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Abnormalities in Plasma Concentration of Lipids and Fibrinogen of Egyptian Microalbuminuric NIDDM Type 2 Diabetic Patients

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Abstract

Introduction: Diabetes mellitus is associated with derangements in the serum levels of several biochemical parameters. Fibrinogen is a strong cardiovascular risk factor in the general population, and increased fibrinogen plasma concentrations have been reported in type 2 diabetic patients.

Purpose: To assess fibrinogen, lipids and lipoprotein composition and the relationship between fibrinogen and lipoprotein abnormalities and urinary albumin excretion (UAER) in type 2 diabetic patients.

Study Design: 48 control persons (24 male, 24 female), 96 diabetic patients (48 male: 24 normoalbuminuric, 24 microalbuminuric, 48 female: 24 normoalbuminuric, 24 microalbuminuric). They were divided into 9 groups. All groups were matched for age, sex, BMI. The diabetic patients were matched with the duration of diabetes. Diabetic patients were classified according to their level of urinary albumin excretion rate (UAER) into normoalbuminuric (<20 µg/min), microalbuminuric (20-200 µg/min). Diabetic patients with other complications were excluded.

Materials and Methods: Blood and urine samples were collected from the diabetic patients and non-diabetic healthy controls. Glucose, $HbA1_C$, Hb, creatinine, fibrinogen, urinary albumin excretion rate, cholesterol, HDL-C, LDL-C, VLDL-C, Ch/HDL-C, HDL-C/LDL-C, LDL-C/HDL-C, triacylglycerol and phosphlipids were determined.

Results and Discussion: A significant elevation of glucose, $HbA1_C$, fibrinogen, urinary albumin excretion rate, cholesterol, LDL-C, VLDL-C, Ch/HDL-C HDL-C/LDL-C, LDL-C/HDL-C, triacylglycerol and phosphlipids and a significant decrease in HDL-C were obsereved in the diabetic groups in comparison with control group and the same was found for microalbuminuric vs normoalbuminuric diabetic groups.

Conclusion: Albuminuria is the best predictor of fibrinogen plasma levels in type 2 diabetic patients. Plasma fibrinogen level is increased in type 2 normoalbuminuric diabetic patients (without detectable micro- and macrovascular complications), which indicate that hyperfibrinogenemia may precede the onset of clinical vascular complications and might therefore contribute to the increased cardiovascular risk in type 2 diabetes.

Keywords: type II diabetes mellitus (NIDDM), lipids, diabetes mellitus, fibrinogen, hæmoglobin (Hb), glycosylated hæmoglobin ($HbA1_C$)

Introduction

It is well established that non-insulin-dependent diabetes mellitus, NIDDM, is associated with increased morbidity and mortality compared with the general population. The microvascular and neuropathic complications of diabetes are a major clinical and public health problem in Egypt (Herman *et al.*, 1998). In a cross-sectional, population-based survey done in Egypt, Herman *et al.* (1998), found that among people with previously diagnosed diabetes, mean glycosylated hæmoglobin ($HbA1_C$) was 9.0%; Forty-two per cent had retinopathy; 21% had albuminuria, and 22% are neuropathy. During the past 20 years, major socio-demographic changes have occurred in the Eastern Mediterranean Region (WHO, 1993) associated with

changes in physical activity and dietary patterns that have promoted the development of non-communicable diseases as diabetes which is considered as an emerging clinical and public health problem in Egypt (Herman *et al.*, 1997 & 1998). Several hematological abnormalities have been defined in patients with diabetes mellitus, despite the lack of classic hematologic pathologic findings in this condition (Jones & Peterson, 1981). Patients with diabetes commonly have a greater degree of anemia for their level of renal impairment than those presenting with other causes of renal failure (Craig *et al.,* 2005). Dyslipidaemia is common in patients with Type 2 diabetes and is held to be responsible for considerable cardiov-ascular disease (CVD)-related morbidity and mortality (Bustos *et al.,* 2005) and should therefore receive preventive interventions and are frequently treated with oral antihyperglycaemic medications (Krentz 2003 and Buse *et al.,* 2004).

Microalbuminuria represents a sensitive marker of cardiovascular disease (Mogensen, 1984) that is associated with hyperfibrinogenemia in type 2 diabetes (Allawi and Jarrett, 1990). Fibrinogen plays a crucial role in many atherothrombosis-associated processes as hæmostasis fibrinolysis, inflammation, platelet aggregation, blood viscosity, smooth muscle proliferation and migration (Maresca *et al.*, 1999). Fibrinogen is a strong and independent cardiovascular risk factor (Ernst, 1991 and Barazzoni et al., 2000 & 2003) and is regulated by interplay of genetic and environmental factors. Plasma fibrinogen may also be increased in type 2 diabetes and non-diabetic populations (Boulogne & Vantyghem 2004; Howard *et al.* 2000; Missov, 1996; Maresca *et al.*, 1999; Imperatore *et al.*, 1998; Kannel and McGee, 1979), but it remains controversial whether fibrinogen is in a causal relationship or merely in association with the atherosclerotic process (Van Der Bom *et al.*, 1998). Fibrinogen production is greatly enhanced by the acute phase response to inflammatory processes (Vasse *et al.*, 1996), which might reflect the low-grade inflammation associated with vascular disease. Increased fibrinogen level may be true modifier of the atherosclerotic disease and contribute to its progression. Moreover, fibrinogen and fibrin degradation products might in turn enhance the inflammatory aspect of vascular lesions by regulating cytokine production and leukocyte-endothelial interactions (Flick *et al.,* 2004). However, the mechanisms leading to hyperfibrinogenemia in type 2 diabetic subjects have not been elucidated so far, even though potential role of low-grade inflammation and albuminuria has been discussed (Yudkin *et al.,* 2004; Zanetti *et al.,* 2001).

