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Evaluation of aldose reductase levels and some other biochemical variables in patients with type 2 diabetes

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Abstract

Background: Diabetes is a disease characterized by high blood sugar levels. This elevation occurs as a result of the body's inability to produce insulin or use glucose effectively, resulting in the presence of high glucose in the blood.

Objective: The current study aimed to measure the activity of the aldose reductase enzyme in addition to other biochemical variables, including adiponectin, lipoproteins type (a) in the blood of patients with type 2 diabetes compared to the control group.

Methods: The study included collecting 90 blood samples from both sexes, patient's blood samples were (60), including (33) females and (27) samples were males from people with type 2 diabetes, whose ages ranged between (18-75) years, and (30) blood samples from healthy people as a control group the patients were diagnosed under the supervision of specialist doctors at Al-Sharqat General Hospital- Iraq.

Results: The results showed a significant increase ($P<0.05$) in the level of aldose reductase, adiponectin, and lipoproteins -a compared to the control group.

Conclusion: Increased concentrations of both adiponectin and lipoprotein-a in diabetic patients recognized the preventive effect of both against atherosclerotic alterations and increased risk of cardiovascular disease.

تقييم مستويات إنزيم ألدوز ريدكتاز وبعض المتغيرات البيوكيميائية الأخرى لدى مرضى السكري من النوع الثاني

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الخلاصة

مرض السكري هو مرض يتميز بارتفاع مستوى السكر في الدم ويحدث هذا الارتفاع نتيجة لعدم قدرة الجسم على إنتاج الأنسولين أو استخدام الكلوكوز بشكل فعال مما يؤدي إلى وجود نسبة عالية من الكلوكوز في الدم وقد شملت الدراسة جمع 90 عينة دم من كلا الجنسين وكانت عينات دم المرضى (60) منهم (33) أنثى و (27) عينة من الذكور من المصابين بداء السكري من النوع الثاني والذين تراوحت أعمارهم بين (18-75) سنة و (30) عينة دم من أشخاص أصحاء كمجموعة سيطرة تم تشخيص المرضى تحت إشراف الأطباء المختصين في مستشفى الشرقاط العام- العراق. هدفت الدراسة الحالية إلى قياس نشاط إنزيم الالدوز المختزل بالإضافة إلى متغيرات كيميائية حيوية أخرى منها الأديبونيكتين والبروتينات الدهنية نوع (a) في دم مرضى داء السكري من النوع الثاني مقارنة مع مجموعة السيطرة.وأظهرت النتائج ارتفاعا معنويا عند مستوى احتمالية ($P<0.05$) في مستوى إنزيم الالدوز المختزل والأديبونيكتين والبروتينات الدهنية-a مقارنة مع مجموعة السيطرة. زيادة تركيز كل من الأديبونيكتين والبروتينات الدهنية-a في مرضى السكري له تأثير وقائي معروف لكليهما ضد التغيرات التصلبية وزيادة خطر الإصابة بأمراض القلب والأوعية الدموية.

Introduction:

One of the most prevalent illnesses in the modern world, diabetes has been dubbed the "disease of the era" because of how frequent it is. Patients with diabetes have a chronic illness to which they are always exposed, and it can occasionally result in unexpected death. Diabetes has a variety of causes, including inherited and genetic variables in addition to environmental factors that makes the pancreas secrete either too little or no insulin, so the illness develops. This insulin shortage has an impact on how proteins, lipids, and carbs are metabolized [(1)]. Diabetes can have long-term detrimental effects on the heart, arteries, kidneys, nerves, limbs, and senses in addition to biological causes. Diabetes is a leading cause of strokes, heart attacks, kidney failure, blindness, and amputation of lower limbs. The disease has other causes as well, most of which are behavioural in nature include smoking, poor food, sedentary lifestyles, and lack of physical activity [(2)]. There are two types of diabetes: insulin-dependent diabetes is the first type. The majority of patients with this kind of diabetes are young adults and children, and the condition lasts the patient's entire life. Patients with it require frequent insulin injections [(3)]. Regarding to the second type, the none insulin-dependent diabetes. It is one of the metabolic disorders that primarily affects people who are forty years of age or older. As a result, this type is referred as adult diabetes and is defined by the body's resistance to insulin receptors or insufficiency in insulin secretion [(4)].Aldose reductase (AR) plays a critical role in the pathophysiology of type 2 diabetes by mediating the conversion of glucose to sorbitol through the polyol pathway [(5)] . This enzymatic activity contributes to various diabetic complications, including neuropathy, nephropathy, retinopathy, and cardiovascular issues. The accumulation of sorbitol leads to osmotic and oxidative stress, exacerbating tissue damage and disease progression [(6)].

