Determination of Angiopoietin Like Protein-4 Levels and Some Parameters in Iraqi Patients with Type 2 Diabetes Mellitus

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Abstract

A. Background: Diabetes initiates the thrombotic complications of atherosclerosis through changing the function of endothelial cells, smooth muscle cells and platelets. Also insulin resistance, hyperglycemia and dyslipidemia can lead to arterial atherosclerosis in diabetic patients. Angiopoietin like protein- 4 (ANGPTL4) is a multifunctional protein involved in lipid regulation, energy metabolism, angiogenesis, and inflammation. Its expression is stimulated in liver, heart, muscle and adipose tissue, during the acute phase response. C-reactive protein directly induces the expression of adhesion molecules by endothelial cells. Also recruiting monocytes into the vessel wall are triggered by the expression of specific chemokines particularly monocyte chemoattractant protein-1 (MCP-1), all these processes induce the risk of atherosclerotic complications with type 2 diabetes mellitus (T2DM).

B. Aim of this study: To study the role of ANGPTL4 in T2DM patients with and without atherosclerosis risk factor (dyslipidemia), and to demonstrate the relationship of ANGPTL4 with inflammatory process.

Keywords**:** Angiopoietin like protein- 4; Dyslipidemia; Type 2 diabetes mellitus**;** Inflammation.

Introduction

Type 2 Diabetes Mellitus is a chronic condition which is considered as a major cause of mortality and morbidity for its micro-vascular (retinopathy, nephropathy and neuropathy) and macro-vascular (coronary heart disease, peripheral vascular disease and stroke) complications. It is a multi-factorial disease that in its development, in addition to genetic predisposition, a number of environmental factors such as poor nutrition, lack of physical activity and obesity play major roles. Among these factors, obesity, dyslipidemia and hypertension have more potent relationship with T2DM which may link the ANGPTL4 and in flammatory marker to diabetic complications [1]. Cardiovascular disease CVD (broadly defined as stroke, coronary artery disease, and peripheral vascular disease) is the major cause of morbidity and mortality in patients with T2DM. CVD leads to 65%of deaths in diabetic patients. According to the updated US National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III guidelines, T2DM patients are categorized as having the highest level of risk for recurrent CVD events and they are in the same risk category as patients with acute coronary syndrome (ACS) [2].

Inflammation plays a significant role in both CVD and T2DM. Inflammation can lead to atherogenesis, atheromatous plaque rupture, and thrombus formation that cause ACS [3].

ANGPTL-4 is a multifunctional protein involved in lipid regulation, energy metabolism, angiogenesis, and inflammation. Its expression is stimulated in liver, heart, muscle and adipose tissue, during the acute phase response; it is an endogenous inhibitor of the triglyceride-hydrolyzing enzyme lipoprotein lipase (LPL) that catalyzes uptake of circulating lipids into tissues [4]. Irreversible inhibition of LPL activity by ANGPTL4 through converting active LPL dimer into inactive monomers consequently, overexpression of ANGPTL4 leads to hypertriglyceridemia and reduced fatty acid uptake in tissues, whereas ANGPTL4 deletion causes lowering of circulating triglyceride levels [5]. By inhibiting LPL activity, ANGPTL4 was previously shown to reduce macrophage uptake of triglycerides-derived fatty acids and impair macrophage activation [6], which may indirectly lead to decreased uptake of oxidized LDL [7]. C-Reactive Protein can induce the expression of tissue

factor by monocytes, and it is present in atherosclerotic plaques but not in the normal vessel wall [7,8]. CRP has several direct effects that may affect vascular disease progression. These reported functions include an ability to bind and activate complement, induce expression of several cell adhesion molecules as well as tissue factor, mediate LDL uptake by endothelial macrophages, induce monocyte recruitment into the arterial wall, and enhance production ofmonocyte chemoattractant protein-1 MCP-1 [9].