Aim Of The Work

To assess fibrinogen, lipids and lipoprotein composition and the relationship between fibrinogen and lipoprotein abnormalities and urinary albumin excretion (UAER) in type 2 diabetic patients.

Research Design And Methods

Patients and Controls

This study was conducted on 96 cases (48 male; and 48 female) of NIDDM patients, who were attending governmental, and Non-Governmental Organization (NGO's) as hospitals and clinics, and 48 healthy (24 male and 24 female) controls. They were divided into 9 groups as follows: Group 1 (All: G 1): all normal control (48 persons); Group 2 (All: G2): all normoalbuminuric diabetic patients (48 patients); Group 3 (All: G3): all microalbuminuric diabetic patients (48 patients); Group 4 (M: G 1-1): normal male control (24 persons); Group 5 (M: G2-1): all male normoalbuminuric diabetic patients (24 patients); Group 6 (M: G3-1): male microalbuminuric diabetic patients (24 patients); Group 7 (F: G 1-2): normal female control (24 persons); Group 8 (F: G2-2): all female normoalbuminuric diabetic patients (24 patients); Group 9 (F: G3-2): female microalbuminuric diabetic patients (24 patients). The study groups were well matched for age, sex distribution and BMI with their respective control groups and

with each other. The age range was (25-40 y), Duration of diabetes was (≈6.0; 1.0-10.0 Y), Body Mass Index (BMI, ≈25.0; 22.0-26.0). The selected subjects were non-smokers. The diabetic patients are not taking any medicines other than oral anti-diabetic pills for the past 4 years (at least). Diabetic patients were classified according to their level of urinary albumin excretion rate (UAER) into normoalbuminuric (<20 µg/min), microalbuminuric(20-200 µg/min) i.e. 96 diabetic patients (48 male: 24 normoalbuminuric, 24 microalbuminuric; 48 female: 24 normoalbuminuric, 24 micro-albuminuric). The diagnosis of type II diabetes mellitus was based on the criteria of the Expert Committee on the diagnosis of diabetes mellitus (2000). Diabetic patients with other complications were excluded.

Materials And Methods:

Anthropometrics Measurements

Weight and height were measured in indoor clothing without shoes and body mass index (BMI) was calculated where BMI=wt (kg)/ht (m^2).

Blood Sampling

Fasting blood samples were drawn and collected in 2 tubes with anticoagulant, one to get blood for Hb determination and the other to get plasma for the remaining analysis. They were kept at –80 °C if not analyzed immediately. Glucose, $HbA1_C$, crearinine, cholesterol, HDL-C, LDL-C, VLDL-C, triacylglycerol, phospholipids was determined. Ch/HDL, HDL/LDL, LDL/HDL were calculated. Repeated freezing and thawing was avoided.

Urine Sampling

24 hr urine samples were colleted in special sterilized container containing preservative, 0.5 ml 1% w/v sodium merthiolate. Contaminated urine was excluded. They were kept at –80 °C if not analyzed immediately. Freezing and thawing was avoided.

Methods Of Biochemical Parameters Assay

Blood Analysis

Glucose was determined using Randox kit (Barham & Trender, 1972). Hb was determined using Eagle Diagnostics kit (Drabbkin, 1949; Van Kampen & Zijlstra, 1965; Tietz, 1987). Fibrinogen was determined using method of Wotten, 1974; Hurlet & Josso, 1972; Desting *et al.*, 1960 (a, b). Creatinine was determined using method of Broad & Sirota, 1948 and Bohner, 1968. Total cholesterol, TC, was determined using Bio Mérieux kit (Richmond, 1973 and Allain *et al*., 1974). Total triacylglycerol, TG, was determined using Bicon kit (Bucolo & David, 1973). Serum HDL was determined using Bio Mérieux kit (Burstein *et al*., 1970 and Lopes Virella *et al*., 1977). Serum LDL-C was determined using Bio Mérieux kit (Friedewald *et al*., 1972; Levy *et al.*, 1981 and Fruchart, 1982). VLDL-C was calculated by using the following equation: VLDL-C = total cholesterol - (HDL-C+LDL-C). Phospholipids were determined using method of Connerty *et al.* (1961). $HbA1_C$ was determined using HPLC (Pérez *et al.*, 1998 and John, 2003).

