Evaluation of Some Biochemical Variables Regulated by The Kidneys in Patients with Type 2 Diabetes Mellitus in Kirkuk city

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ABSTRACT

The study was conducted on patients with type 2 diabetes at Kirkuk General Hospital, through the period from November 2017 to February 2018. The total number of diabetic patients was 30 (16 males and 14 females), and their ages ranged between (15-90 year). These patients were compared with 15 healthy individuals (10 males and 5 females). The results of the current study showed that type 2 diabetes had a significant effect on kidney function and raised glucose, urea and creatinine levels to high levels compared to the control group, which amounted to 306.37 mg/dL, 41.87 and 2.25 mmol/L, and the patients' age and body mass index significantly affected the variables studied. While there were no significant differences between the two sex groups among patients and healthy subjects, the results of the Pearson correlation coefficient analysis showed the presence of significant and direct correlations between the study factors and their variables.

Keywords: Kidney functions, Type 2 Diabetes, biochemical.

Introduction

One hundred million people with a history of diabetes worldwide [9]. Lifestyle modifications, diet modification, regular physical activity, and weight loss are indicated for the prevention of diabetes [8].

Diabetes mellitus, commonly known as diabetes mellitus, is a metabolic disease that causes high blood sugar. The hormone insulin transports sugar from your blood into your cells to be stored or used for energy [10]. With diabetes, your body either does not produce enough insulin or cannot effectively use the insulin it makes. Untreated high blood sugar from diabetes can damage nerves, eyes, kidneys, and other organs. Diabetes mellitus, diuresis and others (Latin: diabetes mellitus) is a syndrome characterized by a metabolic disorder and abnormalities in the concentration of glucose in the blood caused by a deficiency of the hormone insulin, decreased sensitivity of tissues to insulin, or both [11]. Diabetes leads to serious complications or even early death. However, diabetics can take specific steps to control the disease and reduce the risk of complications. These steps can be summarized as reducing weight and moving a lot [12].

Diabetic nephropathy is a microvascular complication that occurs in about 30% of patients with type 1 diabetes and about 40% in patients with type 2 diabetes (T2DM) (Alicic *et al*., 2017). It is characterized by albuminuria, an irreversible decrease in glomerular filtration rate and arterial hypertension (Adler *et al*., 2003).

Diabetes mellitus is a multifactorial syndrome characterized by abnormal hyperglycaemia. In particular, the incidence of Type 2 diabetes is increasing at an alarming rate (Al-Musawi *et al*., 2021). The incidence of diabetes in Iraq is very high, with one in five

adults affected by Type 2 diabetes [1]. Early diagnosis of patients with risk factors appears to be of paramount importance; Hence, routine screening for diabetes begins at the age of 45 years and is repeated at least every three years, while starting earlier in those at risk [2]. Type 2 diabetes is usually characterized by certain limits of blood parameters; HbA1c ≥ 6.5%, FBG 126 mg/dL, or 2-hour postprandial glucose of 200 mg/dL after 75 g oral glucose [1]. The HbA1c value is a measure of glucose bound to haemoglobin and indicates the average blood glucose for three months before the test [3]. Insulin is synthesized in the rough endoplasmic reticulum of beta cells, and the blood purification of insulin depends on its receptors and the enzyme that degrades, and the deficiency of these two molecules will lead to poor insulin purification and then hyperinsulinemia, which leads to the development of insulin resistance [4]. Insulin resistance is defined as a condition in which the sensitivity of target tissues to insulin is reduced, resulting in elevated levels of both insulin and glucose in the blood [5].

In Type 2 diabetes, the glomerular filtration rate also deteriorates significantly, which, if not treated medically, causes nephropathy that will progress to chronic kidney disease, which in turn complicates the clinical treatment of Type 2 diabetes [6]. Urea and creatinine are raised in uncontrolled T2DM, which in addition to hyperglycemia is usually associated with severe renal damage. Urea excretion is a vital physiological function of the kidneys because urea acts as a carrier of nitrogenous waste. Creatinine is a product of the breakdown of creatinine phosphate, which is released from skeletal muscle at a constant rate [7].

The current study aims to know the effect of type 2 diabetes on the college's control of the levels of some biochemical variables, the role of gender, age and body mass index factors, as well as the analysis of Pearson's correlation coefficient for the studied factors and variables.

Material and methods

Subjects and Methods: The study was conducted on patients with type 2 diabetes at Kirkuk General Hospital, through the period from November 2017 to February 2018. The total number of diabetic patients was 30 (16 males and 14 females), and their ages ranged between (15-90). Patients were selected after excluding those treated with insulin, hypertensive patients, those with a thyroid disorder or other endocrine disease, those with active liver disease, pregnant women, and smokers. These patients were compared with 15 healthy individuals (10 males and 5 females).

