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Assessment the Role of Kidney Function and Total Proteins in Patients with Diabetic Nephropathy in Kirkuk City/ Iraq

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Abstract: ***The current study aims to determine the levels of creatinine, urea, glomerular filtration rate eGFR and total proteins in patients with diabetic nephropathy, the experiment was conducted for the period from the beginning of July 2023 until the end of October 2023 Blood samples were collected from patients visiting Kirkuk General Hospital and specialized medical clinics in the city of Kirkuk, and included (70) male patients with diabetic nephropathy at the ages of (35-75) years and an average weight of (79) kg, as well as About (20) healthy people with the same average age and weight of patients and the study samples were distributed as follows: The first group of control group included (20) healthy males and the second group of patients group was distributed into four groups according to age groups age group (35 - 45) years and included 16 patients, age group (46 - 55) years and included 17 patients, age group (56 - 65) years and included 20 patients age group (66 - 75) years and included 17 patients. The study's findings indicated a noteworthy rise ($P \leq 0.05$) in the levels of creatinine and urea and a significant decrease in the rate of glomerular filtration and total proteins in patients with diabetes compared to the control group, either by age groups, the results showed no significant differences in the concentration of creatinine and urea in patients with diabetes, while the rate of glomerular filtration and total proteins by age groups showed significant differences in patients with diabetes, as the first category showed a significant increase Compared to the rest of the categories.***

Keywords: Kidney Function, Egfr, Total Proteins, Diabetic Nephropathy.

1. INTRODUCTION

Diabetes mellitus (DM) is a chronic condition that occurs as a result of the failure of the pancreas to produce enough insulin or when the body's insulin production is ineffective or

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insulin receptor malfunction [1]. DM diabetes is the most prevalent endocrine disease and is a serious health concern worldwide and complications occur that increase unexpectedly if the disease is not well regulated such as hyperglycemia, ketoacidosis, hyperosmolar coma, cardiovascular disease (CVD), end-stage renal failure, retinal damage that can cause blindness, nerve damage of various kinds, and microvascular damage that can be Impotence and slow healing all cause serious long-term complications as well as slow healing of wounds [2]. Diabetic nephropathy (DN) is one of the most common chronic microvascular complications of diabetics and the leading cause of end-stage kidney disease (chronic kidney disease (CKD), DN diabetic nephropathy is characterized by excessive filtration and synovuria in the early stages followed by a gradual decrease in kidney function [3]. Assessment of kidney function is important indicators in the lives of patients with kidney disease or diseases that affect kidney function [4]. Serum creatinine and serum urea are recognized as ideal markers to know the progression of diabetic nephropathy Diabetic nephropathy is clinically diagnosed with low GFR and possible hypertension, cardiovascular disease and mortality resulting from it. Early detection of an imbalance in creatinine and urea levels in Diagnosis, prevention and development of diabetic kidney disease [5]. GFR is widely used as an indicator of kidney function and the normal range for men is about 130 ml per minute per 1.73 m2 and for women 120 ml per minute per 1.73 m2, which depends on age, sex and body size means low values with age [6].Total proteins are one of the most abundant compounds in blood serum or plasma and proteins are involved in many vital functions as proteins are used in the formation of enzymes, hormones and antibodies as well as It plays an important role in maintaining the balance of osmotic pressure and proteins are found in all body fluids but show a very high concentration in plasma, lymphatic fluids and some secretions, the total serum protein test evaluates the total amount of proteins in the blood, as many studies have shown high levels of globulin in the blood and a decrease in the ratio of albumin to globulin (A/G) in patients with infections and advanced malignant tumors, indicating their important role in the immune system and inflammation [7]. The current study aimed to evaluate the concentrations of kidney function creatinine and urea and to know the glomerular filtration rate and total proteins, which are important indicators in patients with diabetic nephropathy.