Urine Analysis

Urinary albumin was determined implying immunoturbidometeric assay method using Randox kit (Bakker,1988; Elving *et al.*, 1989; Mogensen & Christensen, 1984).

Statistical Analysis

Data are expressed as Mean ±SE. Data were assessed by t-test (Avram, 1964) and Duncan test (Steel & Torrie, 1969). The correlation coefficients were determined by Pearson's simple linear regression analysis (Steel & Torrie, 1969). Statistical significance was accepted at $P < 0.05$.

Results

Table (1) shows the clinical characteristics of NIDDM (type 2) patients and controls.

The study groups were well matched for age, sex distribution and BMI with their respective control groups and with each other. The study groups (male, female and all: M+F) were well matched for the duration of diabetes with each other. There are no significant differences in age, duration of diabetes and BMI for all groups. The age range was (25-40 y), Duration of diabetes was (≈6.0; 1.0-10.0), Body Mass Index (BMI, ≈25.0; 22.0-26.0).

Data of table (1) reveals that glucose and $HbA1_C$ level of groups: 2, 3, 2-1, 3-1, 2-2, 3-2 diabetic (normo- or micro-albuminuric) patients are significantly higher than their respective control groups. Sex has no significant effect on glucose level or on $HbA1_C$, no significant differences between male and female of the same group. Very highly significant, positive, direct correlation between glucose and $HbA1_C$ was found for all groups either control or diabetic (r: 0.60-0.79; $P \leq 0.001$; table 2).

Data of table (1) reveals that Hb level of groups: 2, 3, 2-1, 3-1, 2-2, 3-2 diabetic (normo- or micro-albuminuric) patients are similar to each other with tendency of males to be higher than females. Sex has a significant effect on Hb concentration, where males show a significant increase when compared with its respective female group (14.41 vs 13.01, $P \leq 9.7E\text{-}5$; 14.52 vs 13.23, $P \leq 1.8E\text{-}6$; 14.61 vs 13.29, $P \leq 3.9E\text{-}6$; M vs F).

Data of table (1) reveals that creatinine level of groups: 2, 3, 2-1, 3-1, 2-2, 3-2 (normo- or micro-albuminuric) patients are similar to each other in all groups. Sex has a significant effect on creatinine concentration.

Data of table (1) reveals that urinary albumin excretion rate (UAER) and fibrinogen level of groups: 2, 3, 2-1, 3-1, 2-2, 3-2 diabetic (normo- or micro-albuminuric) patients are significantly higher than their respective control groups.

Data of table (1) reveals that cholesterol, LDL-C and VLDL-C level of diabetic patient is significantly higher than control while, HDL-C is significantly lower than control for groups: 2, 3, 2-1, 3-1, 2-2, 3-2. This also applies on microalbuminuric vs normoalbuminuric patients.

Data of table (1) reveals that plasma triacylglycerol levels were significantly higher in the NIDDM patients (normo- or micro-albuminuric) compared to control.

Data of table (1) reveals that plasma phosphlipids levels were significantly higher in the NIDDM type 2 patients (normo- or micro-albuminuric) than control or between diabetics with normo- or micro-albuminuria. Sex has no significant effect on phosphlipids level, no significant differences between male and female of the same group were found.

Table (2): Correlation coefficient between age, duration of diabetes, BMI, glucose, $HbA1_C$, fibrinogen and the remaining parameters.