***Collection and preparation of blood samples*:** Fasting venous blood samples were collected from all participants in EDTA tubes to prepare the serum, blood was collected in disposable gel tubes, left to clot at room temperature for 10–15 min, and centrifuged at 2000 × g for ~10–15 min. The obtained serum was stored at −20 °C for the determination of glucose, urea and creatinine, by COBAS C 311 ROCH analyzer [13].

Biomarkers Analysis: The HbA1C level was assessed by an automated Epithod®616 Analyzer (DxGen /Korea) based on the boronate affinity principle. Insulin concentration was measured using an ELISA kit(CALBIOTECK/USA), which isrelied on the standard sandwich enzyme-linked immune sorbent assay. IR was detected by the homeostasis model estimation of IR (HOMA-IR) (Bruder-Nascimento *et al.,* 2014), and calculated by applyingthe equation [IRHOMA = (Fasting insulin × Fasting glucose) / 405] (Saleh *et al*., 2019).

Berthelot's method was employed to assess levels of urea (mmol/L) using the Linear kit, Spain, while Randox kit (Randox, UK) was used to evaluate creatinine levels (mmol/L) (Saleh *et al*., 2019).

Statistical analysis: Statistical analysis was performed using Statistical Analysis Software (SAS) for the Social Sciences (version 9.0 for Windows). The data are presented as means. Significance was set at $p < 0.05$. Cases and controls were compared using Duncan's multiple range test. Pearson's coefficient test

was used to test the relationship between the studied variables and factors.

Result and Discussion

Result

Effect of diabetes disease: The total number of the study sample was 45 individuals, including 30 patients, who were divided into (16 males and 14 females), in addition to (15 individuals as a control group, including 10 males and 5 females). Table (1) shows type II diabetes mellitus in the biochemical variables of the student's kidney function, which shows that the levels of these variables glucose, urea and creatinine are higher in the patients group than normal levels with significant differences from their values in the control group (healthy) where the group values reached patients have 306.37 mg/dL, 41.87 and 2.25 mmol/L while in the control group they are 141.20 mg/dL, 27.83 and 1.07 mmol/L for the three variables, respectively.

Table (1): The effect of diabetes on the studied biochemical variables

Groups	Glucose (mg/dl)	Urea (mmol/L)	Creatinine (mmol/L)
Patient (N=30)	306.37 a	41.87 a	2.25 a
Control (N=15)	141.20 b	27.83 b	1.07 b

The values followed by the same letter are not significantly different from each other

Effect of Age: Table (2) shows the average effect of age on the biochemical variables studied among patients with type 2 diabetes, where the study sample was divided into three age groups (less than 45, 45-60 and more than 60 years old or old). For the age group over 60 years, they were recorded at 364.63 mg/dL, 44.96 and 2.30 mmol/L for glucose, urea and creatinine levels, respectively, while the lowest rates were 130.45 mg/dL, 27.71 and 1.03 mmol/L. for the three glucose variants. And urea and creatinine, respectively, for the age group less than 45 years within the control group, and we note the clear effect of the increase in age on raising the levels of the variables studied with the disease and in its absence.

Table (2): The effect of age on the studied biochemical variables

Groups	Age (year)	Glucose (mg/dl)	Urea (mmol/L)	Creatinine (mmol/L)
Patient	Less than 45 (N=4)	299.5 a	33.65 ab	2.18 a
	45-60 (N=18)	282 ab	42.35 a	2.25 a
	More than 60 (N= 8)	364.63 a	44.96 a	2.30 a
Control	Less than 45 (N=11)	130.45 c	27.71 b	1.03 b
	45-60 (N= 4)	170.75 bc	28.15 b	1.19 b
	More than 60	-	-	-

The values followed by the same letter are not significantly different from each other

Effect of Gender: Table (3) shows the effect of the gender category on the levels of glucose, urea and creatinine in the two groups (type 2 diabetes patients and control), as the results of the statistical analysis indicated that the effect did not reach the significant limits within both groups

Table (3): The effect of Gender on the studied biochemical variables

Groups	Gender	Glucose (mg/dl)	Urea (mmol/L)	Creatinine (mmol/L)
Patient	Male (N=16)	300.81 a	42.46 a	2.25 a
	Female (N=14)	312.71 a	41.23 a	2.25 a
Control	Male (N=10)	139.9 b	27.33 b	1.08 b
	Female (N=5)	143.8 b	28.82 b	1.07 b

The values followed by the same letter are not significantly different from each other

Effect of BMI: Table (4) shows the average effect of body mass index on the biochemical variables studied for the two groups (type 2 diabetes and control), including the presence of small significant differences for this factor, as the group recorded more than 30 g/cm2 within the group of patients, the highest levels of glucose and urea. With values of 378.7 mg/dl and 46.13 mmol/L for each of them, respectively, there were no significant differences between BMI categories for creatinine level. Also, there were no significant effects of BMI categories on the levels of the three variables under study within the healthy group

