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Determine the level of some Glycemic Control Parameters and Biochemical Parameters of Kidney Function of T2DM Patients

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Abstract

In this work, 150 sample from serum of T2DM patients and control were collected to determine level of biochemical parameters such as Glycated Hemoglobin, Glucose and kidney function (urea creatinine, uric acid). The present study showed statistically significant differences ($p<0.001$) for Fasting Serum Glucose(FSG), Glycated Hemoglobin (HbA1C),Urea and Uric acid in the T2DM patients groups when compared with control group. Creatinine showed statistically significant differences between study groups ($p< 0.05$). Whilst, when we studied the differences between T2DM patients groups [Good Glycemic Control , Moderate Glycemic Control and Poor Glycemic Control]showed statistically significant differences ($p<0.001$) for Glucose and Glycated Hemoglobin in the T2DM patients groups, whilst Urea, Creatinine and Uric acid showed nonsignificant differences between study groups ($p<0.001$).

Keywords: T2DM, Glucose, Glycated Hemoglobin, Urea and Uric acid.

Introduction

Hyperglycemia is a primary feature of a group of physiological dysfunctions referred to as diabetes mellitus. It is a direct result of insulin resistance, inadequate insulin secretion, or elevated glucagon production. An autoimmune disease called type 1 diabetes (T1D) destroys the pancreatic beta cells. Type 2 diabetes (T2D), which is far more common, is primarily caused by inadequate glucose regulation, which is exacerbated by insulin resistance and dysfunctional

pancreatic beta cells [1]. The obesity pandemic is intimately associated with the growing worldwide health issue of type 2 diabetes mellitus (T2DM). Hyperglycemia and individual components of the insulin resistance (metabolic) syndrome put people with type 2 diabetes at increased risk for microvascular consequences (retinopathy, nephropathy, and neuropathy) as well as macrovascular issues (cardiovascular comorbidities). A number of pathophysiological abnormalities, including obesity, poor diet, and physical inactivity, as well as genetic variables, are linked to the disturbed glucose homeostasis in type 2 diabetes [2]. In medical contexts, urea, also known as blood urea nitrogen (BUN), is used in conjunction with creatinine (Cr) to assess renal function. Urea is a waste product of protein metabolism produced in the liver and eliminated by the kidney. However, a number of variables, including the intake of protein, corticosteroids, gastrointestinal bleeding, and dehydration, may impact BUN levels. The liver's urea cycle enzymes produce urea by deaminating amino acids [3, 4]. Over 90% of the urea secreted by the kidneys is eliminated by their large-scale excretion. It is eliminated from the blood via the glomerulus, but tubular reabsorption is greatly enhanced by passive diffusion [5]. The chemical waste product known as creatinine is created during the nonenzymatic dehydration process of phosphocreatine and creatine. The chemical known as creatine, which is needed for the creation of energy in muscles, is created by the liver and pancreas through the synthesis of three amino acids: arginine, glycine, and methionine. Approximately 2% of the creatine in your body is converted into creatinine each day by your body. The bloodstream transports creatinine to the kidneys, where it is filtered and eliminated as urine [6, 7]. For a considerable amount of time, creatinine has been utilized as an indicator of renal function, especially after dialysis, thyroid issues, and muscular injury. The kidneys are responsible for keeping blood creatinine levels within the normal range. Because of this, creatinine has been found to be a very reliable indicator of renal function; the blood's amount of creatinine rises as kidney function declines. An issue with one or both kidneys may be indicated by abnormally high creatinine levels, sometimes even before a patient experiences any symptoms [8, 9]. The primary byproduct of purine nucleoside catabolism is uric acid (UA) (adenosine and guanosine). Large amounts of filtered UA are reabsorbed in the proximal convoluted tubules, after which the distal tubules of the proximal tubules secrete uric acid and the distal tubules

resorb the filtered UA. As a result, between 6% and 12% of the total amount filtered is excreted in urine as UA [10]. Chronic exposure to hyperglycaemia affects the microvasculature, eventually leading to diabetic nephropathy, retinopathy and neuropathy with high impact on the quality of life and overall life expectancy [11].

