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Determination of serum plasminogen activator inhibitor -1 and homocysteine concentrations of Diabetes mellitus patients type 2 in Tikrit city population-Iraq.

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Abstract:

Type -2 diabetes mellitus is usually preceded by pre diabetes, in which levels of blood glucose are above normal but not high enough yet for a diagnosis of diabetes. The study aimed to measure the concentration of serum plasminogen activator inhibitor -1 and homocysteine concentration. This study was achieved by collecting 90 subjects who participate in the study, 35 patients diagnosed with type -2 Diabetes mellitus and obese, while 35 patients diagnosed with obese only and 20 healthy subjects as Control. The study was carried out in Salah-Aldin Hospital in Salah -Aldin governorate from beginning of March to end of June 2019. Serum homocysteine and plasminogen activator inhibitors (PAI-1) were measured by using human Elisa Kits manufactured by Bioassay Technology Laboratory company- China.There is elevation in body mass index in obese patients with DMT2, (G1), patients with obesity only, (G2), as compare with control group. Also, there was an elevation in serum homocysteine, (Hcy) in obese DMT2 as compare with obese patient and control healthy subjects, ($P \leq 0.01$). Moreover, the present study found a significant elevation in serum PA-1 concentration in obese DMT2 patients and in obese as compare with normal healthy control subjects.

Key words: Obese, DMT2, plasminogen activator inhibitor-1, and serum homocysteine,

تعين تركيزات مثبط منشط البلازمينوجين المصلي -١ وهوموسيستين لمرضى السكري من النوع ٢ في مجتمع مدينة تكريت - العراق.

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خلاصة :

توجد لداء السكر من النوع 2 السكري علامات ما قبل المرض ، حيث تكون مستويات الجلوكوز في الدم فوق المعدل الطبيعي ولكنها ليست عالية بما يكفي لتشخيص مرض داء السكر. علامات تنشيط التخثر كما هو مبين في العديد من الدراسات مثل مركبات الثرومبين- مضاد الثرومبين وجزيات تنشيط البروثرومبين، والتي تكون مرتفعة لدى مرض داء السكر. تهدف الدراسة لتحديد تركيز مثبط منشط البلازمينوجين في المصل – 1 وهوموسيستين في تحديد بعض المواد كمؤشرات لأعراض التجلط في الأشخاص الذين يعانون من السمنة ومرضى السكري. تم تحقيق هذه الدراسة من خلال جمع 90 شخصًا ممن شاركوا في الدراسة ، وتم تشخيص 35 مريضًا من مصابين يداء السكر النوع – 2 والسمنة ، بينما تم تشخيص 35 مريضًا يعانون من السمنة فقط و 20 من الأشخاص الأصحاء غير البدينين كمجموعة سيطره. أجريت هذه الدراسة في مستشفى صلاح الدين في محافظة صلاح الدين من بداية اذار حتى نهاية حزيران 2019. تم قياس مثبطات الهوموسيستين ومحفز البلازمينوجين (PAI–1) في مصل الدم باستخدام مجموعات Elisa البشرية المصنعة من قبل شركة Bioassay Technology Laboratory– الصين. هنالك ارتفاع في مؤشر كتلة الجسم في المرضى الذين يعانون من داء السكرو السمنة (DMT2 ، G1) ، والمرضى الذين يعانون من السمنة فقط ، (G2) ، مقارنة مع مجموعة السيطره. أيضا ، كان هناك ارتفاع في الحمض الاميني في المصل (Hcy) في في المرضى الذين يعانون من داء السكرو السمنة DMT2 السمنة بالمقارنة مع المرضى البدناء والسيطرة على الأصحاء ، ($P \leq 0.01$). علاوة على ذلك ، وجدت الدراسة الحالية ارتفاعًا كبيرًا في تركيز PA–1 في مصل الدم لدى مرضى الذين يعانون من داء السكرو السمنة والسمنة مقارنة مع الأشخاص الطبيعيين الذين لديهم تحكم صحي.

الكلمات المفتاحيه: السمنة ، مثبط منشط البلازمينوجين – 1 ، الهموسيستين في الدم و داء السكر .

Introduction

Type -2 diabetes mellitus, (T2DM) is usually preceded by pre diabetes, in which levels of blood glucose are above normal but not high enough yet for a diagnosis of diabetes [1, 2]. Thrombosis is abnormal condition in diabetes, which plays a role in enhanced activation of platelets and clotting factors seen in diabetes [3, 4]. Coagulation activation markers as indicated by many studies such as thrombin-antithrombin complexes and prothrombin activation fragments, which were elevated in diabetes [5]. Plasminogen activator inhibitor -1, (PAI -1) main function entails the inhibition of urokinase plasminogen activator (uPA), an enzyme responsible for the cleavage of plasminogen to form plasmin [6, 7]. Hyperhomocysteinemia has been correlated with the occurrence of blood clots and heart attacks [8].

The aim of the study is to determine the concentration of serum plasminogen activator inhibitor -1, (PAI), and homocysteine in diabetes mellitus obese patients, (DMT2).

Materials and methods

This study was achieved by collecting 90 subjects who participate in the study, 35 patients diagnosed with type -2 Diabetes mellitus and obese, (Group 1), while 35 patients diagnosed with obese only, (Group 2) and 20 healthy subjects as Control, (Group 3). The study was carried out in Salah-Aldin Hospital in Salah –Aldin governorate from beginning of March to end of June 2019. Body weight and height were measured & Body mass index calculated from body weight in Kilogram divided by body height in meter square.