adiponectin (ADP): a significant protein hormone that the fat cells secrete, and it has a variety of physiological functions as well as health concerns. It functions through certain receptors, AdipoR1 and AdipoR2, and is found in three isoforms including a low molecular weight (LMW, trimer), a medium molecular weight (MMW, hexamer), and a high molecular weight (HMW, 12–32 mer) isoform [(7)]. ADP has anti-inflammatory and anti-atherosclerotic functions and is also engaged in vital processes including insulin sensitivity, cholesterol and energy management, and so on, Higher levels are frequently linked to a

lower risk of chronic diseases like diabetes and cardiovascular disease, Its levels are controlled by a number of factors, including gender, body mass index (BMI), and nutrition [8]. Moreover, adiponectin may be protective against neurodegenerative illnesses and has surfaced as a possible biomarker of inflammation and insulin sensitivity [9]. Lipoprotein(a) (Lp-a) is a genetically determined lipoprotein that plays an important role in cardiovascular disease (CVD) risk. It has a unique structure, consisting of apolipoprotein B and a specific protein called lipoprotein(a), which varies in size among individuals. The study of lipoprotein(a) [Lp(a)] in diabetic patients is of great importance because of its close association with various complications of diabetes, particularly cardiovascular and renal diseases. Elevated Lp(a) levels have been associated with an increased risk of atherosclerosis, diabetic nephropathy, and overall cardiovascular events in individuals with type 2 diabetes mellitus (T2DM). Understanding these relationships could advance risk assessment and management strategies for patients with diabetes [10]. The aim of the study was to estimate the level of aldose reductase enzyme in diabetic patients, and to determine of some biochemical variables in diabetic patients including adiponectin, lipoprotein-a, and comparison with the healthy individuals .

Materials and Methods

(90) blood samples of both control and patient groups, whose ages ranged between (18-75) years, patients' blood samples were (60), including (33) females and (27) samples were males from patients with type 2 diabetes, and (30) blood samples from healthy people as a control group. The blood samples were collected from the Blood Bank Unit at Al-Sharqat General Hospital / Salah Al-Din Governorate, between 11/2/2023 and 1/1/2024 excluding any sample have another disease-like heart, liver, kidney and respiratory disorders or taking any medications that interrupt with the tests applied on the samples. Using a medical syringe a (5 ml) blood was drawn from the vein. The blood was then transferred to fresh, sterile tubes devoid of any additives, and left for ten minutes. A centrifuge was then used to separate the blood serum from the clotted portion of the sample. The samples were then kept at 4 degrees Celsius until the biochemical variables were measured.

Ethical approval

All design of the present study was ethically approved by the Laboratory Dept. - Al-Sharqat General Hospital / Salah Al-Din Governorate.

Biochemical tests

Estimation of aldose reductase activity (AR), Adiponectin (ADP) and lipoprotein-a (Lp-a) concentration was done using the analysis kits produced by) SUNLO, China, using ELISA technique [11].

Statistical analysis

The results were statistically analyzed using the statistical program (MINI TAB-17), and the t-test was used to show the difference between the two groups and determine the statistical differences between them at a probability level ($p \leq 0.05$).