Materials and Methods

In this potential clinical investigation, 100 out of 150 samples received a type 2 diabetes diagnosis. The fifty patients who were left in the trial served as a control group because they were not diabetics. Furthermore, the three categories of people with type 2 diabetes were good, moderate, and bad, according to how well or poorly they were able to control their blood sugar.

Study Samples

The study has included 150 subjects, 100 of them were diagnosed with T2DM disease in age range 47.06±11.17 year. The remain 50 were non-diabetic participants used as control for the study in age range 45.60±11.62 year. Moreover, T2DM patients were divided into three groups according to their glycemic control, namely; good glycemic control, moderate glycemic control, and poor glycemic control. The anthropometric information were gathered from each subject including hieght, weight. After that, the blood was collected and sera were extracted and stored in 3 tubes at freezing temperature until the time of analysis.

Anthropometries Measurements

Anthropometric measurements were made of the following: age, weight, height. The formula used to calculate the Body Mass Index (BMI) consists of the fundamental division of weight by height squared.

Estimation

Determination of Fasting Serum Glucose (FSG)

The glucose oxidase (GOD) oxidizes glucose to gluconic acid and forms hydrogen peroxide which, in the presence of peroxidase (POD), reacts with 4- aminoantipyrine and phenol and produces a colored complex, whose color intensity is directly proportional to glucose concentration in the sample. This method is known as an enzymatic colorimetric method [12].

Determination of Urea

Urea in the specimen is hydrolyzed enzymatically in to the ammonium (NH^{+}_{4}) and carbon

dioxide (CO_2). In a reaction catalyzed by glutamate dehydrogenase (GLDH), formed ammonia ions react with α-ketoglutarate while NADH is oxidized simultaneous to NAD^+

The decrease in NADH concentration is proportional to the amount of urea in the specimen. This method is known as kinetic method UV [13].

Determination of Creatinine

Creatinine reacts in an alkaline environment with picric acid forming a salt of a yellow-orange color. The intensity of the color that develops in a predetermined time interval is proportional to the amount of creatinine in the sample [14].

Determination of Uric Acid

Uricase transforms uric acid to allantoin with formation of hydrogen peroxide which, in presence of peroxidase (POD), reacts with 4- aminoantipyrine and stain to produce a colored complex whose color intensity is directly proportional to the uric acid concentration in the sample [15].

Determination of Glycated Hemoglobin (HbA1c).

This method utilizes the interaction of antigen and antibody to directly determine the HbA1c in whole blood. Total hemoglobin and HbA1c have the same unspecific absorption rate to latex particles. When mouse antihuman HbA1c monoclonal antibody is added (Reagent B) latex-antibody complex is formed.

Agglutination is formed when goat anti-mouse IgG polyclonal antibody interacts with the monoclonal antibody. The amount of agglutination is proportional to the amount of HbA1c absorbed on the surface of latex particles. The amount of agglutination is measured as absorbance. The HbA1c value is obtained from a calibration curve [16, 17].

Results and Discussion

Table (2) shows (mean ± SE) of age among groups for patient and control group 47.06±11.17, 45. 60±11.62 respectively. The age distribution among patients groups shows no significant difference between the different groups at ($p>0.05$). The body mass index results were measurement of the (means ± SE). Table (2) showed increase but no significant different

(p>0.05) between the studied groups patients and control healthy group (25.83±2.15, 25.95±3.91 respectively).

Table 2: Characteristics of patients and control.

Parameter	Control	T2DM patients	*p*-value
Number	50	100	-
Age (year)	45.60±11.62	47.06±11.17	0.464
BMI (kg/m^2)	25.95±3.91	25.83±2.15	0.836

When compare patient groups between themself showed the age among groups (good glycemic control, moderate glycemic control, and poor glycemic control) was 47.48±12.50, 46.60±9.96, 47.73±12.74 respectively, was found increase but no significant (p>0.05) , as shown in table (3).

The body mass index results were measurement of the (means ± SE). Table (3) showed no significant different (p>0.05) between the studied groups patients (good glycemic control, moderate glycemic control, and poor glycemic control) (25.55±2.50, 25.94±1.97, 26.07±2.00 respectively).