	BMI Kg/m^2	Glucose mg%	$HbA1_C$	Hb gm%	Fibri-nogen mg%	Creat-inine mg%	UAER µg/min	Choles-terol mg%	HDL mg%	LDL mg%	VLDL mg%	TG mg%	PhLP mg%
Age													
All: G 1	0.07	0.14	0.25 [1]	0.14	-0.10	0.13	-0.29 [2]	0.04	0.11	0.01	0.06	-0.01	-0.32 [2]
G 2	0.21	0.001	0.06	0.29 [2]	0.19	-0.28 [1]	-0.17	-0.11	-0.25 [1]	-0.10	0.01	-0.02	-0.06
G 3	0.26 [1]	-0.16	-0.16	-0.09	-0.08	0.40 [4]	-0.02	-0.39 [4]	-0.32 [2]	-0.39 [4]	-0.40 [4]	-0.54 [4]	-0.54 [4]
M: G 1-1	0.12	0.13	0.41 [2]	-0.17	0.08	0.55 [4]	-0.51 [3]	-0.05	0.15	-0.13	-0.05	-0.04	-0.27
G 2-1	0.04	0.13	0.26	-0.15	0.17	-0.27	0.11	-0.46 [2]	-0.64 [4]	-0.45 [2]	-0.23	0.08	-0.40
G 3-1	0.50 [3]	0.35 [1]	0.56 [4]	0.41 [2]	-0.01	0.40 [1]	0.54 [4]	-0.51 [4]	-0.47 [2]	-0.52 [4]	-0.53 [4]	-0.46 [2]	-0.25
F: G 1-2	-0.22	0.03	-0.10	0.19	-0.17	-0.51 [3]	-0.07	0.03	-0.01	0.04	0.03	-0.06	-0.23
G 2-2	0.41 [2]	-0.11	-0.13	0.64 [4]	0.26	-0.33	-0.52 [4]	0.18	0.15	0.18	0.18	-0.18	0.40
G 3-2	0.03	-0.50 [3]	-0.44 [2]	-0.57 [4]	-0.05	0.38 [1]	-0.60 [4]	-0.41 [2]	-0.31	-0.42 [2]	-0.43 [2]	-0.66 [4]	-0.79 [4]
Duration													
All: G 2	0.22	-0.05	0.04	0.34 [3]	0.19	-0.34 [3]	-0.20	-0.08	-0.22	-0.06	0.06	-0.01	-0.06
G 3	0.15	-0.06	-0.10	-0.12	0.04	0.40 [4]	0.05	-0.20	-0.11	-0.20	-0.24 [1]	-0.39 [4]	-0.50 [4]
M: G 2-1	-0.05	0.09	0.26	-0.22	0.03	-0.46 [2]	0.04	-0.49 [3]	-0.68 [4]	-0.48 [3]	-0.24	0.04	-0.42 [2]
G 3-1	0.43 [2]	0.45 [2]	0.61 [4]	0.26	0.31	0.44 [2]	0.61 [4]	-0.22	-0.18	-0.22	-0.23	-0.15	-0.08
F: G 2-2	0.47 [2]	-0.15	-0.15	0.73 [4]	0.39 [1]	-0.28	-0.50 [3]	0.24	0.19	0.24	0.23	-0.15	0.43 [2]
G 3-2	-0.19	-0.40 [1]	-0.37 [1]	-0.62 [4]	0.03	0.32	-0.58 [4]	-0.29	-0.14	-0.30	-0.36 [1]	-0.63 [4]	-0.84 [4]
BMI													
All: G 1		-0.04	0.24 [1]	-0.13	-0.03	0.42 [3]	0.18	-0.06	-0.22	-0.09	0.21	0.14	-0.27 [1]
G 2		0.01	-0.09	0.42 [4]	-0.08	0.21	0.17	0.21	0.16	0.22	0.25 [1]	0.12	-0.21
G 3		-0.14	-0.29 [2]	0.50 [4]	-0.30 [2]	0.42 [4]	0.26 [1]	-0.11	-0.25 [1]	-0.12	0.02	0.04	0.02
M: G 1-1		0.04	0.26	-0.76 [4]	0.14	0.16	-0.02	0.09	-0.24	0.10	0.32	0.27	-0.16
G 2-1		0.46 [2]	-0.03	0.10	0.23	0.55 [4]	0.52 [4]	0.45 [2]	0.40 [2]	0.48 [3]	0.39 [1]	0.25	-0.08
G 3-1		0.37 [1]	0.15	0.11	0.03	0.55 [4]	0.24	-0.30	-0.39 [1]	-0.32	-0.15	-0.27	0.04
F: G 1-2		-0.33	0.03	0.001	-0.06	0.73 [4]	0.42 [2]	-0.38 [1]	-0.41 [2]	-0.39 [1]	-0.20	-0.18	-0.24
G 2-2		-0.35 [1]	-0.02	0.32	-0.19	-0.42 [2]	-0.32	-0.42 [2]	-0.57 [4]	-0.44 [2]	-0.15	-0.23	-0.10
G 3-2		-0.37 [1]	-0.36 [1]	0.39 [1]	-0.24	0.11	0.07	-0.36 [1]	-0.51 [3]	-0.37 [1]	-0.19	0.06	0.38 [1]
