International Journal of Science Academic Research
Vol. 01, Issue 08, pp.575-579, November, 2020
Available online at http://www.scienceijsar.com

ISSN: 2582-6425

Research Article

CORRELATION BETWEEN THYROID FUNCTION, INSULIN AND LEPTIN IN DIABETIC PATIENT

[1]Mansour ahmed Al_Senussi and [2,*]Mohy Eldin AbdEl Fattah

[1]Department of Chemistry, Faculty of Science, Sabha University, Libya
[2]Department of Organic Chemistry, Faculty of Science, Suez Canal University, Egypt

Received 26th September 2020; **Accepted** 19th October 2020; **Published online** 30th November 2020

Abstract

The aim of the present study was conducted to assess the correlation and the influence of the coexistence of diabetes,, thyroid, leptinand biochemical variables related to carbohydrate and lipid metabolism in patients suffered from either type 1 diabetes (T1DM; 1DDM) or type 2 diabetes (T2DM;NIDDM). The study was performed on 100 individual collected from the outpatient and inpatient clinics of diabetes. They divided into 5 groups as follow; volunteer apparently healthy, IDDM with complications and NIDDM without complications. The obtain results revealed an increase in the level of glycosylated haemoglobin (HBA1C) in individuals with higher levels of blood glucose, hypercholesterolemia and hypertriglyceridemia in diabetic patients with more increase in patients suffered from IDDM with complications. Patients suffered NIDDM with complications show higher level of leptin than other groups. There is an increase in serum TSH level in patients suffered from IDDM with complications than other groups with reduction in T3 and T4 levels. On the other hand, there is a decrease in serum TSH level in patients suffered from NIDDM with complications than other groups with elevation in T3 and T4 levels. In conclusion, the present study indicates a significant negative correlation between serum T4 and leptin in NIDDM with complications. A negative correlation is showed between serum T3, T4 and leptin in IDDM with complications.

Keywords: Thyroid function, Diabetes, Obesity, leptin.

INTRODUCTION

Diabetes mellitus is a syndrome initially characterized by loss of glucose homeostasis, resulting from defects in insulin secretion, insulin action or both leading to impaired metabolism of glucose and other energy-yielding fuels such as lipids and proteins. The disease is progressive and associated with a high risk of vascular diseases. There are macrovascular complications as coronary artery disease, cerebrovascular disease and microvascular complications, that found to cause nephropathy, retinopathy and neuropathy (White *et al.,* 2003; D'Elia *et al.,* 2011). Diabetics suffer from either type1 or type 2diabetes. Type1 diabetes (T1DM;IDDM) is a debilitating autoimmune disease caused by T-cell-mediated gradual destruction of B-cell, leading to either insufficient or complete lack of insulin production. T1DM is increasing in incidence worldwide, particularly in young children whom have gained more weight (Devendra and Eisenbarth, 2003; Gilliam *et al.,* 2006). Type2 diabetes (T2DM; NIDDM) is a progressive chronic disease that can manifest at any age due to largely persistent metabolic imbalance engendered by myriad of internal and external environmental factors, including diet and lifestyle changes (Lu *et al.,* 2012). Increasein episodic basal and postprandial insulin secretion imitated by these environmental shifts gradually and expedites B-cells dysfunction and loss that eventuates into unremitting hyperglycemia (Kahn *et al.,* 2006; Kalra, 2009). Obesity is one of the most important health risks of our time through increased risk of diabetes, dyslipidemia, kidney disease, cardiovascular disease, thyroid dysfunction and cancer (Biondi, 2010). Leptin is a 15-kDa hormone secreted mainly by adipocytes, although leptin expression in placenta, fetal tissue, stomach and other tissues was initially described as a protein important in food intake and body weight regulation.

Corresponding Author:** ***Mohy Eldin AbdEl Fattah
Department of Organic Chemistry, Faculty of Science, Suez Canal University, Egypt.

