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Adropin Levels in the Serum of Obese Type 2 Diabetic Patients and their Relationship to Oxidative Stress

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Abstract:

Background: Adropin, a peptide hormone translated from energy Homeostasis and insulin sensitivity. This study aims to investigate serum adropin level of type2diabetes mellitus (T2DM) patients, especially in obese patients, finding the relationship between oxidative stress and adropin levels. This study consisted of 30 patients with 30 healthy people; their ages ranged from (30-65) year of both sexes (12) females and (18) males for each patients and healthy peoples. The patients with T2DM showed significantly lower serum adropin levels and glutathione (GSH) concentration than those in healthy people. At the same time, glucose, malondialdehyde (MDA), peroxynitrite, and total lipids were higher concentrations in patients with T2DM than healthy people. It was concluded that the levels of adropin are inversely proportional to the concentration of glucose in the blood and positively correlated with GSH, MDA, peroxynitrite, total lipids, and body mass index.

Keywords: Adropin, Obese T2DM, Total lipids, Glutathione, Peroxynitrare.

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Introduction

The defect in glucose metabolism in most people with high blood glucose causes type 2 diabetes mellitus (T2DM) [1]; it is considered an expensive ailment as it constitutes more than 8.89 of the value of spending on health [2].

Insulin resistance and beta cell failure are the two main characteristics of type 2 diabetes, finally, it led to an intolerance to an excessive rise in glucose in the blood. In recent years, interest has been given to studying the molecules that regulate the metabolic balance and complex reaction which lee to T2DM [3][4].

Adropin is a 76-amino-acid peptide hormone discovered by Kumar et al. in 2008. It was originally characterized as a secreted peptide [5][6]. It is considered to be a powerful regulator that maintains insulin sensitivity and energy balance [7][8]. Low levels of adropin in humans are linked with a higher risk of metabolic illnesses such as metabolic syndrome, polycystic ovarian syndrome, gestational diabetes, and nonalcoholic fatty liver disease [9].

It was found that T2DM leads to an increase in the incidence of atherosclerosis, death of blood vessels and the heart [10][11]. In addition to an increase in the activity of free radicals, and thus an increase in lipid peroxidation [12].

The oxidative breakdown of polyunsaturated fatty acids produces malondialdehyde (MDA) a rather stable end product [13].

Glutathione (GSH) is an important intracellular antioxidant that helps to mitigate the consequences of oxidative stress [14]. Several studies have found that people with T2DM had lower erythrocyte (GSH) concentrations [15].
Peroxynitrite is considered as a transmitter inside cells and in all directions, and it has biological activity under pathological and physiological conditions [16]. While modest amounts of Peroxynitrite are advantageous for a variety of physiological and cellular processes, such as maintaining vascular tone, coagulation, and inflammation, large levels might have negative consequences [17][18].
Our study aimed to investigate the value level of adropin for patients with diabetes mellitus type 2 and oxidative stress.

Material and methods

Population study:

The study was conducted on 30 patients with type2diabetes mellitus of both sexes (12) females (18) males and their ages ranged from (30-65) year who visit the clinics of AL- wafa center in Mosul city during the period January to April 2020.
The healthy group included 30 people without diabetes mellitus and other diseases of both sexes (12) Females (18) males; their ages ranged from (30- 55) year.

Blood samples were drawn for the group of patients and the healthy after 10 hours of abstaining from eating, meaning that the person was fasting.

Samples collection

Serum samples
were obtained by withdrawing 5 ml of venous blood, then placing it in a gel tube and leaving it for 15 minute at a temperature of 37°C and centrifuging 3000 Xg. then separating the serum and keeping it at a temperature of-20°C until the necessary tests are performed.

Methodology:
1. Fasting blood Glucose was measured by using a kit manufactured by Biolabo France [19].
2. An ELISA kit was used to determine the amounts of Adropin in the blood (biosciences).
3. Malondialdehyde through using the modified method [20].
4. Glutathione uses Elman's reagent [21].
5. Peroxynitrite by using a modified method [22].
6. Total lipid by using colorimetric method [23].

Statistical analysis:
Statistic the data were analyzed using SPSS version 25. An independent T-test was used to compare two groups. 0.05 was deemed statistically significant [24].

Results and discussion

Table 1 presents results which shows an important increase in glucose in T2DM patients (11.2997±0.17537), with a percentage of 99.32% compared to healthy people (5.6690±0.0975mmol/L), this is consistent with several studies that showed height in the values of glucose in the serum of T2DM patients [7][25][26].
The reason for the rise in the level of glucose is due to the lack of insulin secretion or a defect in the insulin resistance in the body [27].
Also, table 1 shows decrease difference of adropin values in patents with T2DM compared to healthy People, respectively, at P≤ 0.05 (3.0013∓ 0.21056) ng/ml & (6,2560∓ 0.12865) and with a decrease percentage of (-52.03%) this is agree with previous studies that showed a decrease in the level of adropin in T2DM [28][5][7].
Celik et al. hypothesized that a deficiency level of adrop with cause of patients of gestural diabetes mellitus [29]. Furthermore, previous studies have linked low plasma adropin levels in metabolic syndrome, such as polycystic ovarian and non-alcoholic fatty liver disease. [30][31].
Adropin level was also found to be lower in endometrial cancer patients than in the control group [32].
The concentration of malondialdehyde (MDA) was estimated as a final product of the lipid peroxidation process, and the results showed a non- significant increase in MDA concentration with increased percentage +82.2% of a probability level of

P≤ 0.05 in the serum of T2DM patients (4.1927∓0.9998) µmol/L compared to its level in the healthy people (2.3010 ∓0.1268) µmol/L as shown in table 1.