2. RELATED WORKS

The results of study [8] revealed an increase in the average value of serum creatinine in patients suffering from diabetic nephropathy, in relation to the level of urea in the blood. The results of study [9] showed an increase in the average concentration of blood urea in diabetic patients compared to the healthy group, and the results showed Study [10] found a decrease in the concentration of total protein in the serum of patients with diabetic nephropathy. The results of a study [11] showed a decrease in the glomerular filtration rate in people with diabetes compared to healthy people, and all of these previous studies reported that a decrease in the estimated glomerular filtration rate (eGFR) is an indicator of poor kidney function in patients with diabetic nephropathy, so evaluating the eGFR is crucial. Importance in diabetic patients, and all the results of these studies were consistent with the results of our current study

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3. METHODOLOGY

Study Design

The research took place from July 2023 inception through October 2023 conclusion.at Kirkuk General Hospital and specialized medical clinics in Kirkuk City. It included (70) male patients with diabetic nephropathy at the ages of (35-75) years, and an average of weights (79) kg, as well as a number of healthy people with the same average age and weight of patients, and the study samples were distributed into two groups. The first group, the control group, included (20) healthy males, and the second group, the patient group, were distributed into four groups according to age groups: there were 16 patients in the 35-45 age group, 17 patients in the 46-55 age group, 20 patients in the 56-65 age group, and 17 patients in the 66-75 age group.

Blood Samples

Blood samples were obtained from patients via a 5 ml venous draw and were then transferred into glass tubes that contained gel, as well as into vacuum tubes with gel and clot activator but no anticoagulant. The sample was left at room temperature for 30 minutes to coagulate, and the tubes were placed in a centrifuge for a duration of 15 minutes, rotating at a speed of 3000 rpm to acquire serum.

Biochemical Tests

Determination of concentrations of a set of biochemical indicators of the studied groups, including estimation of creatinine and urea concentration in blood serum using ready-made analysis kit (Kit) from the French-origin Biolabo [12] and determination of glomerular filtration rate (GFR) from plasma concentration of endogenous substances such as creatinine, and was performed via eGFR calculator [13]. And the determination of the total protein concentration in serum samples using a ready-made analysis kit (Kit) from the manufacturer Biolabo, of French origin, this method is based on chromatography and absorption measurement Optical using an optical spectrometer [14].

Statistical Analysis

Statistical analysis of the results was performed using the SPSS software program based on the T-test test, where the averages of patients and healthy people were compared at a significant level ($P \leq 0.05$). The ANOVA test was used to compare between age groups and at a significant level ($P \leq 0.05$), and the values of the variables were described as a standard deviation ± Mean [15].

4. RESULTS AND DISCUSSIONS

Creatinine Concentration in Diabetic Patients and Control Group

The findings in Table 1 reveal a notable elevation ($P \leq 0.05$) in the levels of creatinine in patients with diabetes, as it reached (1.15 ±0. 36) mg / 100 ml, compared to the control group that amounted to (0.50 ± 0.20) mg / 100 ml, and the results of the current study agreed with the study [16] who found an increase in the average value of creatinine in the diabetic group

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compared to the healthy group, According to age groups the results in Table 2 show that there are no significant differences between the different age groups among patients with diabetes, as the concentration of creatinine in the first age group (35-45) amounted to (1.00 ± 0.31) mg / 100 ml, compared to the second age group (46-55) amounted to (1.27 ± 0.38) mg / 100 ml, in the third age group (56-65) it amounted to (1.13± 0.31) mg / 100 ml, and in the fourth age group (66-75), which amounted to (1.19 ±0.42) mg / 100 ml. The results of this study are consistent with the findings of [17] who indicated that the differrence in age does not affect the level of creatinine in people with diabetes. High blood creatinine concentration in diabetics may be due to poor kidney filtering ability, causing the accumulation of nitrogenous waste, and decreased nephronal function causing high blood creatinine levels [18]. When the kidneys are unable to function properly, the level of creatinine in the blood rises abnormally [19]. Changes in serum creatinine concentration more reliably reflect changes in the glomerular filtration rate (GFR) instead of modifications in blood urea levels, and creatinine is formed naturally at a constant rate of creatine and its concentrations in the blood rely primarily on the glomerular filtration rate (GFR only) [20].