It transport from plasma crossing the blood-brain barrier through a asaturable transport system and acting on receptors in the lateral and medial regions of the regulate appetite and energy balance (Friedman and Halaas, 1998; Konukoglu *et al.,* 2006). Insulin is adipogenic, promotes fat deposition in the body, while liptin expression increases after peak insulin secretion during feeding cycle (Kalra, 2008). Diabetes mellitus type1 may be associated with thyroid dysfunction either hypothyroidism (Hashimoto's disease)or hyperthyroidism (Graves' disease) that is autoimmune disorders, with development influenced by genetic and environmental factors (Hawa *et al.,* 2006; Roman-Gonzalez *et al.,* 2009). It has been known that, HBA1C can be used as a potential biomarker for predicting dyslipidemia in type 2 diabetic patients in addition to glycemic control (Varashree and Bhat, 2011). Indeed, hyperlipidemia is the commonest complication of diabetes mellitus and it predisposes them to premature atherosclerosis and macrovascular complications. Common lipid abnormalities in diabetes areraisedtriglycerides, LDL-C serum cholesterol and low HDL-C. Therefore good glycemic control can prevent development and progression of lipid-abnormalities among patients with diabetes mellitus (Khursheed *et al.,* 2011).

MATERIALS AND METHODS

The study was performed on 100 individuals collected from the outpatients and inpatient clinic at SabhaUniverist.in our study.Those individuals are divided into 5 groups as follow; GroupI consisted of 20 volunteer apparently healthy individual with age ranging from 5-39 years were chosen as control group; GroupII; consisted 25 patients suffered from IDDM with CVD as a major complication of diabetes; Group III consisted of 15 patients suffered from IDDM without complications; Group IV consisted of 20 patients suffered from NIDDM with complications; Group V consisted of 20 patients suffered from NIDDM without complications. Two hours postprandial samples are taken, two blood samples were

collected from each person; the first was taken with anticoagulant (EDTA) for determination of glycosylated hemoglobin (HBA1C) that was estimated by using a fast ion exchange resin separation method (Niederau and Reinauer, 1981) by using commercial kit of Stanbio Laboratory, Inc, 1261 Main St, Boerne, TX. The second sample was taken into a clean tube, centrifuged at 3000r.p.m for 15 minutes and serum separated for determination of 2hpp fasting blood glucose according to (Trinder, 1969)and total cholesterol (T.C) according to (Richmond, 1973; Allain *et al.,* 1974) by using a commercial kit of Stanbio Laboratory. Serum triglycerides (T.G) was estimated according to (Fossati and Prencipe, 1982)by using a commercial kit of Axiom diagnostic. HDL-C was estimated according to (Burstein *et al.,* 1970; Lopes-Virella *et al.,* 1977) by using a commercial kit of Bio System.LDL-C was calculated by formula of (Friedewald *et al.,* 1972). Serum LDL-C (mg/dl) = TC-HDL-C –TAG/5TSH, T3, T4 and Leptin were measured in serum using a commercially available ELISA kit (BioCheck, Inc.,323 Vintage Park, Dr.)

Statistical analysis

Statistical analysis was carried out with SPSS using the one way ANOVA, paired T-test and correlation. Data are given as mean ± standard error (S.E) (Snedcor and Cochran, 1980).

RESULTS

Table 1. Determination of fasting blood glucose, HBA1C,Liptin level in studied groups

Groups	Glucose(mg/dl)	HBA_{1C} (%)	Leptin (µg/dl)
Group I	95.5±3.04	6.84±0.1	5.82±0.32
Group II	295.05±11.41	11.80±0.28	104.86±2.65
Group III	189.85±5.72	7.71±0.19	83.2±3.72
Group IV	216.82±6.72	9.63±0.19	136.91±3.57
Group V	177.25±5.22	8.49±0.08	16.92±0.84

Group I= control group; Group II= diabetic patients (IDDM) with complications; Group III= diabetic patients (IDDM) without complications; Group IV= diabetic patients (NIDDM) with complications & Group V= diabetic patients (NIDDM) without complications. Value represents mean ±SE