Subjects and Methods

A. Subjects:

This study was conducted on Iraqi patients, 24 T2DM patients without atherosclerosis risk factor (dyslipidemia) group P1; duration of diabetes was less than 5 years) and 30 T2DM patients with atherosclerosis risk factor (dyslipidemia), (group P2; duration of diabetes was more than 10 years) who attended to the National Diabetes Center of Al- Mustansiyria University, as well as 26 non diabetic healthy persons to serve as control (Group C). All subjects were informed of the purpose of the study and their consent was obtained. T2DM is diagnosed and classified according to the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus [10]. A detailed history and complete clinical examination were done. All demographic and clinical data of subjects were collected in the form of age and gender. Their weight, height, waist to hip ratio (WHR), waist to height ratio (WHtR), and body mass index (BMI) were calculated.

Dyslipidemia is change in plasma level of lipid elevated in TG (TG≥150 mg/dl) and decreased in level of HDL-C (HDL-C ≤ 40 mg/dl).

Systolic and diastolic blood pressures were recorded as a mean of three successive measurements. Group C was judged to be in good health according to their medical history and physical examination as well as their fasting and postprandial blood glucose. All T2DM patients were under treatment with Metformin (Glucophage) or a combination of Glibenclamideknown as sulfonylureas (Daonil) and Metformin as glucose lowering drugs.

B. Exclusion criteria were: Cushing's disease, acromegaly, chronic pancreatitis, pancreatactomy, pregnancy, history or even manifestation ofnephropathy, chronic renal failure, malignancies and chronic or acute inflammatory disease, patients who were taking aspirin, lipid lowering therapy and insulin therapy, history of smoking or alcohol drinking were excluded.

C. Sampling: Blood samples were drawn from subjects on overnight fasting (12hours). All blood samples were divided into 2 tubes: and divided in to 2 and 8 ml.; one with anticoagulant to aspirated plasma and the second without any anticoagulant (tubes gel) were put in centrifuge for 10 minutes after clotting; then serum was aspirated and divided into aliquots (250µl) in Eppendorff tubes, and stored in deep freeze (-20^{o}c) till used.

D. Laboratory investigations: Serum total cholesterol (TC) and triglyceride (TG) were analyzed using fully enzymatic methods with commercially available kits (SPINREACT, S.A/S.A.U, Spain). Serum HDL -cholesterol (HDL-C) was measured using direct enzymatic methods (RANDOX, United Kingdom) and serum LDL-cholesterol (LDL-C) and (VLDL) were calculated using the Friedewald formula (11). [LDL-C (mg/l) = TC – (TG/5 +HDL)], VLDL (mg/l) = TG/5

Atherogenic index of plasma (AIP) was calculated by the equation:

AIP= Log (TG/HDL-C) [12].

Risk Ratio1 (RR1) was obtained by dividing total cholesterol by HDL-cholesterol (TC/ HDL-C) and risk Ratio2 (RR2) was obtained by dividing LDL-cholesterol by HDL-cholesterol (LDL-C/ HDL-C), and these ratios are considered the greatest valuable for evaluation of CVD risk (National Cholesterol Education Program, 1994 and Grundy, 1989). Fasting Plasma glucose (FPG) concentration was analyzed by a hexokinase method (Spinreact, S.A.U, Spain), and insulin was analyzed by ELISA (DRG instruments GmbH, Germany). Concentration of ANGPTL4, MCP-1 and C-reactive protein (CRP) were determined by ELISA method (Ray Biotech, Inc. USA).The intra- and inter-assay coefficients of variation for the assays were

less than 10% and 12% respectively. Computer-based Homeostasis Model Assessment (HOMA) of insulin resistance (HOMA IR) and insulin sensitivity was previously detailed (http://www.dtu.ox.ac.uk).

E. Statistical analyses: A one-way analysis of variance (ANOVA) and multiple comparison were used to determine the difference between various groups .The results are expressed as Mean ± Standard deviation (SD.). Bivariate Pearson's product correlation coefficient(r) was used to test the strength of association between serum (ANGPTL4, MCP-1and hs-CRP) levels and other variables in the three groups (P1 and P2). Simple scatter plot was used to illustrate the significant correlation, while simple bar chart was used to show the significant differences of ANGPTL4, MCP-1and hs-CRP between groups. All statistical analyses were performed by using SPSS 17.0 (SPSSInc., Chicago, IL, USA). Differences were considered statistically significant at $p<0.05$ and highly significant at $p<0.01$.