Glucose													
All: G 1			0.79 [4]	0.27 [1]	0.62 [4]	0.15	0.53 [4]	0.85 [4]	0.82 [4]	0.82 [4]	0.78 [4]	0.79 [4]	0.43 [4]
G 2			0.71 [4]	0.18	0.61 [4]	-0.09	0.14	0.52 [4]	0.43 [4]	0.50 [4]	0.63 [4]	0.81 [4]	0.57 [4]
G 3			0.69 [4]	0.02	0.50 [4]	-0.22	-0.10	-0.12	-0.14	-0.11	-0.12	-0.04	0.001
M: G 1-1			0.76 [4]	0.35 [1]	0.82 [4]	0.60 [4]	0.65 [4]	0.87 [4]	0.76 [4]	0.81 [4]	0.90 [4]	0.91 [4]	0.71 [4]
G 2-1			0.66 [4]	0.53 [4]	0.66 [4]	0.19	0.83 [4]	0.56 [4]	0.47 [3]	0.54 [4]	0.67 [4]	0.84 [4]	0.53 [4]
G 3-1			0.60 [4]	-0.15	0.48 [3]	0.10	-0.37 [1]	-0.49 [3]	-0.54 [4]	-0.50 [3]	-0.41 [2]	-0.09	-0.20
F: G 1-2			0.79 [4]	0.04	0.65 [4]	-0.34 [1]	0.42 [2]	0.83 [4]	0.86 [4]	0.84 [4]	0.63 [4]	0.68 [4]	0.42 [2]
G 2-2			0.74 [4]	0.22	0.57 [4]	-0.34 [1]	-0.43 [2]	0.67 [4]	0.56 [4]	0.64 [4]	0.76 [4]	0.89 [4]	0.60 [4]
G 3-2			0.74 [4]	0.42 [2]	0.48 [3]	-0.43 [2]	0.27	0.23	0.22	0.25	0.16	0.08	0.05
$HbA1_C$													
All: G 1				0.40 [4]	0.55 [4]	0.44 [4]	0.58 [4]	0.72 [4]	0.62 [4]	0.71 [4]	0.66 [4]	0.63 [4]	0.44 [4]
G 2				0.04	0.62 [4]	-0.17	0.54 [4]	0.26 [1]	0.11	0.25 [1]	0.45 [4]	0.61 [4]	0.53 [4]
G 3				0.09	0.36 [3]	-0.47 [4]	0.56 [4]	-0.10	-0.10	-0.08	-0.13	-0.07	0.08
M: G 1-1				0.26	0.74 [4]	0.75 [4]	0.65 [4]	0.54 [4]	0.35 [1]	0.53 [4]	0.61 [4]	0.56 [4]	0.52 [4]
G 2-1				0.42 [2]	0.66 [4]	-0.28	0.39 [1]	0.42 [2]	0.28	0.40 [1]	0.62 [4]	0.57 [4]	0.44 [2]
G 3-1				0.41 [2]	0.08	0.06	0.74 [4]	-0.36 [1]	-0.37 [1]	-0.35 [1]	-0.34	-0.20	0.27
F: G 1-2				0.34	0.60 [4]	0.03	0.51 [4]	0.85 [4]	0.83 [4]	0.87 [4]	0.66 [4]	0.71 [4]	0.72 [4]
G 2-2				0.03	0.55 [4]	-0.01	0.73 [4]	0.28	0.06	0.28	0.48 [3]	0.74 [4]	0.58 [4]
G 3-2				0.31	0.35 [1]	-0.76 [4]	0.64 [4]	0.12	0.12	0.15	0.05	0.08	-0.15
Fibrinogen													
All: G 1				0.14		0.58 [4]	0.77 [4]	0.56 [4]	0.37 [1]	0.48 [4]	0.75 [4]	0.55 [4]	0.36 [1]
G 2				0.33 [2]		0.11	0.64 [4]	0.50 [4]	0.43 [4]	0.50 [4]	0.50 [4]	0.39 [4]	0.52 [4]
G 3				0.05		0.16	0.63 [4]	0.30 [2]	0.16	0.30 [2]	0.40 [4]	0.55 [4]	0.03
M: G 1-1				0.14		0.58 [4]	0.84 [4]	0.56 [4]	0.37 [1]	0.48 [4]	0.75 [4]	0.55 [4]	0.36 [1]
G 2-1				0.43 [2]		0.40 [1]	0.72 [4]	0.35 [1]	0.30	0.36 [1]	0.38 [1]	0.23	0.25
G 3-1				0.27		0.48 [3]	0.85 [4]	0.33	0.36 [1]	0.31	0.32	0.11	0.01
F: G 1-2				0.26		0.07	0.77 [4]	0.38 [1]	0.53 [4]	0.41 [2]	0.04	0.16	0.40 [2]
G 2-2				0.67 [4]		0.05	0.66 [4]	0.84 [4]	0.80 [4]	0.85 [4]	0.76 [4]	0.56 [4]	0.67 [4]
G 3-2				0.59 [4]		0.36 [1]	0.87 [4]	0.41 [2]	0.24	0.40 [2]	0.54 [4]	0.64 [4]	0.23