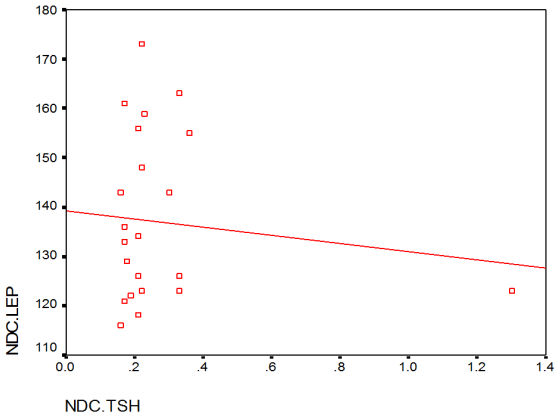


Figure (A)

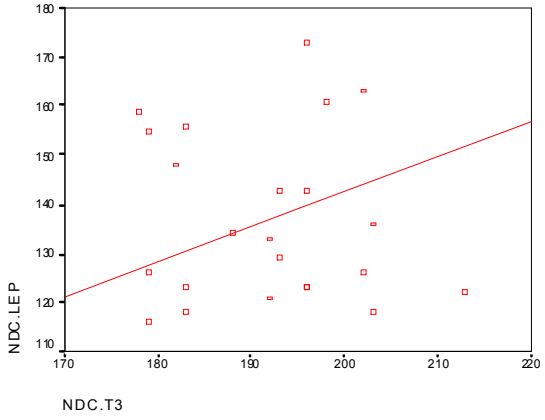


Figure (B)

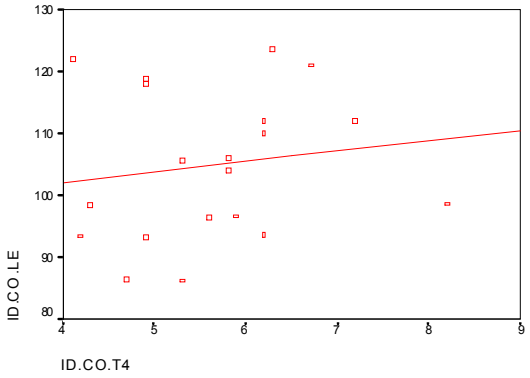
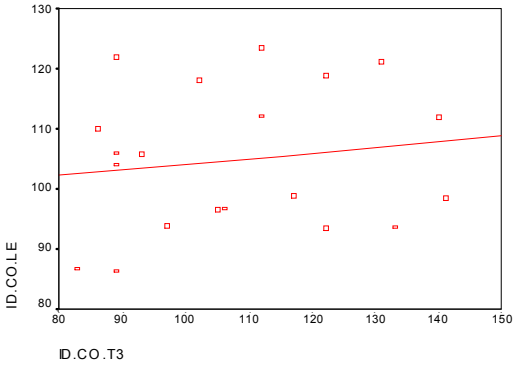


Figure (C)



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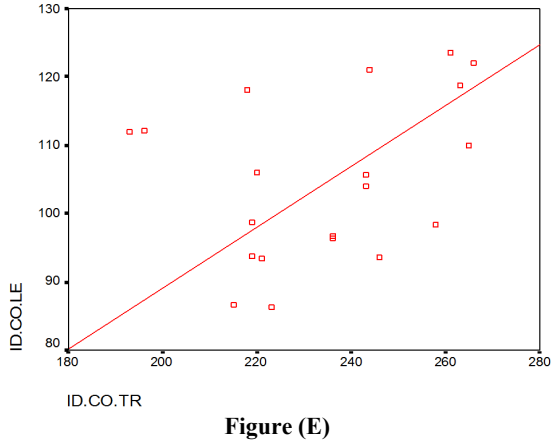

Figure (E)