Results

The results showed that significant increase in waist, WHR, WHtR, FPG, Insulin, HOMA2 parameters (IR, S%, and β%), VLDL, AIP, MCP-1 and hs-CRP was found in group (P1) in comparison with group (C), while ANGPTL-4 showed significant decrease in group (P1) in comparison with group (C) (Table (1)) (Fig.(1)).

Table (1) shows significant increase in duration of diabetes, diastolic B P, FPG, TC, TG, LDL, VLDL, AIP, RR1and RR2 of diabetes patients group (P2) in compression with group (P1) ($P<0.001$),while HDL shows significant decrease. Also ANGPTL-4, MCP-1, hs-CRP (Fig.(1)), BMI, smoking, SBP and HOMA2 -β % was significantly increased in group (P2) in comparison to group (P1) ($P<0.05$).However, age, weight, height, waist, hip, WHR, WHtR, F.P.G, Insulin, HOMA2-

IR and HOMA2 S% showed no significant differences between the two groups (P1 and P2) ($P> 0.05$) Table (1).

Also, the results showed positive correlation between ANGPTL-4 and hs-CRP in diabetes patients group (P1) Table (2), Fig.(2). ANGPTL-4 of group (P2) showed positive correlations with WHR, TC, TG, VLDL, AIP, RR1and RR2, and negatively correlated with hs-CRP Table (3), Fig.(3).

MCP-1 shows positive correlation with TG and VLDL of diabetes patients group (P1) (Table (2)), and a positive correlation with TC, LDL and RR2 of diabetes patients group (P2) Table (3).

hs-CRP shows positive correlation with Insulin and HOMA2 I.R in both patients groups (Table2). Also hs-CRP in group (P2) shows positive correlation with insulin, age, waist, hip and WHtR Table (3).

Table (1)
Mean and STD of Various parameters for studied groups.

Parameter	*Group (C) n=26 (mean± STD)*	*Group (P1) n=24 (mean± STD)*	*Group (P2) n=30 (mean± STD)*	*P value using ANOVA*
Number (male/female)	(14/12)	(19/4)	(17/13)	-
Age (year)	36 – 63	36 – 65	42 – 64*^{b}	0.102
Duration of diabetes (year)	-	2.58±1.71	11.46±1.79**^{c}	-
Weight(Kg)	75.27 ±8.34	79.17±7.48	78.77±9.04	0.192
Height (Cm)	169.15±7.97	168.88±5.77	168.3±7.29	0.900
BMI(kg/m^2)	26.3±1.67	27.22±1.99	28.42±1.92*$^{b\ c}$	<0.01
Waist (Cm)	95.73±6.40	100.33±6.07 *^{a}	101.43±8.77*^{b}	0.130
Hip (Cm)	102.85±4.91	101.92±5.74	102.77±8.87	0.869
WHR	0.926±0.04	0.98±0.04*^{a}	0.98±0.02*^{b}	<0.01
WHtR	0.561±0.04	0.59±0.04*^{a}	0.602±0.05* ^{b}	<0.01
Smoking	-	1.13±0.33	1.4±0.49* $^{b\ c}$	<0.01
Systolic B.P.(mm Hg)	124.23±5.03	124.58±6.50	138±17.69* $^{b\ c}$	0.311
Diastolic B.P. (mmHg)	76.92±4.70	78.33±3.80	84.67±5.71* ^{b}**^{c}	0.136
FPG (mg/dl)	87.46±7.96	158.708±47.9*^{a}	224.26±72.82*^{b}**	<0.01
Insulin (µIU/ml)	6.37±4.85	15.94±10.64*^{a}	10.75±11.94* ^{b}	<0.01
HOMA2-IR	0.93±0.73	2.26±1.40*^{a}	1.99±2.26* ^{b}	0.012
HOMA2 (S%)	147.13±68.25	63.79±50.76 *^{a}	82.23±36.59*^{b}	<0.01
HOMA2 (B%)	95.08±51.10	64.65±44.85*^{a}	26.62±26.52* $^{b\ c}$	<0.01
TC (mg/dl)	148.84±18.85	157.25±22.94	225.8±33.28*^{b}**^{c}	<0.01
TG(mg/dl)	92.5±17.23	118.79±26.29 *^{a}	218.6±134.09*^{b}**	<0.01
HDL (mg/dl)	54.03±8.43	51.75±7.09	39.16±5.33**^{b}**^{c}	<0.01
LDL (mg/dl)	77.3±18.01	82.37±20.91	139.56±22.48*^{b}**	<0.01
VLDL (mg/dl)	18.96±4.47	23.79±5.18 *^{a}	43.73±26.84*^{b}**^{c}	<0.01
AIP	0.236±0.09	0.35±0.13*^{a}	0.65±0.3*^{b}**^{c}	<0.01
RR1	2.82±0.48	3.09±0.57	5.47±1.34*^{b}**^{c}	<0.01
RR2	1.457±0.41	1.6±0.48	3.337±0.67* ^{b}**^{c}	<0.01
ANGPTL-4(ng/ml)	3.08±0.93	2.60±0.72*^{a}	5.41±5.11*^{b}**^{c}	<0.01
MCP-1(pg/ml)	121.34±54.50	219.1±47.98*^{a}	254.7±63.12*^{b}**^{c}	<0.01
hs-CRP(mg/l)	1.443±0.72	2.142±1.53*^{a}	2.935±1.14* ^{b}**^{c}	<0.01

