non-HDL cholesterol and study concluded that TC/HDL-C can be used as a treatment guides for diabetic dyslipidemia. Total number of apo-B containing particles and small LDL-C Particles are increased in diabetes and these metabolic abnormalities are better reflected by TC/HDL-C ratio than LDL-C alone (31, 32). Significant association of HbA1c with various lipid parameters, LDL-C/ HDL-C ratio and TC/HDL-C ratio in present study suggests the importance of glycemic control in order to control dyslipidemia.

The Diabetes complications and control trial (DCCT) established HbA1c as the gold standard of glycemic control. In the present study, the diabetic patients with HbA1c value > 7.0% exhibited a significant increase in TC, , TAG, LDL-C, HDL-C, LDL-C/HDL-C ratio, and Risk ratio without any significant alteration in HDL-C in comparison to patients with HbA1c value ≤7.0%. Khan HA et al. (33) showed the impact of glycemic control on various lipid parameters in which the diabetic patients were categorized into 3 groups according to their HbA1c levels: group 1, good glycemic control (HbA1c<6%); group 2, poor glycemic control (HbA1c >6%–9%) and group 3, worst glycemic control (HbA1c>9%). Though there was no significant differences in LDL–C in 3 groups with regard to glycae-mic control, alterations in other lipid parameters were statistically significant in three different groups. Severity of dyslipidemia increases in patients with higher HbA1c value.

Gender wise evaluation of the present study with respect to glycemic control showed no significant difference in TC, TAG, LDL-C among both genders of both HbA1c categories , though HDL-C levels were

higher in females. This warrants the need for more critical monitoring of lipid profile in diabetic males so as to prevent cardiovascular complications among them. These finding were in accordance with Meenu et al. (22). The increase in HDL-C in females may be attributed to the effects of sex hormones on body fat distribution, which leads to differences in altered lipoproteins (34).

In diabetes many factors may affect blood lipid levels, because of interrelationship between carbohydrates and lipid metabolism. Therefore, any disorder in carbohydrate metabolism leads to disorder in lipid metabolism and vice versa. Hypertriglyceridemia usually accompanies decreased HDL cholesterol, which is also a prominent feature of plasma lipid abnormalities seen in individuals with diabetes (**35; 36).** The cluster of lipid abnormalities associated with diabetes is defined by a high concentration of TAG and small dense LDL-C and a low concentration of HDL-C. The possible mechanism responsible for hypertriglyceridemia may be due to increased hepatic secretion of very low density lipoprotein (VLDL) and delayed clearance of triacylglycerol rich lipoproteins, which is predominantly due to increased levels of substrates for triacylglycerol production, free fatty acids and glucose (**25).** Moreover, **Molitch, (37)** reported that high Triacylglycerol (TAG) level may be attributed to poor Glycemic control. Poor Glycemic control with inadequate provision of insulin leads to a reduction in the activity of lipoprotein lipase and consequently inability to clear chylomicrons and VLDL-cholesterol **(39).**These findings may partially support the observed elevation in the levels of LDL-cholesterol in the current study.

However, in metabolically poorly controlled diabetic patients, glycation of LDL-cholesterol increased with hyperglycemia. This reduced catabolism of LDL results in high serum level of LDL-cholesterol (**40).** Poor Glycemic control with inadequate provision of insulin leads to a reduction in the activity of lipoprotein lipase and consequently inability to clear chylomicrons and VLDL-cholesterol (**39**). These findings may partially support the observed elevation in LDL-cholesterol in the current study.