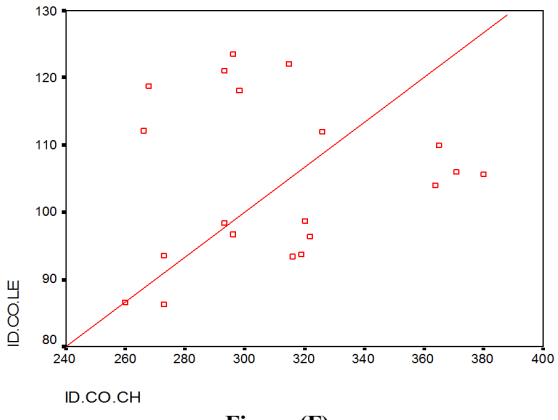

Figure (F)

Table 2. Determination of TSH, T3, and T4 level in studied groups

Groups	TSH(µIU/ ml)	T4(µg/dl)	T3 (ng/dl)
Group I	1.06±0.13	6.87±0.30	126.22±4.92
Group II	3.2±0.15	5.63±0.23	107.9±4.2
Group III	3.03±0.18	10.31±0.31	160.55±3.75
Group IV	0.27±0.04	12.24±0.34	191.69±2.01
Group V	1.81±0.18	7.49±0.21	153.30±3.74

Table 3. Determination of T.C, T.G, HDL-C and LDL-C level in studied groups

Groups	T.C (mg/dl)	T.G (mg/dl)	HDL-C (mg/dl)	LDL-C(mg/dl)
Group I	162.21±5.61	98.64±4.06	37.92±0.80	106.17±4.5
Group II	310.70±8.15	234.25±4.92	57.65±1.41	206.20±8.78
Group III	203.20±2.50	126.55±5.46	54.6±1.21	123.29±3.35
Group IV	288.43±6.85	255.69±4.38	65.47±1.2	171.81±6.67
Group V	213.90±3.04	159.05±9.54	46.60±1.77	134.47±3.35

DISCUSSION

The obtained results revealed an increase in the level of glycosylated hemoglobin in individuals with higher levels of blood glucose, there are a high significant increases in serum fasting blood glucose, HBA1and leptin levels in both diabetic patients (IDDM, NIDDM) either with or without complications than control group. Patients suffered from IDDM with complications show higher level of fasting blood glucose and HBA1than other groups, while patients suffered from NIDDM with complications show higher level than other groups (Table 1). Severalassumptions have been suggested to explain the hyperglycemia in diabetes. This is plausible that, hyperglycemia in IDDM may be attributed to eitherinsufficient or complete lack of insulin production according to the degree of B-cell destruction (Devendra and Eisenbarth, 2003; Gilliam *et al.,* 2006). Concerning that hyperglycemia, in NIDDM that more prevalent among obese subject may be due to insulin receptor insensitivity, insulin resistance and diminished downstream insulin receptor signaling in target cells. The relentless compensatory insulin hyper secretion to normalize blood glucose levels under these conditions expedites B-cell dysfunction that eventuates into unremitting hyperglycemia (Kahn *et al.,* 2006; Kalra, 2009). Further investigation proposed that, the increase in serum leptin was exponentially with increased fat mass in obese subjects whom are at increased risk of type 2 diabetes mellitus. Since, the B-cells may be regulatory restrain on insulin efflux from B-cells eventually leading to diabetes (Soodini, 2004; Otukonyong *et al.,* 2005; Hamed *et al.,* 2011). The conclusion of, (Niswender and Schwartz, 2003; Gilliam *et al.,* 2006) hypothesized that leptinplays a role in the development of autoimmunity by facilitating the generation of autoantibodies targeting pancreatic B-cells promoting a T1DM immune response. Our work recorded an increase in the level of glycationof haemoglobin in individual with higher levels of blood glucose, this result came in accordance with the result of (Varashree and Bhat, 2011) who reported that, human erythrocytes are freely permeable to glucose and within each erythrocyte glucose can bind non enzymatically to haemoglobin and glycatedhaemoglobin is formed that is dependent on the ambient glucose concentration. The glycation process is slow and continuous that occurs over days to 3-4 months. In a normal person about 3-6% of HBA is glycated; in a diabetic patient the percentage of HBA may double or triple degree of hyperglycemia). The evidence of (Tsukahara *et al.,* 2003; Abd El Dayem *et al.,* 2012) suggested that, a small proportion of glycated products are then irreversible transformed, over several weeks to months, into advanced glycosylation end products (AGEs) that accumulate in a variety of collagenous structures, such as vascular wall collagen and basement membranes result in endothelial dysfunction and vascular complications. There is increasing evidence that AGEs play a pivotal role in atherosclerosis and renal failure in diabetes. These data exhibit an increase in serum TSH level in patients suffered from IDDM with complications than other groups with reduction in T3 and T4 levels (Table 2). Thus, the present study is consistent with many others which reported that T4 exerted negative feedback on TSH (ŞimŞek *et al.,* 1997; Imaizumi *et al.,* 2011). It was obvious in the present study that, there is a negative correlation is showed between serum T4 and leptin in IDDM with complications (Figure C), also between serum T3 and leptin in IDDM with complications (Figure D).