*****: P < 0.01, *: P< 0.05. a: significant between P1 & C, b : significant between P2 & C, c: significant between P1 & P2, using multiple comparison.***

Table (2)
Pearson's correlation between fasting ANGPTL4, MCP-1 and hs-CRP with all parameters in diabetic patients (group P1).

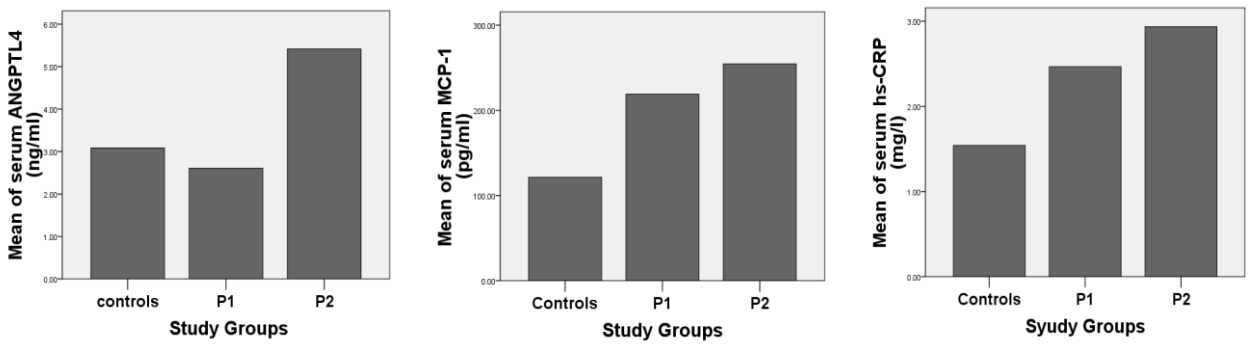
Parameter	*ANGPTL-4(ng/ml)*			*MCP-1(pg/ml)*			*CRP(mg/l)*		
	R	*P value*	*Sig.*	*R*	*P value*	*Sig.*	*R*	*P value*	*Sig.*
Age(year)	-0.273	0.265	NS	-0.222	0.239	NS	-0.163	0.445	NS
Duration of disease (year)	0.147	0.493	NS	0.258	0.224	NS	-0.317	0.131	NS
Weight (Kg)	0.240	0.258	NS	-0.037	0.868	NS	0.059	0.786	NS
Height(cm)	0.167	0.435	NS	0.003	0.988	NS	0.113-	0.601	NS
BMI (Kg/m^2)	0.207	0.331	NS	-0.213	0.317	NS	0.129	0.547	NS
Waist(cm)	0.163	0.446	NS	0.212	0.319	NS	0.074	0.730	NS
Hip(cm)	0.078	0.719	NS	-0.114	0.596	NS	0.129	0.546	NS
WHR	0.176	0.412	NS	0.254	0.230	NS	-0.064	0.766	NS
WHtR	0.014	0.948	NS	0.039	0.856	NS	0.105	0.626	NS
Smoking	0.209	0.326	NS	-0.137	0.525	NS	0.171	0.425	NS
Systolic B.P. (mm Hg)	-0.398	0.115	NS	-0.115	0.593	NS	0.222	0.298	NS
Diastolic B.P. (mmHg)	-0.04	0.851	NS	-0.210	0.325	NS	0.226	0.287	NS
FPG (mg/dl)	-0.084	0.696	NS	-0.391	0.059	NS	0.081	0.707	NS
F.P. Insulin (µIU/ml	0.261	0.218	NS	-0.230	0.279	NS	0.538	0.007	S
HOMA2 (I.R)	0.289	0.171	NS	-0.263	0.214	NS	0.568	0.004	S
HOMA2 (S%)	-0.259	0.221	NS	0.215	0.313	NS	-0.314	0.135	NS
HOMA2 (B%)	0.204	0.34	NS	0.118	0.583	NS	0.142	0.509	NS
TC (mg/dl)	-0.151	0.48	NS	0.193	0.367	NS	-0.323	0.09	NS
TG(mg/dl)	-0.043	0.842	NS	0.426	0.038	S	-0.275	0.193	NS
HDL (mg/dl)	-0.09	0.677	NS	0.153	0.475	NS	0.01	0.962	NS
LDL (mg/dl)	-0.128	0.55	NS	0.129	0.549	NS	-0.371	0.074	NS
VLDL (mg/dl)	-0.027	0.899	NS	0.432	0.035	S	-0.264	0.212	NS
AIP	0.001	0.995	NS	0.32	0.127	NS	-0.232	0.276	NS
RR1	-0.056	0.796	NS	0.131	0.543	NS	-0.189	0.377	NS
RR2	-0.092	0.669	NS	0.16	0.454	NS	-0.182	0.394	NS
ANGPTL- 4(ng/ml)	1.00	-	-	0.055	0.799	NS	0.417	0.04	S
MCP-1(pg/ml)	0.055	0.799	NS	1	-	-	-0.311	0.139	NS
hs-CRP(mg/l)	0.417	0.04	S	-0.311	0.139	NS	1	-	-