Table (4): The effect of BMI on the studied biochemical variables

Groups	BMI (gm/cm^2)	Glucose (mg/dl)	Urea (mmol/L)	Creatinine (mmol/L)
Patient	Less than 25 (N=3)	345 ab	42.1 a	2.12 a
	25-30 (N=17)	257 b	39.35 ab	2.35 a
	More than 30 (N= 10)	378.7 a	46.13 a	2.12 a
Control	Less than 25 (N=3)	141 c	28.4 b	1.03 b
	25-30 (N=17)	144 c	27.02 b	1.08 b
	More than 30 (N= 10)	136 c	28.3 b	1.13 b

The values followed by the same letter are not significantly different from each other

Pearson correlation coefficient: Due to the presence of significant effects of age groups and body mass index on the studied biochemical variables, and to confirm the relationship between the studied factors and variables, Pearson correlation coefficient analysis was conducted, and the results of Table (5) showed the age factor was significantly associated at the 1% probability level with urea and creatinine levels with values of 0.445 and 0.599, respectively, and at the 5% probability level with 0.327 glucose levels, and all these correlations were in a positive direction (directly), meaning that the levels of age Biochemical variables increase with age of the patient.

As for the body mass index, it was found to have a significant correlation at the probability level of 1% and in a positive direction with creatinine levels with a value of 0.396, while the correlation coefficients with glucose and urea did not reach the statistical significance limits

Table (5): Pearson's correlation coefficient between the factors and variables of the study.

Variables / Factors	Glucose (mg/dl)	Urea (mmol/L)	Creatinine (mmol/L)
Age (year)	0.327*	0.445**	0.597**
BMI (kg\ m^2)	-0.063	0.035	0.396**

**** and * are significant at the 1% and 5% probability levels, respectively.**

Discussion

Diabetics are more likely to develop electrolyte disturbances due to the disease state itself and the associated blood glucose imbalance. The use of antidiabetic drugs also leads to the development of electrolyte disturbances [14].

Poorly controlled blood glucose levels may lead to increased levels of urea and creatinine, thus increasing the patient's chances of developing diabetic nephropathy. This confirms that hyperglycemia is one of the main causes of progressive renal damage [22]. Usually, patients with T2DM should be monitored periodically for nephropathy and urea and creatinine levels. The current study is consistent with a previous study [7], which showed a strong positive association between urea levels and blood glucose levels, both during fasting and after eating. Likewise, the present result is in agreement with that of another study, which also revealed a very significant positive relationship between fasting blood glucose and creatinine levels in T2DM [23]. Chronic exposure to high levels of glucose increases the production of reactive oxygen species and generates oxidative stress in islet cells [24].

Various studies have shown that higher urea levels are proportional to higher creatinine levels [21]. However, T2DM patients showed slightly higher levels of urea and creatinine than those in the control group, and the differences were slight. The results of the current study partially agree with the results of previous research which showed that urea and creatinine levels were significantly higher ($P \leq 0.05$) in T2DM patients [20]. The non-significant findings found in this study may be attributed to different sample sizes, technical reasons, population differences in health habits, and genetic predisposition to the disease.

Consider assessing kidney function. Estimated glomerular filtration rate and serum creatinine depend on renal hemodynamics, systemic blood pressure, urinary findings, and susceptibility to therapeutic intervention. On the basis of these findings, it was concluded that microalbuminuria may not be associated with abnormal creatinine or creatinine abnormalities [15].

Among the important parameters that have been shown to directly influence renal hemodynamics and alter the afferent/outbound balance is BMI, which can lead to glomerular hypertension, hyper filtration, and eventually renal injury [16]. The current study shows a positive correlation between (body mass index, weight) and creatinine estimation in a diabetic patient.

Studies have demonstrated assessment of renal function in relation to body dimensions, however, it is important to realize that renal function equations are subject to BMI-related bias, for example, Kwakernaak et al's comparison of Cockcroft-Gault and dietary modification in kidney disease in a healthy subject, He found that the effect of BMI on overestimation of GFR was greatest for Cockcroft-Gault and lowest for diet modification in renal disease [17]. Renal hemodynamics profile in overweight and obese subjects, and in subjects with a central distribution of body fat, may be influenced by other factors such as sodium intake and volume homeostasis, as well as long-term susceptibility to renal damage [18]. Interestingly, in young subjects with low blood pressure levels, weight gain correlates with a higher filtration fraction in response to higher salt intake, while glomerular filtration rate increases in lean subjects without an increase in filtration fraction. Furthermore, in overweight subjects, higher salt intake is associated with a greater increase in extracellular volume than in lean subjects, supporting the effect of small changes in renal hemodynamics on volume balance [19].

Conclusions

We conclude from the current study that type 2 diabetes had a significant effect on kidney function and raised glucose, urea and creatinine levels to high levels compared to the control group, as well as the patients' age and body mass index significantly on the variables studied, while no significant differences appeared between the two sex groups among patients and healthy subjects. The results of the

correlation coefficient analysis showed that there were significant and direct correlations between the study factors and their variables.

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