These result is agree with the results of (Johnson, 2006;Okten *et al.,* 2006) whom confirm that patients with type I DM have higher prevalence of positive thyroid autoantibodies than healthy controls. Moreover, The issues of (Devendra and Eisenbarth, 2003; Marzullo *et al.,* 2010) address the intriguing hypothesis of a link between obesity and hypothyroidism where high leptin level in obese persons increasing the susceptibility to thyroid autoimmunity, which in turn entails a high risk of developing hypothyroidism (Hashimoto's disease) where a lymphocyte infiltrate destroys the thyroid gland.On the other hand, there is a reduction in serum TSH in patients suffered from NIDDM with complications than groups with elevation in T3 and T4 levels (Table 2). As well as, there is a significant negative correlation between serum TSH and leptin in NIDDM with complications (Figure A). A positive correlation is found between serum T4and leptin in NIDDM with complications (Figure B). These result is agree with the result of (De Pergola *et al.,* 2007) who reported that, there was a positive association has been reported between the T3 toT4 ratio and both waist circumference, BMI in obese patients. This finding suggest a high conversion of T4 toT3 in patients with central fat obesity due to increased deiodinase activity by leptin as a compensatory mechanism for fat accumulation to improve energy metabolism, thermogenesis and plays a critical role in glucose, lipid metabolism, food intake, and oxidation of fatty acids. The study reveals high prevalence of hypercholesterolemia and hypertriglyceridemia which are well known risk factors for cardiovascular disease in diabetes. Since, patients suffered from IDDM with complication show higher level of total cholesterol, LDL-C and triglycerides than other groups (Table 3). These results correlated with result of (Vinod Mahato *et al.,* 2011) who revealed that, insulin affects the liver apolipoprotein production. It regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transport protein. All these factors are likely cause of dyslipidemia in diabetes mellitus. Moreover, insulin deficiency reduces the activity of hepatic lipase resulting in hypertriglyceridemia. Also, our study reveals a significant positive correlation between serum leptin and triglycrides (Figure E), as well as between serum leptin and cholesterol (figureF) in IDDM with complications. These results are confirmed with the results of (Soodini, 2004;Uttra *et al.,* 2011;Vinod Mahato *et al.,* 2011) whom demonstrate that, an increased amount of adipose tissue or its disproportionate distribution between central and peripheral body region is related to the development of insulin resistance, type II diabetes mellitus, hypercholesterolemia, hypertriglyceridemia dyslipidemia, atherosclerosis, and coronary artery disease. The most important products of

adipose tissue collectively referred to as adipocytokinase, include adiponectin, leptin, tumer necrosis factor-alpha (TNF-), interleukin-6 (IL-6), resistin, plasminogen- activating inhibitor-1 (PAI-1) and angiotensinogen.

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