H.S.: P < 0.001, S. : P< 0.05, N.S. = P> 0.05.

Table (3)
Pearson's correlation between fasting (ANGPTL4, MCP-1 and hs-CRP) and all parameters in diabetic patients (group P2).

Parameter	*ANGPTL-4 (ng/ml)*			*MCP-1(pg/ml)*			*CRP (mg/l)*		
	R	***P value***	***Sig.***	***R***	***P value***	***Sig.***	***R***	***P value***	***Sig.***
Age(year)	0.103	0.587	NS	-0.222	0.239	NS	0.365	0.048	S
Duration of disease (year)	0.115	0.544	NS	0.133	0.484	NS	-0.006	0.974	NS
Weight (Kg)	0.140	0.461	NS	0.046	0.810	NS	0.062	0.743	NS
Height(cm)	-0.045	0.812	NS	-0.153	0.420	NS	-0.108	0.570	NS
BMI (Kg/m^2)	0.249	0.185	NS	-0.121	0.525	NS	0.244	0.194	NS
Waist(cm)	0.171	0.366	NS	0.140	0.460	NS	0.484	0.006	HS
Hip(cm)	0.103	0.588	NS	0.018	0.606	NS	0.518	0.003	HS
WHR	0.357	0.053	S	-0.035	0.855	NS	-0.112	0.556	NS
WHtR	0.059	0.759	NS	-0.046	0.809	NS	0.524	0.003	S
Smoking	0.004	0.984	NS	0.216	0.251	NS	-0.008	0.965	NS
Systolic B.P. (mm Hg)	-0.272	0.145	NS	-0.091	0.632	NS	0.046	0.808	NS
Diastolic B.P. (mmHg)	-0.291	0.119	NS	0.094	0.62	NS	0.108	0.569	NS
FPG (mg/dl)	-0.056	0.767	NS	0.18	0.342	NS	-0.156	0.410	NS
Insulin(µIU/ml)	-0.006	0.975	NS	0.07	0.712	NS	0.374	0.042	S
HOMA2(I.R)	-0.074	0.697	NS	0.248	0.186	NS	0.237	0.208	NS
HOMA2 (S%)	0.063	0.742	NS	-0.24	0.201	NS	-0.258	0.169	NS
HOMA2 (B%)	0.107	0.573	NS	-0.172	0.362	NS	0.201	0.281	NS
TC (mg/dl)	0.686	0.000	HS	0.445	0.014	S	-0.219	0.244	NS
TG(mg/dl)	0.629	0.000	HS	-0.252	0.179	NS	-0.18	0.34	NS
HDL (mg/dl)	-0.021	0.913	NS	0.325	0.079	NS	0.198	0.293	NS
LDL (mg/dl)	0.204	0.281	NS	0.405	0.026	S	-0.187	0.323	NS
VLDL (mg/dl)	0.629	0.000	HS	-0.257	0.171	NS	-0.178	0.346	NS
AIP	0.427	0.018	S	-0.25	0.183	NS	-0.262	0.161	NS
RR1	0.568	0.001	HS	-0.208	0.271	NS	-0.263	0.16	NS
RR2	0.403	0.027	S	0.420	0.02	S	-0.301	0.105	NS
ANGPTL-4(ng/ml)	1	-	-	-0.136	0.473	NS	-0.454	0.012	S
MCP-1(pg/ml)	-0.136	0.473	NS	1	-	-	0.12	0.528	NS
hs-CRP(mg/l)	-0.454	0.012	S	0.12	0.528	NS	1	-	-