References

i. *Abou-Seif MA and Youssef AA (2004): Evaluation of some biochemical changes in diabetic patients. Clin Chim Acta, 346:161–170.*
ii. *Ghazanfari Z, Haghdoost SA, and Mohammad A (2010): Comparison of HbA1c and Fasting Blood Sugar Tests in General Population. International Journal of Preventive Medicine, 1 (3): 187-94.*
iii. *Adeghate E, Schattner P, and Dunn E (2006): An update on the etiology and epidemiology of diabetes mellitus. Ann N Y Acad. Sci., 1084: 1–29.*
iv. *Feldt-Rasmussen, B. (2006): Is there a need to optimize glycemic control in hemodialyzed diabetic patients? Kidney Int., 70: 1392–1394.*
v. *Stolar, M. (2010): Glycemic control and complications in type 2 diabetes mellitus. Am J Med. 123(3 Suppl): S3-11.*
vi. *Mohsin, A.B. and Muhammad, A.G. (2013): Estimation of biochemical changes in diabetic patients. Intern J. Sci. and Technol., 2(6):498-501.*
vii. *Taskinen, M.R. (2002): Diabetic dyslipidemia. Atheroscler Suppl., 3(1):47–51.*
viii. *Mahato R.V., Gyawali, P., Raut, P.P., Regmi, P., Khelanand, P.S., Dipendra, R.P. and Gyawali, P. (2011): Association between glycaemic control and serum lipid profile in type 2 diabetic patients: glycated haemoglobin as a dual biomarker. Biomed. Res., 22(3):375–380.*
ix. *American Diabetes Association (2012): Diagnosis of diabetes mellitus. Diabetes Care, 1(27): 57-59.*
x. *Rohlfing CL, Wiedmeyer HM, Little RR, England JD, Tennill A, and Goldstein DE (2002): Defining the relationship between serum glucose and HbA1c: analysis of glucose profiles and HbA1c in the Diabetes Control and Complications trial. Diabetes Care, 25: 275-278.*
xi. *Barham D, and Trinder P (1972): An improved color reagent for the determination of blood glucose by the oxidase system. Analyst, 97: 142-145.*
xii. *Abraham E C, HuffT A, Cope ND, Wilson JB Jr, Bransome ED Jr, and Huisma TH (1978): Determination of the glycosylated hemoglobin (HbA1) with a new microcolumn procedure: Suitability of the technique to assess the clinical management of diabetes mellitus, Diabetes, 27 (9): 931-7.*

xiii. *Allain C.C., Poon I.S., Chan C.H.G. and Richmond W. (1974): Enzymatic determination of serum total cholesterol. Clin. Chem. 20:470-71.*

xiv. *Fossati, P., and Prencipe, L. (1982): Serum triglycerides determination colormetrically with an enzyme that produces hydrogen peroxide. Clin. Chem., 28: 2077-2080.*

xv. *Finley, P.R., Schifman, R.B., Williams, R.B. and Lichti, D. A. (1978): Cholesterol in high-density lipoprotein: use of Mg+2/dextran sulfate in its enzymatic measurement. Clin. Chem., 24 (6): 931-3.*

xvi. *Friedewald, W.T.; Lovy, R.I.; and Fredriekson, D.C. (1972): Estimation of concentration of LDL-lipoproteins separated by three different methods. Clin. Chem., 28: 2077.*

xvii. *17-Stanford, B. and Charles, B. (2003): Pharmaceutical statistics: practical and clinical applications. Edition Number: 4, Publisher: Taylor & Francis, Inc.*

xviii. *Taskinen MR (2002): Diabetic dyslipidemia. Atheroscler Suppl, 3(1):47–51*

xix. *Ozder Acian. (2014). Lipid profile abnormalities seen in T2DM patients in primary healthcare in Turkey: a cross-sectional study. Lipid Health Dis; 13: 183.*

xx. *Haffner SM, Lehto S, Ronnemaa T, Pyorala K, L.aakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med 1998; 339: 229-234..*

xxi. *Windler E. What is the consequence of an abnormal lipid profile in patients with type 2 diabetes or the metabolic syndrome? Atheroscler. Suppl. 2005;6: 11-14.*

xxii. *Meenu, J; Jayendrasinh, J M. and Neeta, M: (2013): Correlation between AbA1c values and lipid profile in type 2 diabetes mellitus. Intrn. J. of Basic and Applied physiology. Vol. (2) Issue 1 , 47-50.*

xxiii. *Masram, S.W.; Bimanpalli, . M.V. and Ghangle S (2012): Study of Lipid Profile and Glycated Hemoglobin in Diabetes Mellitus. Indian Medical Gazette 257-265.*