This is consistent with other studies that indicated a high concentration of (MDA), but with a significant difference in T2DM patients. [33][34]

The results in table 1 showed the important decrease in the glutathione concentration in patients with T2DM (2.4010∓ 0.0508) µmol/L compared to healthy people (5.2438∓ 0.0792) mol/L at the level of probability P≤ 0.05. with a decreased percentage 54.2%. This is agreed with other studies [35][36]. Our findings imply that decreased GSH concentrations in T2DM patients are because of the lack of production of glutathione or reuse as an antioxidant [37].

The results in table 1 showed that the concentration of peroxynitrite in the serum of T2DM (26.7337∓0.67780) µmol/L is higher than that of healthy people (20.5333∓ 0.32424) µmol/L at probability level P ≤0.05 and this increase was significant and this agrees with what Cerielle et al., 2001 found.

The excessive glucose in the blood may increase NO production by up-regulated inducible INOs [38].

The results also showed in table 1 there is a significant increase at a paternal level of total lipids in patients with T2DM (914.3448∓ 7.10084) mg/100ml, at percentage 13.6% compared to the healthy people (805.1000∓ 1.9407) mg/100 ml, and this is consistent with other studies that indicated high total lipids in the serum of patients with diabetes mellitus [39], and also body mass index (BMI) give a significant difference between patients and healthy people Diabetes mellitus leads to hyperlipidemia and increased oxidative stress-induced endothelial dysfunction [40].

Body mass index (BMI) was found by dividing the weights of diabetic patients by the square of their heights. The results in table 1 showed a significant increase in the concentration of MDA, NO, Total lipids and BMI, this is agreed with previous studies that indicated a direct relationship between BMI and oxidative stress status [41][8], While Zang et al., study do not show any significant relationship between adropin and body mass index [42].

This study tries to understand the role of the peptide hormone, adropin, in patients with T2DM and healthy people, the level of adropin is inversely fit with the height of the glucose and was also positively correlated with blood glucose, GSH, MDA, NO, T. lipids and BMI As shown in Table 2.

Geo et al. demonstrated that adropin administration improves glucose tolerance, insulin resistance, and preferential carbohydrate metabolism over lipid metabolism in the setting of energy selection in diet-induced diabetic mice. Geo et al. [43].
They suggested that skeletal muscle is the pivotal peripheral tissue in mediating a dropin effects, in which adropin exerted Its protective role by sensitizing insulin signaling pathways and substituting glucose instead of Fat in muscle as the energy source, while it was shown to suppress fat oxidation [4], while our study does not agree with Ugur et al., [44]. Where they founded a higher adropin level in patients with T2DM compared to healthy people.
Table 1 shows the comparison of glucose, adropin, MDA, GSA, Peoxy nitrate BMI in T2DM and healthy people.

Biochemical Parameters	Mean ∓ SE		% increaled ordecrealed
	Patients (no.30)	Healthy people (no.30)	
Glucose mmol/L	11.2997∓0.1754	5.6690∓0.09745*	+ 99.3%
Adropin ng/ml	3.0013∓0.21056	6.2560∓0.12865*	-52.0%
MDA µmol/L	4.1927∓0.09998	2.3010∓0.12684*	+82.2%
GSH µmol/L	2.4010∓0.0508	5.2438∓0.07915*	-54.2%
peroxynitrite µmol/L	26.73337∓0.6778	20.5333∓0.3242*	30.2%
BMI kg/m2	33.2667∓1.5357	20.100∓0.3785*	65.5%
Total lipids mg/dL	914.3448∓7.1008	805.100∓1.9407*	13.6%

(*) Significant difference between patients and healthy people at P≤ 0.05.

Table 2 Correlation of adropin level with Biochemical parameter study in T2DM patients

Biochemical Parameters	Adropin (r-value)
Glucose mmol/L	*-0.089*
MDA µmol/L	-0.180*
GSH µmol/L	0.346*
Peroxynitrite µmol/L	-0.290*
BMI kg/m2	-0.010*
Total lipids mg/dL	-0.201*

(*) Correlation is significant at P≤0.05 (2-tailed);
T2DM: Type II diabetes mellitus.
MDA: Malondialdehyde.
GSH: Glutathion.
BMI: Body Mass Index.

Conclusion

Patients with T2DM have low concentration of adropin, and inversely proportional to glucose and positively correlated with Glucose, MDA, GSH, NO, BMI, and T lipids. Furthermore, obese patients with T2DM have significantly low concentration of adropin with increased oxidative stress.

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Abbreviations

T2DM: Type 2 diabetes mellitus.

GSH: Glutathione.

MDA: Macondialdehyde.

ONOO: Peroxynitrite.

BMI: body Mass index.

NAFLD: Non- alcoholic fartty liver disease.

PCOS: Poly cystic ovary syndrome.

GDM: Gestational diabetes mollify.

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