[1]: $P < 0.05$; [2]: $P < 0.02$; [3]: $P < 0.01$; [4]: $P < 0.001$

Discussion

In this study, the results for glucose and $HbA1_C$ level of diabetic patients are in agreement with Al-Muhtaseb *et al.* (1991).

In this study, the results for Hb concentration of diabetic patients are in agreements with Reverter *et al.* (1994).

Microalbuminuria represents a sensitive marker of cardiovascular disease (Mogensen, 1984) that is associated with hyperfibrino-genemia in type 2 diabetes (Allawi and Jarrett, 1990). Fibrinogen has an independent effect on cardiovascular mortality suggesting that both endothelial dysfunction and chronic inflamm-ation are involved in the excess cardiovascular mortality of type 2 diabetic patients (Bruno *et al.*, 2005). All diabetic groups had signif-icantly higher fibrinogen level. Fu and Nair (1998) indicated that increased fibrinogen plasma concentration is not associated with enhanced fibrinogen production in elderly non-diabetic or diabetic humans, which indicate that differential mechanisms may determine hyperfibrino-genemia in diabetic subjects. Ceriello *et al*. (1995) stated that hyperglycemia activate the coagulative cascade, thus increasing thrombin forma-tion and fibrinogen degradation products, which, in turn, may stimulate hepatic fibrinogen synthesis. In this study the results are in agreement with Jones and Peterson (1979). Control groups had normal plasma fibrinogen level. In this study, the results reveals a significant increase when microalbuminuric groups were compared with normoalbuminuric grougs and this result differ with that of Unuigbe *et al.* (2005) where they found that plasma fibrinogen concentration did not differ significantly in the different groups of diabetics (diabetics with normal renal function and diabetics with mild renal imp-airment. Sex has a significant effect on plasma fibrinogen level, where female shows a significant increase when comp-ared with its respective male group (305.13 vs 283.88, $P \leq 0.04$; 321.88 vs 298.38, $P \leq 0.04$; 429.0 vs 392.75, $P \leq 0.016$; F vs M). Very highly significant, positive, direct correlation between plasma fibrinogen level and urinary albumin excretion was found for all groups either control or diabetic. Zanetti *et al. (*2001) stated that the correlation between fibrinogenemia and albuminuria could be attributed to their common association with the inflammation underlying diabetes and/or vascular and renal disease. Several authors as Festa *et al.* (2000); Tkáč *et al*. (2003) and Javorský *et al*. (2005), had reported results resemble the results of this study in which a correlation between fibrinogen and albuminuria in type 2 diabetes patients have been found.

All diabetic groups had significantly higher cholesterol, LDL-C and VLDL-C while, HDL-C is significantly lower than control. A low level of high-density lipopr-otein cholesterol (HDL-C) is a key feature of type 2 diabetes. HDL particles exert an anti-atherogenic, antioxidative as well as anti-inflammatory effect (Gordon *et al*., 1989). Low HDL-C (and high TG) levels are associated with increased cardiovascular disease risk (Gordon *et al*., 1989; Assmann and Schulte, 1992; Jeppesen *et al*., 1997; Manninen *et al*., 1992). In this study, the results are in agreement with Akanji *et al.* (1989) and Al-Muhtaseb *et al.* (1991). In this study, the results for micro- vs normo-albuminuric diabetic patient disagree with Reverter *et al. (*1994). Reduced HDL chol-esterol levels are often accompanied by elevations in plasma TG levels (Lamarche *et al*., 1996), a process mediated by chole-sterol ester transfer protein, CETP (Tall, 1995). A very highly significant correlation ($P \leq 0.001$) between HDL-C and triacylgly-cerol was found in all groups.

Abnormal lipid metabolism often presents in patients with type 2 diabetes with an excess of atherogenic small low-density lipoprotein (LDL) particles (Rosenson, 2005). Resistance to insulin likely underlies the changes that occur in lipid parameters of type 2 diabetes and usually it is associated with higher conc-entrations of cholesterol and TG and lower concentrations of HDL cholesterol (Garvey *et al*., 2003) and it may contribute to the atherogenic dyslipidemia of diabetes by

increasing the hepatic secretion of very low-density lipoprotein, VLDL (Taskinen *et al.,* 1984). Type 2 diabetes is characterized by increased secretion of apolipoprotein (apo) B as a result of increased free fatty acid (FFA) flux to the liver (Cummings *et al.,* 1995; Laws *et al.,* 1997; Duvillard *et al.,* 2000; Krauss and Siri, 2004) and an inhibition of microsomal triglyceride transfer protein activity (a protein identified as a key component of the VLDL assembly process may occur) and this leads to increased plasma levels of TG and reduced level of HDL-C.

Sex has no effect on cholesterol, LDL-C, VLDL-C and HDL-C level of control group since no significant difference between male and female of control group was found. But for diabetic patient (either normo- or micro-albuminuric) the case is different where a significant difference between male and female group was found. Males show a significant increase when compared with its respective female group.

Data of table (1) reveals that atherogenic indices of diabetic patients as Ch/HDL-C and LDL-C/HDL-C showed a significant increase, while HDL-C/LDL-C showed a significant decrease when compared with the control group. In this study, the results are in agreement with Akanji *et al.* (1989) and Al-Muhtaseb *et al.* (1991).