H.S.: P < 0.001, S.: P< 0.05, N.S. = P> 0.05.



A ***B*** ***C***

Fig.(1) (A-B-C) Serum ANGPTL-4, MCP-1and hs-CRP levels in diabetic patients with and without dyslipidemia (P1and P2) and control (C) groups.

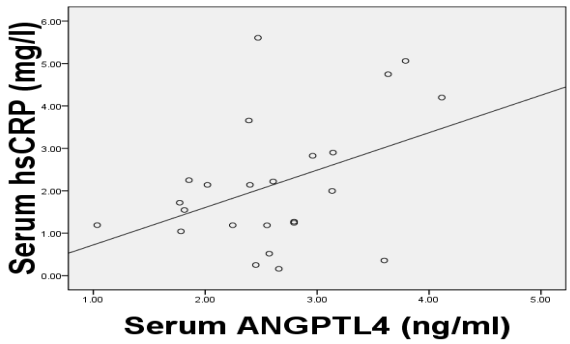
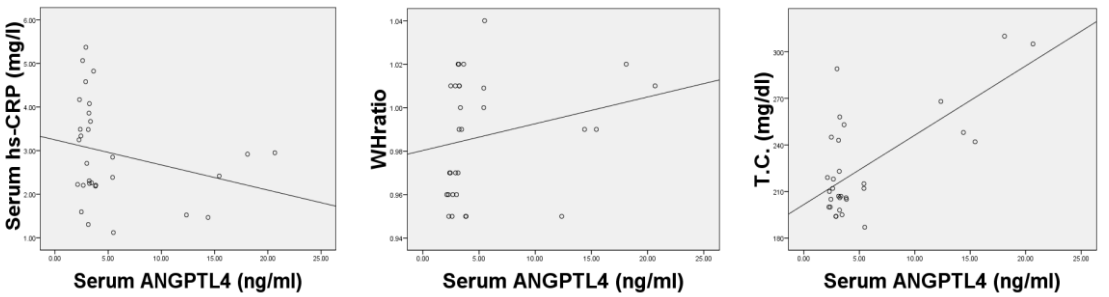
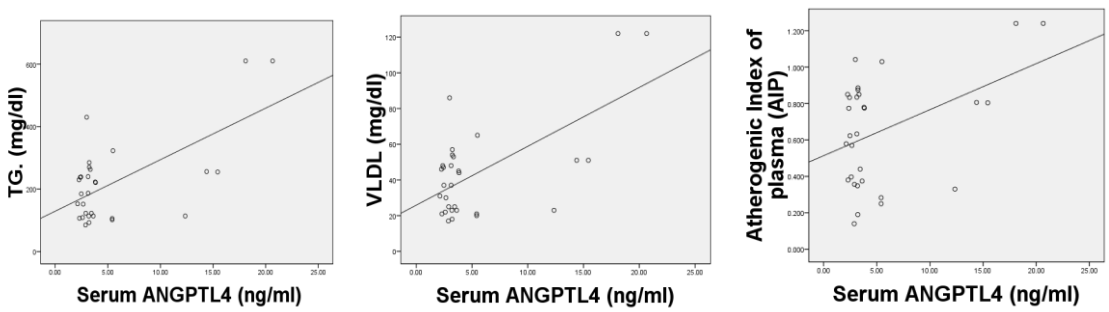


