The Linear Correlation of Serum Level Thrombospondin-1 with Lipid Profile in Patients with Diabetic Disease Type II

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ABSTRACT

The study was conducted on randomly selected 65 type 2 diabetic patients attending the diabetes mellitus center in Al-Sadder Teaching City in Al- Najaf province , Iraq and a group of 24 apparently healthy subjects were included as a control group . The Study was carried out from August 2013 to February 2014. The patients' age was ranging of 35 to 64 years old. The results indicated a significant increase ($p < 0.05$) in serum TSP-1 , Cholesterol, TG, VLDL-C, LDL-C levels and a significant decrease ($p > 0.05$) in serum HDL-C level in diabetic patients in comparing with healthy groups. The results have been shown significant positive correlation ($P < 0.05$) TSP-1 and cholesterol, TSP-1 and TG, TSP-1 and LDL-C, TSP-1 and VLDL-C in DM patients. The results have been shown significant negative correlation ($P < 0.05$) between TSP-1 and HDL-C in type 2 diabetic patients.

Keywords: Type II diabetic mellitus , Lipid profile and TSP-1

Article Information

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INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders of carbohydrates metabolism, this condition occurs when inadequate uptake of glucose by the cells of the body causes high levels of glucose in the blood (hyperglycemia) (CDA, 2008; CDA, 2013). Patients with type II diabetes mellitus are insulin resistant, have relatively low insulin production, or both, some patients with type II diabetes may eventually require insulin when other medications fail to control blood glucose levels adequately (Leahy and William, 2002). Type II diabetes is most commonly associated with obesity in middle-aged individuals. It is due to reduction in the number or affinity of insulin receptors on the plasma membrane of cells in target tissues, or an abnormal binding of insulin to the receptors (Thabrew and Ayling, 2001). The major forms of diabetes are divided into those caused by deficiency of insulin secretion due to pancreatic β -cell damage (type 1 DM), and those that are a consequence of insulin

resistance occurring at the level of skeletal muscle, liver, and adipose tissue, with various degrees of β -cell impairment (type 2 DM) (Alemzadeh *et al.*, 2008; CDA, 2013).

Thrombospondin-1 (TSP-1) is a well-studied glycoprotein that have many motifs (*i.e.*, adhesive domains; N-terminal domain, procollagen homology, type I repeats, type II, type III repeat , C-terminal domain) (Qian and Tuszynski, 1996). TSP-1 suppresses endothelial cell proliferation, migration, and tube-formation and induces endothelial apoptosis (Jimenez *et al.*, 2000). Thus, TSP-1 is an endogenous inhibitor of angiogenesis under physiological and pathological conditions , including in the context of malignancy (Adams and Lawler, 2004). TSP-1 also modulates the extracellular matrix and leads to degradation and remodeling of connective tissues (Lawler, 2000). TSP-1 plays an important role in the regulation of various biological activities, including vascular homeostasis, immunity, and

wound healing (Bauer *et al.*,2010; Lopez-Dee *et al.*,2011).

METHODS

Collection of blood samples

Five milliliters of venous blood samples were drawn using a disposable needle and plastic syringes from each patients and controls subject. Blood was left at room temperature for 10 minutes to clot, centrifuged 6000 rpm for 10 minutes, and then serum was separated and transported into new disposable tubes.

Biochemical markers

Lipid profile

Measurements of total cholesterol (TC)

Specific kit for measuring human TC concentrations in serum was supplied by Biolabo SA, France.

Measurements of high density lipoprotein (HDL)

Specific kit for measuring human HDL concentrations in serum was supplied by Biolabo SA, France .

Measurements of triglycerides(TG)

Specific kit for measuring human TG concentrations in serum was supplied by Biolabo SA, France

Calculation of low density lipoprotein (LDL)

Low density lipoprotein was calculated by this formula: $LDL(mg/ml) = TC(mg/dl) - VLDL(mg/dl) - HDL(mg/dl)$.

Determination of serum Thrombospondin-1 level

Thrombospondin ELISA Kit For the quantitative determination of human thrombospondin-1 (TSP-1) concentrations in serum was supplied by CUSABIO, USA.

Statistical Analysis

The data of present study were articulated as (Mean $\pm$ Standard Error), the statistical analysis (descriptive statistics, Correlation coefficients, p value) were calculated by using megastat and Graphpad prism, when P value < 0.05 was statistically a significant

RESULTS

Comparison between diabetics mellitus patients and healthy groups

The results of table (1) indicate a significant increase ($P < 0.05$) in serum TSP-1, cholesterol, Triglyceride , VLDL-C , LDL-C levels and a significant decrease ($P < 0.05$) in serum HDL-C level in diabetic patients in comparing with healthy groups.

Table (1): Serum levels of TSP-1 and lipid profile parameters in diabetic mellitus patients and control groups.