Plasma triacylglycerol levels were significantly higher in the NIDDM patients compared to control. In this study, the results are in agreement with Akanji *et al.* (1989); Owens *et al.* (1991) and Al-Muhtaseb *et al.* (1991). The mechanisms responsible for hypertriglyceridemia may be an increased hepatic secretion of VLDL and a delayed clearance of triacylglycerol (TG)-rich lipop-roteins, which might mainly be due to, increased levels of substrates for triacylglycerol (TG) production, free fatty acids, and glucose. The latter (glucose) could be secondary to decreased activity of lipoprotein lipase (LPL), a key enzyme for lipoprotein–TG hydrolysis (Howard, 1987; Taskinen, 1992 and Yoshino *et al.,* 1996). Hypertrigl-yceridemia usually accompanies decreased HDL cholesterol, which is also a prominent feature of plasma lipid abnorm-alities seen in diabetic subjects (Howard, 1987; Taskinen, 1992 and Yoshino *et al.,* 1996). It has been reported that the diabetic dyslipidemia seems to be more obvious when accompanied by diabetic nephropathy (Attman, 1992 and Ekberg, 1990). Kinetic studies on nephrotic syndrome have revealed that both overproduction of VLDL and a defect in VLDL removal (Vega and Grundy, 1988) are associated with increased plasma TG concentrations, suggesting that similar mechanisms are exerted in diabetic nephro-pathy. On the other hand, several reports have demonstrated that plasma TG concentration is significantly increased even in the early stage of diabetic nephropathy, e.g., in patients with microalbuminuria (Niskanen, 1990). Because the amount of urinary albumin excretion is too small to reduce plasma albumin concentration, the mechanism for hypertriglyceridemia in microalbuminuric diabetic subjects must be different from that in nephrotic syndrome. However, the mechanisms for hypertriglyceridemia in diabetic subjects with microalbuminuria have not been elucidated. Lipoprotein lipase (LPL) is produced in parenchymal cells, translocated to the endothelial cell surface and anchored there via interaction with heparin sulfate proteoglycans, HSPG, (Goldberg, 1996). Deckert *et al*. (1989 & 1992) proposed that microalbuminuria in diabetic patients may reflect widespread vascular damage. Moreover, they speculated that LPL attached to HSPG moiety is decreased by the gener-alized endothelial cell damage, thereby causing hypertriglyceridemia in diabetic subjects with microalbuminuria (Deckert *et al*., 1992 and Blann and Taberner, 1995). In this study the significantly higher triacylglycerol levels of diabetic patients than controls are not influenced by degree of glycaemic control, which are in agreement with Akanji *et al.* (1989).

Epidemiological studies have revealed that plasma triglyceride (TG) is an independent risk factor of coronary heart disease in diabetic subjects (Fontbonne, 1989 and Laakso, 1993). All diabetic patients showed significant increases in triacylgly-cerol/ total cholesterol ratio with respect to

control and this agree with Sanchez *et al*. (1994).

Plasma phosphlipids levels were significantly higher in the NIDDM patients than control, which agree with Al-Muhtaseb *et al*. (1991).

Table (2) shows that hæmoglobin of G 2, 3-1, 2-2 and 3-2 significantly positively correlates with age. Creatinine of G 3, 3-1, 3-2 (microalbuminuric) significa-ntly correlates (positively) with age. In control group sex has an effect where male significantly correlates (positively) while female significantly correl-ates (negatively) with age. A significant inverse correlation between Urinary albumin excretion rate (UAER), serum cholesterol, LDL-C, VLDL-C, TG, phospholipids with age of microalbuminuric (groups: 3, 3-1, 3-2) patients except UAER of group 3, phosp-hlipids of male group (3-1) was found. No correlation between fibrinogen and age was found. Sex has an effect on microalbuminuric patients where male significantly correlates (positively) while female significantly correlates (negatively) with age.

Most of the studied parameters significantly correlated with glucose especially $HbA1_C$ (where strong positive correlation was found which agree with Akanji *et al*., 1991) and fibrinogen where also a strong positive direct correlation was found.

A significantly positive correlation between fibrinogen and $HbA1_C$ was found for all 9 groups. No correlation between the serum creatinine of all diabetics and plasma fibrinogen concentration was found which agree with Unuigbe *et al*. (2005). A significantly positive correlation between TC, HDL-C, LDL-C, VLDL-C, TG, phospholipids and $HbA1_C$ was found in control groups (1, 1-1, 1-2). VLDL-C, TG and phospholipids of normoalbuminuric diabetic patient correlates positively (significantly) with $HbA1_C$. TC, HDL-C and LDL-C of microalbuminuric male diabetic patients significantly correlated (negatively) with $HbA1_C$ and this result agree with Chan *et al.* (2005). A significantly positive correlation between UAER and $HbA1_C$ was found for all 9 groups. Van Wersch *et al.* (1991) found a significant correlation only between UAER and $HbA1_C$ of microalbuminuric diabetic patients.

A significantly negative correlation between TC, HDL-C, LDL-C and BMI was found for female groups (control, normo-, micro-albuminuric). Also a significantly neg-ative correlation between HDL-C and BMI was found for microalbuminuric groups (3, 3-1, 3-2). No significant correlation between TG and BMI was found and this result differs with Chan *et al*. (2005) or between fibrinogen and BMI.

A significantly positive correlation between phospholipids and fibrinogen was found for control groups (1, 1-1, 1-2). Very highly significant, positive, direct correlation between plasma fibrinogen level and urinary albumin excretion (UAER) was found for all 9 groups either control or diabetic which, agree with Telejko *et al*. (1998); Zanetti *et al. (*2001), Festa *et al*. (2000); Tkáč *et al*. (2003) and Javorský *et al*. (2005). A significantly positive correlation between Hb and fibrinogen was found for normoalbuminuric groups (2, 2-1, 2-2). TC, LDL-C of all groups except microalbuminuric male diabetic patients are significantly correlated (positively) with fibrinogen.