Results

This study included measuring the level of aldose reductase activity ,Lp-a and adiponectin in the blood of patients with type 2 diabetes compared to healthy people, as shown in the table below. The tables show the rate of AR activity in the serum of patients with type 2 diabetes and healthy people. When statistically compared, it was found that there was a significant increase in the activity of the enzyme in patients compared to healthy people at a probability level of ($P \leq 0.05$).Also, the results showed that a significant increase in ADP levels at a probability level of ($P \leq 0.05$) in patients with diabetes when compared to control. In addition the level of Lp-a were significantly higher ($P \leq 0.05$) in patients group in compare with healthy people.

Table 1: shows the level of aldose reductase, adiponectin and lipoprotein-a.

Groups	Aldose Reductase (IU/L) Mean± SD	Adiponectin (ADP) (ng/mL) Mean± SD	Lipoproteins(Lp-a) (ng/mL) Mean± SD
Patients(60)	414±36.0*	41.6±5.7*	1401±68.6*
Control(30)	372±31.4	33.0±4.2	1164±48.7
P-Value	0.05	0.026	0.05

Table 2: Information about the participants:

Groups	Number of samples	Males	Females	Age
patients	60	27	33	18-75
control	30	18	12	18-75

Discussion

The hyperactivity of the sorbitol pathway in diabetes is the cause of the elevated aldose reductase enzyme in diabetic patients relative to healthy individuals. These findings align with earlier research that put the high rate of sorbitol pathway with diabetes mellitus incidence [12]. Aldose reductase may be activated by elevated oxidative stress linked to diabetes. The harmful consequences of sorbitol buildup in tissues can also be made worse by oxidative stress [13] . Insulin resistance and other diabetic problems, such as neuropathy, cataracts, and diabetic vascular disease, result from this. Aldose reductase activity is considerably higher in diabetes individuals, according to these studies, which may be a causing factor in the emergence of these complications also, inflammatory cytokines, often elevated in diabetes, can enhance aldose reductase activity. This creates a vicious cycle where inflammation further exacerbates cellular damage [14]. Furthermore, obesity and high-fat diets might raise methylglyoxal synthesis, which exacerbates the effects of aldose reductase in diabetes individuals, some individuals may have genetic variations that lead to increased expression or activity of aldose reductase, making them more susceptible to diabetic complications. Diabetic cataracts and other diabetic problems are linked to the polyol pathway, which is mostly mediated by aldose reductase. As a result, inhibiting aldose reductase may be a useful therapeutic approach for diabetic patients' care and prevention of these consequences [15].The results of this study prove the elevation of ADP levels in diabetic patients, due to disruptions in adiponectin levels, which are secreted by adipose tissue appear to have a crucial role in a number of biological processes, including blood sugar regulation and the body's reaction to insulin, patients with type 2 diabetes have higher levels of the hormone than healthy individuals [16].While obesity is often linked with lower levels of adiponectin, in some cases, especially in early stages of insulin resistance, adiponectin levels may be elevated. This can be due to compensatory mechanisms in an attempt to improve insulin sensitivity [17]. The study results showed that higher levels of lipoprotein (Lp-a) in diabetic patients compared with the control group, represent an important risk factor for coronary artery disease among patients with type 2 diabetes, due to several factors. First, there is an association between higher Lp-a levels and an increased risk of coronary artery disease in this population [18]. Second, studies have shown that Lp-a levels are associated with cardiovascular biomarkers, which reinforces the importance of monitoring them [19]. Therefore, it is highly recommended to regularly monitor Lp-a levels in patients with type 2 diabetes, as this information can contribute to the assessment of cardiovascular risk and the implementation of appropriate preventive measures to reduce this risk [20, 21].

Changes in other hormones, such as cortisol or thyroid hormones, may affect adiponectin production. These hormones can modulate adiponectin secretion and activity, leading to fluctuations in its levels. Some individuals may have genetic variants that lead to naturally higher levels of adiponectin, even in the presence of type 2 diabetes [22].

Conclusion: Increased activity of aldose reductase enzyme in patients with type 2 diabetes, also there were an Increased concentrations of both adiponectin and lipoprotein-a in diabetic patients recognized the preventive effect of both against atherosclerotic alterations and increased the risk of cardiovascular disease.

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