Urea Concentration in Diabetic Patients and Control Group

The findings in Table 1 reveal a notable elevation ($P \leq 0.05$) in the levels of urea in patients with diabetes, as it reached (43.82 ± 9.87) mg / 100 ml, compared to the control group amounted to (29.45± 4.27) mg / 100 ml, and these results agreed with the results of [21] with regard to the level of urea in the blood, which found an increase in the average concentration of blood urea in diabetics compared to the healthy group, According to the age groups in Table 2, the results indicate because there are no discernible variations between the different age groups among patients with diabetes, as the concentration of urea in the first age group (35-45) amounted to (39.56 ± 8.44) mg / 100 ml, compared to in the second age group (46-55) amounted to (46.35 ± 9.87) mg / 100 ml, in the third age group (56-65) amounted to (43.30 ± 10.35) mg / 100 ml, and in the fourth age group (66-75) amounted to (46.05± 9.92 (mg/100 ml). Because the concentration of urea in serum demonstrates the ratio between the urea generated by the liver and urea elimination in the urine by the renal system, an excess of urea in plasma may be caused by raised urea manufacturing, reduced urea elimination, or an amalgamation of the two; the highest concentrations occur in the setting of decreased the urea removal in the urine because of chronic kidney disease and the associated significant decrease in glomerular filtration rate. GFR is a key medical indicator as it determines kidney purpose; individuals with reduced renal function, no matter the cause, have a decline in the glomerular filtration rate (GFR); and there is an association between the glomerular filtration rate (GFR) and the severity of kidney disease [22].

Calculation of Glomerular Filtration Rate in Diabetic Patients and Control Group

The findings in Table 1 show a significant decrease ($P \leq 0.05$) in the estimated glomerular filtration rate eGFR in patients with diabetes, as it reached (80.35 ±22.19) ml / min / 1.73 m2 compared to the control group as it reached)129.05 ± 19.31(ml/min / 1.73 m2, The current study's findings corresponded with the findings of [23], which showed a decrease in glomerular filtration rate in people with diabetes compared to healthy people, and all of these previous studies suggested that a low glomerular filtration rate is associated with diabetes.

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The estimated eGFR is not only an indicator of reduced renal function in diabetic nephropathy patients, but also in diabetic neuropathy, diabetic retinopathy, and other diabetes-related problems, hence evaluating eGFR in diabetic patients is crucial. According to age groups, the results of the current study in Table 2 show significant differences in different age groups among patients with diabetes, as the glomerular filtration rate increased in the first age group (35-45) amounted to (96.93± 22.35) ml / min / 1.73 m2, compared to in the second age group (46-55) amounted to) 75.64 ± 24.44) ml / min / 1.73 m2 and in the third age group (56-65) amounted to) 78.60± 20.48(ml / min / 1.73 m2 and in the fourth age group (66-75) amounted to (70.23 ± 21.50(ml/min / 1.73 m2, The results of the current study agreed with the findings of [24] as they found a strong positive relationship between aging and an increased risk of low glomerular filtration rate among patients with diabetes and also stated that aging, synovuria, high uric acid in the blood, systolic hypertension, and HbA1c greater than 7% are the main factors associated with poor glomerular filtration rate. The major pathogen responsible for the development of diabetic kidney disease is hyperglycemia. Multiple pathophysiological disorders, such as hypertension, variable glomerular tubular reflux, renal hypoxia, steopatoxicity, foot cell injury, inflammation, mitochondrial dysfunction, autophagy dysfunction, and increased sodium and hydrogen exchanger activity, contribute to progressive glomerular sclerosis and low glomerular filtration rate once hyperglycemia occurs.The major pathogen responsible for the development of diabetic kidney disease is hyperglycemia. Multiple pathophysiological disorders, such as hypertension, variable glomerular tubular reflux, renal hypoxia, steopatoxicity, foot cell injury, inflammation, mitochondrial dysfunction, autophagy dysfunction, and increased sodium and hydrogen exchanger activity, contribute to progressive glomerular sclerosis and low glomerular filtration rate once hyperglycemia occurs [25]. Furthermore, diabetic kidney disease is silent until it is advanced. The estimated glomerular filtration rate eGFR is used to estimate the moderate to severe stages of chronic renal disease. According to studies, the risk of cardiovascular disease and death increases as early as stage III of CKD3, which corresponds to a glomerular filtration rate of less than 60 ml/min/1.73 m2..[26]. It is important to note that the average eGFR values in this study are within the normal range in the diabetic group, which indicates that the glomerular filtration rate eGFR is not a useful indicator early in detecting diabetic nephropathy DN, as it is detected and reduced in chronic kidney disease and renal decline late in the disease stage and this is consistent with the findings of study [27].