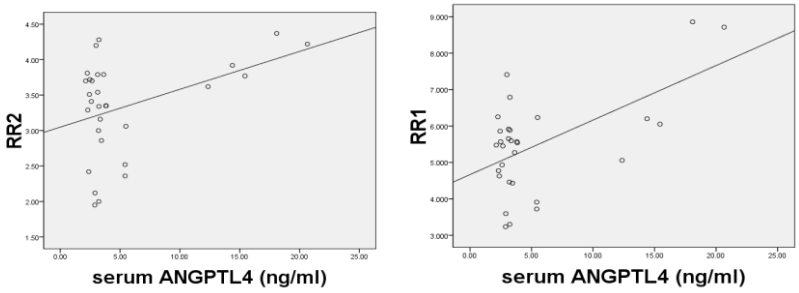
Fig.(2) Pearson correlation of fasting serum ANGPTL-4 with hs-CRP of diabetic patients without dyslipidemia (group P1).



A ***B*** ***C***



D ***E*** ***F***



G ***H***

Fig.(3) (A-B-C-D-E-F-G-H) Pearson correlation of fasting serum ANGPTL-4 with hs-CRP, TC, TG, VLDL, atherogenic parameters of diabetic patients with dyslipidemia (group P2).

Discussion

In the present study the levels of ANGPTL-4 in two groups of T2DM patients were determined; with and without dyslipidemia. It is clearly shown that the alterations in the levels of ANGPTL-4were associated with changes in the lipid profile of patients Table (1) & Fig.(1).

Diabetic dyslipidemia is a modifiable risk factor of CVD [13]. Atherosclerosis and associated coronary heart disease (CHD) are impacted by the changes in the plasma level of lipoproteins. Elevated plasma (LDL-C) levels increase the risk of CHD, while high levels of (HDL-C) are considered to be protective [14]. In addition for high LDL there is evidence that high plasma TG is an independent risk factor for CHD [15]. A consider number of studies have been showed that the blood pressure and its progression were strong and independent predictors of incident type 2 diabetes among initially healthy persons [16, 17].

The results revealed a significant decrease in ANGPTL-4 of diabetes patients without dyslipidemia in comparison with group (C) Table (1) & Fig.(1). Recently, it was shown that triglyceride-rich lipoproteins may interfere with the ability of ANGPTL-4 to inhibit LPL, a property that may also extend to LDL [18]. Also ANGPTL-4 shows no significant correlation with all parameters. Our results are in agreement with that of Yamagishi S. 2011 [19] and Xu et al. [20] who reported that serum ANGPTL-4 concentrations are low in patients with type 2 diabetes mellitus but not in obese individuals and there is no correlation between serum ANGPTL-4 concentrations and serum levels of triglyceride and total cholesterol suggesting that the decreased ANGPTL-4 could be a causative factor of this diseaseand that its beneficial effect on glucose homeostasis might be useful for the treatment of diabetes. Insulin down regulates ANGPTL-4 mRNA expression, and the reduction of ANGPTL-4 mRNA by insulin is attenuated in insulin resistance [21].