Table 3: The characteristics of T2DM patients.

Parameter	Good Glycemic Control	Moderate Glycemic Control	Poor Glycemic Control	*p*-value
Number	33	52	15	-
Age (year)	47.48±12.50	46.60±9.96	47.73±12.74	A- 0.724 B- 0.944 C- 0.732
BMI (kg/m^2)	25.55±2.50	25.94±1.97	26.07±2.00	A- 0.425 B- 0.441 C- 0.831

A: Good Glycemic Control vs Moderate Glycemic Control; B: Good Glycemic Control vs Poor Glycemic Control; C: Moderate Glycemic Control vs Poor Glycemic Control.

Age is one of the main risk factors in pre diabetes and T2DM incidence [18]. It is widely known that T2DM sometimes goes untreated for many years since hyperglycemia develops gradually and frequently isn't severe enough in the beginning for the patient to experience the symptoms of traditional diabetes [19]. The findings can be explained by the fact that the risk of getting type 2 diabetes increases with age, weight, and inactivity [20].

In persons who are genetically predisposed to type 2 diabetes, obesity is probably a diabetogenic factor because it increases insulin resistance. Insulin resistance raises plasma levels of insulin, which increases appetite and leads to weight gain [21].

The body mass index (BMI) of the poor glucose groups in this study was higher, which was in line with the findings of Fadhil et al. that the BMI of diabetic patients was significantly greater than that of excellent glucose patients [22]. Zaho et al. found that higher BMI was associated with increased resistance and decreased insulin sensitivity in the elderly T2DM population in Asia [23].

Levels of Glycated Hemoglobin, Fasting Serum Glucose (FSG), Urea, Creatinine and Uric acid.

The (mean ± SD) of levels of Glycated Hemoglobin, Fasting Serum Glucose (FSG), Urea, Creatinine and Uric acid in serum of T2DM patients and control group, were illustrated in table (4).

The present study showed statistically significant differences ($p<0.001$) for Fasting Serum Glucose (FSG), Glycated Hemoglobin, Urea, and Uric acid in the T2DM patients groups when compared with control group, the mean value of Fasting Serum Glucose (FSG), Urea, Glycated Hemoglobin and Uric acid (155.56±22.51, 8.05±1.77, 37.71±12.67 and 5.54±1.31) respectively in the T2DM patients and (88.20±9.87, 4.91±0.28, 29.73±8.12 and 4.29±1.18) respectively in Control group. Creatinine showed statistically significant differences between study groups ($p< 0.05$). The T2DM patients groups when compared with control group. The mean value of Creatinine (0.91±0.30) in the T2DM patients than in Control group was (0.83±0.16).

Table 4: Characteristics of patients and control.

Parameter	Control	T2DM patients	*p*-value
Glucose (mg/dL)	88.20±9.87	155.56±22.51	<0.001
HbA1c %	4.91±0.28	8.05±1.77	<0.001
Urea (mg/dL)	29.73±8.12	37.71±12.67	<0.001
Creatinine (mg/dL)	0.83±0.16	0.91±0.30	0.033
Uric acid (mg/dL)	4.29±1.18	5.54±1.31	<0.001

Whilst, when we studied difference between T2DM patients groups [Good Glycemic Control , Moderate Glycemic Control and Poor Glycemic Control]showed statistically significant

differences (p<0.001) for Fasting Serum Glucose (FSG) and Glycated Hemoglobin in the T2DM patients groups, whilst Urea, Creatinine and Uric acid showed nonsignificant differences between study groups (p>0.001). The mean value showed in table (5).

Table 5: The levels of biochemical parameters in T2DM patients.