Criteria \ Groups	Mean $\pm$ S.E.	
	Control	Patients
Lipid profile	N=24	N=40
TSP-1 ng/ml	1.181 $\pm$ 0.226	10.942 $\pm$ 0.043 *
Cholesterol mg/dl	112.54 $\pm$ 5.26	435.35 $\pm$ 24.12 *
TG mg/dl	64.83 $\pm$ 7.13	497.80 $\pm$ 28.53 *
VLDL-C mg/dl	18.33 $\pm$ 2.05	99.553 $\pm$ 5.706 *
LDL-C mg/dl	95.46 $\pm$ 3.74	179.535 $\pm$ 1.335 *
HDL-C mg/dl	47.21 $\pm$ 0.90	25.095 $\pm$ 0.997 *

(*) Statistically significant differences ($p < 0.05$) between patients and control groups.

Thrombospondin-1 and lipid profile levels

The results of correlation and linear regression between TSP-1 and lipid profile levels in patients are indicated:

1. The presence of a positive correlation ($P < 0.05$) between TSP-1 and cholesterol levels of DM patients ($r = 0.942$), (figure 1).
2. 1-The presence of a positive correlation ($P < 0.05$) between TSP-1 and triglyceride levels of DM patients ($r = 0.896$), (figure 2).
3. The presence of a positive correlation ($P < 0.05$) between TSP-1 and VLDL levels of DM patients ($r = 0.897$), (figure 3).
4. The presence of a positive correlation ($P < 0.05$) between TSP-1 and LDL levels of DM patients ($r = 0.971$, $\text{TSP-1} = -45.863 + 0.311 \text{ LDL}$), (figure 4).
5. 1-The presence of a negative correlation ($P < 0.05$) between TSP-1 and HDL levels of DM patients ($r = -0.977$), (figure 5).

Figure (2): Correlation between TSP-1 and triglyceride in type 2 DM patients.

Figure (1): Correlation between TSP-1 and Cholesterol in type 2 DM patients.

Figure (3): Correlation between TSP-1 and VLDL in type 2 DM patients.

Figure (4): Correlation between TSP-1 and LDL in type 2 DM patients.

Figure (5): Correlation between TSP-1 and HDL in type 2 DM patients.

DISCUSSION

The present study revealed a significant increase ($p < 0.05$) in Thrombospondin-1 level and lipid profile levels in diabetic patients in comparing with control groups as presented in

table(1). Previous studies suggested that expression of Thrombospondin-1 is markedly up regulated in tissue from diabetic patients and animal models (Kong *et al.*,2013a;Gonzalez-Quesada *et al.*,2013). Other researchers suggests that hyperglycemia potentially induced TSP-1 synthesis by endothelial cells through pathways that may involved glucose mediated activation of hexosamine (Dabir *et al.*, 2008 ;Raman *et al.*,2011).

Elevated blood glucose concentrations increased TSP-1 synthesis which was associated with reduced cell proliferation, increased TGF- β 1 bioactivity and stimulation of fibronectin synthesis (Murphy-Ullrich and Poczaitek ,2000 and 2008; Yevdokimova *et al.*,2001) and our previous study indicated a highly relation between TSP-1 and FBG in type 2 diabetic patients (Al-Kraity, W.R.H, 2016). TSP-1 loss also improved metabolic dysfunction , reduced blood glucose (Kong *et al.*,2013a,b). A multivariate regression analysis study of patients with type 2 diabetic showed that male gender with low level of HDL-C, high level LDL-C and cholesterol are associated with high level of TSP-1 and risk factors of cardiovascular disease (CVD) (Choi *et al.*,2012). Both male and female diabetic patients with uncontrolled diabetes had severe hyperglycemia and significantly increased triglycerides, cholesterol LDL,VLDL and significantly decreased HDL (Khan,2006;Smith 2007) and these studies were agreement with presented study.

Study of Choi *et al.*(2012) indicated the association between TSP-1 level and coronary heart disease and atherosclerosis in type 2 diabetic patients. Many studies proved the relation between thrombospondin-1 and LDL-C and these researches indicated that TSP-1 stimulation mediated signaling through a receptor CO-complex involving calreticulin and low density lipoprotein receptors and postulated that transition to inter-mediate adhesive state enhanced cellular responses (Orr *et al.*,2003a,b). Study of Meng *et al.*(2010) postulated that LDL-receptor related protein (LRP-1) regulates thrombospondin-1 (TSP-1) enhanced notch signaling and proved a significant relation between LDL-receptor and increment of thrombospondin-1.Previous study indicated that thrombospondin-1 play important

roles in development of hyperplasia and the relation was suggested between TSP-1 and hypercholesterolemia atherosclerotic rabbits by over express of TSP-1(Roth *et al.*,1998; Maier *et al.*,2009).

TSP-1 contributed to development of atherosclerosis and may be important in this complication of diabetes by expressed in the arterial wall and highly correlation was noted between increment of TSP-1 and hypercholesterolemia (Maier *et al.*,2009).Further studies from laboratory and others have been demonstrated the role of TSP-1 in cellular events that contribute to increase cholesterol level and atherosclerosis (Wahab *et al.*.,2005;Ii *et al.*,2006).

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CONCLUSION

The study proved that TSP-1 good marker for monitoring the diabetes mellitus and it's a highly relation between thrombospondin-1 and lipid profile and in type 2 diabetic patients.

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