Total Protein Concentration in Diabetic Patients and Control Group

The findings in Table 1 show a significant decrease ($P \leq 0.05$) in the total protein concentration in patients with diabetes, as it reached (7.72± 0.49) g / 100 ml compared to the control group that amounted to (8.13 ± 0.21) g / 100 ml, the results of the study agreed with the results of the study [28] [29] where they found a decrease in the concentration of total protein in the serum for patients with diabetes, The results of the current study by age groups in Table 2 show that there are significant differences between the different age groups in the concentration of total protein in patients with diabetes, as the total protein concentration in the first age group (35-45) amounted to (7.90 ± 0.47) g / 100 ml), compared to in the second age group (46-55) amounted to(7.73 ± 0.35) g / 100 ml and in the third age group (56-65)

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amounted to (7.47± 0.52) g / 100 ml and in the fourth age group (66-75) amounted to (7.78 ± 0.62) grams/ 100 ml, and the results of this study agreed with the findings of a study [30], which showed that low levels of total proteins in serum are associated with age and duration of diabetes and cardiovascular disease.One possible cause of low total protein level associated with diabetics is the low glomerular filtration rate (GFR), which is the selective filtration of substances and minerals dissolved in the blood Usually, these substances are filtered into the kidneys during primary blood purification, but are often reabsorbed by the renal tubules in later stages of the filtration process as a result of impaired kidney function [31]. High blood sugar in diabetes also contributes to the formation of free radicals and these radicals cause oxidative stress and thus weaken the internal antioxidant defense system, if the amount of insulin available is insufficient, the cells respond poorly to the effects of insulin leading to continued elevation of blood sugar levels, and reduced total protein synthesis in serum [28].

Table 1 concentration Creatinine, urea, glomerular filtration rate and total proteins in diabetics and control group.

Group Variables	**Patient**	**Control**
Creatinine	1.15 ±0.36 a	0.50±0.20 b
Urea	43.81± 9.64 a	29.45±4.27 b
Egfr	80. 35± 22.19 a	129.05±19.31 b
Total Protein	7.72±0.49 a	8.13±0.21 b

*The values in the table indicate to (Mean ± S.D)
*Different letters Horizontally indicate significant differences at ($P \leq 0.05$)

Table 2 concentration Creatinine, urea, glomerular filtration rate and total proteins by age groups in diabetics.

Age group Variables	**Age (35 – 45)**	**Age (46 –55)**	**Age (56 – 65)**	**Age (66 –75)**
Creatinine	1.00 ± 0.31 a	1.27 ± 0.38 a	1.13 ± 0.31 a	1.19 ± 0.42 a
Urea	39.56 ± 8.44 a	46.35 ± 9.87 a	43.30 ± 10.35 a	46.05 ±9.92 a
eGFR	96.93 ± 22.35 a	75.64 ± 24.44 b	78.60 ± 20.48 b	70.23 ± 21.50 b
Total Protein	7.90 ± 0.47 a	7.73 ± 0.35 b	7.47 ± 0.52 b	7.78 ± 0.62 b

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*The values in the table indicate to (Mean ± S.D)
*Different letters horizontally indicate significant differences at ($P \leq 0.05$).

5. CONCLUSIONS

From the present study, we conclude that there is a moral rise ($P \leq 0.05$) in the concentration of creatinin and urea among diabetic patients compared to healthy, a decrease in the concentration of total protein and the glomerular filtration rate of diabetes patients compared to healthy. By age group, however, we conclude that there are no moral differences ($P \leq 0.05$) in the concentration of creatinine and urea among diabetic patients, and that there are moral differences in the concentration of total proteins and glomerular filtration rate by age groups among diabetic patients.

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