ANGPTL-4 levels in T2DM patients with dyslipidemia shows positive correlation with increased levels of TC, TG, LDL, VLDL, AIP, RR1and RR2, this data is in line with Lichtenstein *et al*., 2010 (6), Mehta *et al*., 2014 [22], and with Stejskal *et al*., 2008 [23]. They reported a positive correlation between ANGPTL-4 levels and TG in patients with metabolic syndrome. Such elevation may be due to hepatic lipase inhibition by ANGPTL-4 which encourages the liver to increase its levels of cholesterol [24]. Robciuc *et al*. 2010 [25] showed that ANGPTL-4 levels were positively correlated with increase in waist-to-hip ratio which is also in line with our results. We suggest that the increase in ANGPTL-4 levels in group P2 may be part of a protective feedback mechanism aimed at minimizing lipid overload.

Serum levels of ANGPTL-4 show positive correlation with hs-CRP levels in diabetes patients without dyslipidemia. Our results are in line with Lichtenstein. 2010 [6], which demonstrated that ANGPTL-4 protects against the severe pro-inflammatory effects of dietary saturated fat in mesenteric lymph nodes by inhibiting macrophage LPL activity, thereby reducing lipolytic release of fatty acids, macrophage foam cell formation, endoplasmic reticulum ER stress, and initiation of a marked inflammatory response.

In contrast, serum ANGPTL-4 levels in diabetes patients with dyslipidemia showed a negative correlation with CRP. Nguan*et al*., 2013 [26] found that ANGPTL-4 was negatively associated with carotid artery sclerosis in subjects with the metabolic syndrome and low-grade systemic inflammation.

A hypothesis about the role of ANGPTL -4 as a new class of lipid metabolism modulator and their values could be a new key predictors of metabolic syndrome was suggested by a study of Miida *et al*., 2010 [27].

Accordingly, based on the present study and the results from previous studies, ANGPTL -4 pharmacologically can represent interesting candidate for the therapeutic targeting of dyslipidemia. However, further studies are still needed to clarify the influence of an altered of free fatty acid and other lipid profiles on ANGPTL-4 protein and its gene in humans as well as determine the normal value of this protein in blood plasma in order to assess ANGPTL-4 value as a new risk predictor and prognostic factor for the diagnosis of metabolic syndrome and increase atherosclerosis risk in T2DM patients.

Conclusions

There is elevated level of ANGPTL-4 in diabetic patients and positive association between ANGPTL-4 and CRP in diabetic patients without dyslipidemia could reflects the suppressive effect of ANGPTL-4 on microphage migration and chemotaxis that increase atherosclerosis risk of in T2DM patients, but this effect no longer exist in diabetic patients with dyslipidemia since two associated disease make the inflammatory state more active.

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الخلاصة

أ- مقدمة:

يبدأ مرض السكري مراحل تطورات تصلب الشرايين وذلك من خلال تغيير وظيفة الخلايا البطانيه للاوعيه الدمويه, خلايا العضلات الملساء والصفيحات الدمويه, كذلك مقاومة الانسولين والمستوى العالي من الكلوكوز وخلل في مستوى الدهون في الدم يمكنها ان تؤدي الى الاصابة بتصلب الشرايين في مرضى السكري الانجيوبويتين-٤ (ANGPTL-4) بروتين متعدد الوظائف يتطلب وجوده في تنظيم مستوى الدهون, تمثيل الطاقه, تولد الاوعيه وحالات الالتهابات, تعبيره في الجسم يحفز في الكبد والقلب والعضلات والانسجه الدهنيه خلال حالات الاستجابه الشديدة. CRP البروتين سي- التفاعلي ذو تأثير مباشر على تغيير تلاصق الجزيئات في الخلايا البطانيه. وكذلك توظف مجموعة الكريات البيضاء (monocyte) الى جدار الاوعيه الدمويه من خلال تحفيز تعبير وتخليق (chemokines) خاصه ويسمى (MCP-1), كل هذه العمليات تؤدي الى خطر الاصابة والتطور وتعقيدات تصلب الشرايين في مرضى السكري النوع الثاني

ب- الهدف من الدراسة:

هو لدراسة دور ANGPTL-4 في مرضى السكري الذين لديهم احد اخطار الاصابه بتصلب الشرايين (خلل في مستوى الدهون في الدم) والذين لايعانون من هذا الخطر, وكذلك لمعرفة العلاقه بين مستوى ANGPTL-٤ وعمليات الالتهابات.