According to the following equation:

BMI = weight (kg)/(height)2 (meter).

A. inclusion criteria of subjects

1- Diagnosed as newly type 2 diabetic patients
2- Aged 40 – 65 years old
3- Obese normotensive subjects (BMI more than 30 kg/m2).

B-Exclusion criteria

1- Type 2 DM on treatment.
2- Hypertensive patients on treatment.
3- Patients with cardiac diseases.
4- type 2 diabetic patients with physical, mental or cognitive limitation.
5- Patients with other endocrine disorders.

Approximately 5 ml of fasting human blood was collected from each subjects (patients & control) and

transferred into sterilized test tubes and allowed for 30 minutes to clot at room temperature , the sample was centrifuged for 5 minutes at 3500 rotations per minute and the serum was immediately separated and stored at (-20ºC) till used for biochemical analysis.

These kits were enzyme linked immunosorbent assay (ELISA). Homocysteine and plasminogen activator inhibitors were measured by using human homocysteine kit and human plasminogen activator inhibitor-1kit manufactured by bioassay technology laboratory company-China.

All data were presented as mean and standard deviation, (SD). P value less than 0.05 was accepted as significant value.

Result and discussion

Ninety subjects were participated in the present study, 35 patients diagnosed with type -2 Diabetes mellitus and obese, (G1), while 35 patients diagnosed with obese only, (G2) and 20 healthy non obese healthy subjects as control group, (G1).

In table 1, there are no significant difference regarding the age of subjects in group 1 and 2 as compare with control healthy subjects in group 3, all subjects of the present study are of same age and gender. However, there is elevation in body mass index in obese patients with DMT2, (G1), patients with obesity only, (G2), as compare with control group, (G1); ($p \leq 0.01$).

Table (1) show the age, body weight, height and body mass index (BMI), in all groups.

Parameters	G1	G2	G3	P≤ value
Age (years)	52.38±9.6	50.2±7.5	49.7±6.1	NS
Body weight(Kg)	96.4±20.8	80.1±10.5	74.7±4.5	0.01**
Height (Cm)	169.2±5.8	170.5±5.6	173.9±5.9	NS
BMI (Kg/m2)	29.2±4.2	26.3±2.2	24.1±1.4	0.01**

In previous study, it was found that the risk of diabetes increases linearly with increase in body mass index, (BMI); the prevalence of diabetes increased from 2% in those with a BMI of 25 to 29.9 kg/m2, to 8% in those with a BMI of 30 to 34.9 kg/m2, and finally to 13% in those with a BMI greater than 35 kg/m2, (9). The relative risk of T2DM increases as BMI increases above 23 years, and the association was found to be stronger in younger age groups (10).

Table (2) show the concentration of (PAI-1 ng/ml) in all groups. There is a significant elevation in PAI-1 in obese DMT2 patients (G1) & obese patients as compare with control healthy subjects (G3), ($P \leq 0.05$).

Table (2) The mean values and SD of PAI-1 in G1, G2 & G3.

Groups	Mean ±SD	P≤ value
Diabetes Mellitus type 2 & Obese, (G1).	**11.570±6.89**	**0.05***
Obese only, (G2)	**10.103±3.692**	**0.05***
Controls, (G3)	**8.157±4.384**	

The present study found a significant elevation in serum PA-1 concentration in obese DMT2 patients and in obese as compare with normal healthy control subjects. Previous studies found a correlation between serum PAI-1 concentration in diabetic obese patients (11,12).

The present study agrees with the previous studies done by (6, 10).

In the present study, as table 3 show, there was an elevation in serum homocysteine, (Hcy) in obese DMT2 as compare with obese patients and normal control healthy subjects (G3), $P \leq 0.01$).

Table (3) The mean values and SD of Hcy in G1,G2 & G3, (Hcy nmol/ml).

Groups	Mean ±SD	P≤ value
Diabetes Mellitus type 2 & Obese. (G1)	17.53 ± 5.6	0.01**
Obese only (G2)	12.47 ± 2.85	0.01**
Controls (G3)	12.18 ± 2.27	

The present finding agree with previous study that found increased plasma tHcy, triglyceride and waist circumference as well as decreased folic acid and vitamin B12 in type 2 diabetes mellitus (13,14). Moreover, previous study was done in Egypt which found similar result to the present study that Elevated serum homocysteine is associated with the presence of diabetic neuropathy in type 2 diabetic patients (15).

Previous study stated that homocysteine stimulates oxidative stress and inhibits nitric oxide formation, increased plasma homocysteine as observed in type 2 diabetic patients in the present study could promote platelet hyperactivity. It therefore suggests that some of the indicators of CVD risk factor (16). Several studies found that homocysteine levels are associated with a novel risk factor for CAD and premature atherosclerosis (17, 18). However, the mechanism of atherosclerosis plaques correlated with hyperhomocysteinemia is not clearly stated. Some studies reported that the effect of hyperhomocysteinemia is associated with increased thrombogenicity, an increase of platelet aggregation, reduction of protein C activation, oxidative damage of LDL, and endothelial dysfunction (19).

The present study conclude that there are a significant elevations in serum concentrations of PAI-1 and Hcy in obese diabetes mellitus patients.

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