Parameter	Good Glycemic Control	Moderate Glycemic Control	Poor Glycemic Control	*p*-value
Glucose (mg/dL)	133.09±6.43	157.86±10.06	197.00±8.31	p <0.001
HbA1c %	6.55±0.28	7.96±0.58	11.68±1.15	p <0.001
Urea (mg/dL)	36.22±13.32	36.30±10.01	45.87±16.77	p> 0.001
Creatinine (mg/dL)	0.91±0.36	0.90±0.28	0.94±0.22	p> 0.001
Uric acid (mg/dL)	5.18±1.30	5.57±1.30	6.23±1.18	p> 0.001

A: Good Glycemic Control vs Moderate Glycemic Control; B: Good Glycemic Control vs Poor Glycemic Control; C: Moderate Glycemic Control vs Poor Glycemic Control.

Patients with type-2 diabetes mellitus produce up to 3000% more glucose than normal, with both hepatic and renal sources contributing equally to this rise [24, 25]. The kidney plays a role in maintaining glucose homeostasis through the processes of gluconeogenesis, glucose filtration, glucose reabsorption, and glucose intake. Individuals diagnosed with type-2 diabetes (T2DM) may exhibit modifications in any one of these processes, rendering them potential candidates for novel therapeutic modalities. Up to 20% of all glucose is produced by gluconeogenesis, which is primarily controlled by the kidney, according to new studies [26].

A biochemical test for the pathophysiology of diabetes sequelae through glycosylation reactions has been developed using glycated hemoglobin (HbA1C). The hemoglobin molecule's post-translational changes yield HbA1C, which is closely associated with hyperglycemia levels six to ten weeks earlier [27]. In a healthy state, the connection between the N-terminal valine of glucose and hemoglobin molecules causes hemoglobin to become glycosylated [28].

In this study, highly HbA1c levels were linked to poor glycemic control in T2DM and this observation is supported by ***Siva Prasad et al*** [29], as well as ***Rasheed Hameed M*** [30].

Elevated blood glucose-induced levels of urea and creatinine are signs of impaired kidney function in diabetic patients. Chao et al. reported that HbA1c values were greater in patients than in controls, which is in line with our results [31]. Apart from its clinical significance for

treating both type 1 and type 2 diabetes, HbA1c is frequently utilized in the blood glucose control of gestational diabetes mellitus [32].

The higher level of urea and creatinine in diabetics compared to the control group is consistent with ***Chutani, A., et al*** [33], In diabetics, serum creatinine and urea levels can be helpful prognostic indicators and indicators of renal impairment. Blood sugar regulation can stop diabetic nephropathy from developing, which can significantly lower the morbidity and mortality linked to this metabolic disease. Renal function test results typically occur at higher reference limits in patients of type 2 diabetes mellitus, which is suggestive of the onset of nephropathy. Renal function test estimation has become a viable adjuvant for the long-term care of Type 2 diabetes mellitus due to its simplicity, affordability, sensitivity, and reliability [34].

It was discovered that elevated serum uric acid levels were linked to an increased risk of type 2 diabetes. In particular, the original cohort's risk of type 2 diabetes increased by 20%, whereas the offspring cohort's risk increased by 15% for every mg/dL increase in blood uric acid levels. These correlations remained in both genders and were unaffected by age and BMI, two additional established risk factors for type 2 diabetes [35]. Therefore, investigating the risk factors for diabetic macrovascular disease may yield additional knowledge about its prevention and treatment. It has been shown that endothelial dysfunction is associated with uric acid, the final result of purine metabolism in humans and great apes [36], vascular nitric oxide activity, smooth muscle cell proliferation and oxidative stress, which are the key mechanisms of macrovascular disease [37-39]. It is unclear whether uric acid causes, coexists with, or coincides with macrovascular disease, despite epidemiological research showing a link between the two [40]. Furthermore, the question of whether uric acid poses a risk for diabetic macrovascular disease on its own is still being debated [41].

Conclusion

When compared to the control group, the T2DM patient groups' Fasting Serum Glucose (FSG), Glycated Hemoglobin, Urea, and Uric Acid revealed statistically significant differences in this study. Between study groups, there were statistically significant differences in creatinine. However, when we looked at the differences between the T2DM patient groups (Good

Glycemic Control, Moderate Glycemic Control, and Poor Glycemic Control), we found that there were nonsignificant differences between the study groups for urea, creatinine, and uric acid, but statistically significant differences for fasting serum glucose (FSG) and glycosated hemoglobin.

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