xxiv. *Ramirez, L., Nogare, A., Hsia, C. and Arauz, C. (1991): Relationship between diabetes control and pulmonary function in IDDM. Am J Med 91: 371–376.*

xxv. *Goldberg IJ. Lipoprotein lipase and lipolysis: central roles in lipoprotein metabolism and atherogenesis. J Lipid Res 1996; 37: 693-707..*

xxvi. *Tavangar K, Murata Y, Pedersen ME, Goers JF, Hoff-man AR, Kraemer FB. Regulation of lipoprotein lipase in the diabetic rat. J Clin Invest 1992; 90: 1672-1678.*

xxvii. *Ram Vino dMahato1, Prajwal Gyawali2, Pramod Psd. Raut3, Prashant Regmi2, Khelanand Psd. Singh2, Dipendra Raj Pandeya4, Prabin Gyawali5.(2011): Asociation between glycaemic control and serum lipid profile in type 2 diabetic patients: Glycated haemoglobin as a dual biomarker. Biomedical Research 2011; 22 (3): 375-380.*

xxviii. *Elinasri HA and Ahmed AM (2008): Patterns of lipid changes among type 2 diabetes patients in Sudan. East Mediterr Health J. 14(2):314–324.*

xxix. *Mooradian AD (2009): Dyslipidemia in type 2 diabetes mellitus. Nat Clin Pract EndocrMetab. 5:150–159.*

xxx. *Irene, M. Stratton, I R and Adler, I A (2000): Association of glycemia with macrovascular and microvascular complications of type 2 diabetes. (UKPDS); Brit. Med. J. Vol. 321:405-416.*

xxxi. *Gimeno-Orna JA, Faure-Nogueras E and Sancho-Serrano MA. Usefulness of total cholesterol/HDL-cholesterol ratio in the management of diabetic dyslipi-daemia. Diabet Med 2005; 22: 26-31.*

xxxii. *Lemieux I, Lamarche B, Couillard C, Pascot A, Cantin B, Bergeron J, et al. Total cholesterol /HDL cholesterol ratio vs LDL cholesterol /HDL cholesterol ratio as in-dices of ischemic heart disease risk in men. The Quebec Cardiovascular Study. Arch Intern Med 2001; 161: 2685-2692.*

xxxiii. *Peters AL. (2008). Clinical relevance of non-HDL cholesterol in patients with diabetes. Clinial Diabetes; 26:3-7.*

xxxiv. *Khan HA, Sobki SH, Khan SA. Association between glycemic control and serum lipids profile in type 2 diabetic patients: HbA1c predicts dyslipidemia. Clin Exp Med 2007; 7: 24-29.*

xxxv. *Sibley SD, Thomas W, de Boer I, Brunzell JD, Steffes MW. Gender and elevated albumin excretion in the Diabetes Control and Complications trial/ Epidemiol-ogy of Diabetes*

Interventions and Complications (DCCT/EDIC) cohort: role of central obesity. Am J Kidney Dis 2006; 47: 223-232.

xxxvi. *Taskinen MR (1992): Quantitative and qualitative lipoprotein abnormalities in diabetes mellitus. Diabetes 41:12–17.*

xxxvii. *Howard BV (1987): Lipoprotein metabolism in diabetes mellitus. J Lipid Res. 28(6):613–628.*

xxxviii. *Molitch, M.E. (2006): Management of Dyslipidemia in Patients with Diabetes and Chronic Kidney Disease. Clin J. Am SocNephrol 1 (5): 1090-1099*

xxxix. *Nathan, D.M.; Cleary, P.A.; Backlund, J.Y.; Genuth, S.M.; Lachin, J.M.; Orchard, T.J.; Raskin, P.; and Zinman, B. (2005): Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group: Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. N Engl J. Med. 353(25): 2643-53.*

xl. *Taylor, K.G.; John, W.C.; Mathews, K.A.; and Wright, A.D.(1982): A prospective study on the effect of 12 months treatment on serum lipids and apolipoproteins A-I, A-II and B in type II (non insulinodependent) Diabetes. Diabetologia; 23: 507-510*