A strongly significant positive correlation was observed between UAER, HDL-C and TG for all 9 groups and this result agree with Reverter *et al*. (1994).

Conclusion

Albuminuria is the best predictor of fibrinogen plasma levels in type 2 diabetic patients since a strong direct significant correlation exists between them. Fibrinogen production is substantially increased in type 2 diabetic patients, and this alteration is likely to play a key role in the increased fibrinogen concentrations in type 2 diabetes. The current results of normoalbuminuric diabetic patients in the present report indicate that hyper-fibrinogenemia may precede the onset of clinical vascular complications and might therefore contribute to the increased cardiov-ascular risk in type 2 diabetes.

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التركيزات الغير طبيعية للدهون و الفيبرونوجين في بلازما مرضى النوع الثاني لمرض السكر المصريين

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المقدمة: يرتبط مرض السكر باختلالات في تركيز بعض العوامل الكيميائية الحيوية. يعتبر الفيبرونوجين عامل مخاطرة يزيد في امراض القلب في المجتمع العام، و قد تم تسجيل زيادة الفيبرونوجين في بلازما مرضى النوع الثاني لمرض السكر.

الغرض: تقييم الفيبرونوجين و تكوين الدهون و الليبوبروتين و العلاقة بين التغيرات الغير طبيعية للفيبرنوجين و للدهون و معدل افراز الالبيومين في البول.

تصميم الدراسة: 48 شخص طبيعي (24 ذكور، 24 اناث)، 96 شخص مصابين بمرض السكر(48 ذكور: 24 طبيعيى افراز الالبيومين في البول، 24 قليلي افراز الالبيومين في البول ،48 اناث: 24 طبيعي افراز الالبيومين في البول، 24 قليلي افراز الالبيومين في البول). تم تقسيمهم الى 9 مجموعات متماثلين في العمر، الجنس، معامل كتلة الجسم. و كذلك فترة ظهور المرض. تم تقسيم المرضى تبعا لكمية، معدل الالبيومين المفرز في البول الى طبيعي افراز الالبيومين في البول (<20 ميكروجرام/دقيقة)، قليلي افراز الالبيومين في البول (20-200 ميكروجرام/دقيقة). تم استبعاد المرضى الذين لديهم مضاعفات اخرى.

الطرق المستخدمة: تم تجميع عينات دم و بول من المرضى و الاصحاء. تم تقدير نسبة السكر، الهيموجلوبين السكري، الهيموجلوبين، الكرياتنين، الفيبرونوجين، معدل افراز الالبيومين في البول، الكوليسترول الكلي، الكوليسترول في الليبوبروتينات ذات الكثافة العالية ، ذات الكثافة المنخفضة ، ذات الكثافة المنخفضة جدا، الفسفوليبيدات و الجليسريدات الثلاثية و كذلك حساب المؤشرات التي تدل علي خطورة تصلب الشرايين مثل نسبة الكوليسترول/ الليبوبروتينات ذات الكثافة العالية، الليبوبروتينات ذات الكثافة العالية/ الليبوبروتينات ذات الكثافة المنخفضة، الليبوبروتينات ذات الكثافة المنخفضة/ الليبوبروتينات ذات الكثافة المرتفعة.

النتائج و المناقشة: حدوث ارتفاع معنوي في السكر، الهيموجلوبين السكري، الفيبرونوجين، معدل افراز الالبيومين في البول، الكوليسترول الكلي، الكوليسترول في الليبوبروتينات ذات الكثافة المنخفضة ، الليبوبروتينات ذات الكثافة المنخفضة جدا، المؤشرات التي تدل علي خطورة تصلب الشرايين مثل نسبة الكوليسترول/ الليبوبروتينات ذات الكثافة العالية، الليبوبروتينات ذات الكثافة المنخفضة/ الليبوبروتينات ذات الكثافة المرتفعة، الفسفوليبيدات و الجليسريدات الثلاثية، و كذلك حدوث انخفاض معنوي في محتوى الكوليسترول في الليبوبروتينات ذات الكثافة العالية و ذلك في مجموعة المرضى القليلي افراز الالبيومين في البول عند مقارنتهم

بالاصحاء (المجموعة الضابطة) او مجموعة المرضى الطبيعيى افراز الالبيومين في البول.

الاستنتاج: يعتبر الزلال البولي (الالبيومينيوريا) من افضل المتنبئات بتركيز الفيبرونوجين في بلازما مرضى النوع الثاني لمرض السكر. يرتفع تركيز الفيبرونوجين في بلازما مرضى النوع الثاني لمرض السكر الطبيعيي افراز الالبيومين في البول و هذا يدل على أن الهيبرفيبرونوجينيميا تسبق حدوث المضاعفات في الجهاز الوعائي الدموي و بذلك تساهم في زيادة خطورة مضاعفات الاوعية الدموية القلبية في مرضى النوع الثاني لمرض السكر.