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Insights on Renal Profiles of Iraqi Patients With Type II Diabetes

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***Abstract*—Diabetic kidney disease, also known as diabetic nephropathy, is a serious complication that affects around 40% of individuals with diabetes. It stands as the primary cause of chronic kidney disease (CKD) on a global scale. There is an urgent need for widespread innovation to improve health outcomes for patients with diabetic kidney disease, and this will involve predicting the prevalence of renal impairment in diabetic patients.800 patients (312 males and 488 females) with Diabetes Mellitus Type II were enrolled in this cross-sectional study age range from (30-65). All patients were asked to fast for 8-12 hours, and All routine investigating assays (FBG, lipid profile, RFT, HBA1c). eGFR determined by calculator program. The eGFR was classified according to National Kidney Found. The study indicates that hyperglycemia does not affect serum urea levels, so it may not be useful in evaluating renal function for DM. The decline in eGFR is linearly linked with an increased risk of Kidney disease (End Stage. Once the progressive eGFR reduction has commenced, it is crucial to effectively manage the disease process driving this decline. The glomerular filtration rate (GFR) serves as the cornerstone for many of the kidney's regulatory functions and is widely regarded as the most comprehensive indicator of renal function. We recommended that every request for blood creatinine concentration be computed, and an eGFR should be provided using the (CKD-EPI) method.**

***Keywords*—diabetic nephropathy, Diabetes mellitus, GFR, Urea, creatinine.**

I. INTRODUCTION

Diabetes mellitus (DM) is often referred to simply as diabetes. DM is a persistent condition that impairs the body's capacity to utilize glucose efficiently. Symptoms of diabetes include increased thirst (polydipsia), high blood glucose levels (hyperglycemia), and excessive hunger (polyphagia). DM is considered one of the most prevalent metabolic diseases, and its occurrence is on the rise globally at a concerning rate[1]. The international diabetic federation claims that the number of diabetic patients worldwide will reach 439 million adults (9.3%) by 2030 [2]. Between 2010 and 2030, the increasing number of adults with diabetes will be 69% in developing countries and a 20% increase in developed countries, representing a major and growing impairment among diabetic patients within a predetermined sample. health threat to humanity [3, 4]. The number of patients who have diabetes is increasing, and the increment may reach up to 60% from 2007 to 2025 in Asia alone (the 20th world diabetic congress report). In 2017, there were 1.411.500 cases of diabetes in Iraq, and the prevalence of diabetes in adults was 7.5% [5]. Many complications can be presented with diabetes, including nephropathy as a direct consequence of diabetes itself [6, 7]. People with Diabetic kidney disease with afferent arterioles relaxing more than efferent arterioles. Increased albumin levels in urine, hypertension, and a lower glomerular filtration rate are all symptoms [8,9]. Recent studies showed that 25 to 40 % of all patients with diabetes will face nephropathy, making it the major cause of end-stage renal failure in the developed world [10]. Evaluating kidney function in all diabetic patients is very important; glomerular filtration rate GFR is the best way to estimate kidney function in diabetic and healthy people [11].

Globally, diabetic nephropathy—particularly T2DM has emerged as the leading cause of end-stage renal disease. Patients with chronic kidney disease still need to manage conventional risk factors, including smoking, hypertension, and hyperlipidemia, to enhance their cardiovascular and renal outcomes. Nontraditional risk factors, such as hypoalbuminemia, increased urine albumin excretion, raised creatinine levels, and/or reduced hemoglobin levels, are being more recognized as potential contributors to CKD [12].

Recommendations from the National Kidney Foundation and the American diabetic association agree on using diet modification in renal disease equation (MDRD) as a tool to estimate the GFR in adults [13]. The MDRD equation is made of 6 different variables, including age, sex, ethnicity, serum creatinine SC, serum urea, and albumin; then, to make it more suitable for clinical use, the equation was made more simple by making it composed of 4 variables only age, sex, ethnicity, and serum creatinine only [14]. Taken together all of the above, the study aims to predict the prevalence of renal impairment in a sample of Iraqi type 2 diabetic patients. This research uses pertinent clinical biomarkers and demographic data to precisely predict the prevalence of renal

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II. MATERIALS AND METHODS

A.Study design and population

This cross-sectional study was conducted at the National Diabetes Center / Mustansiriyah University from October 2021 to October 2022.This research included 800 patients (312 males and 488 females) with an age range from (30 to 65), suffering from Diabetes Mellitus Type 2. All the patients filled out a consent form as an agreement to draw a sample and were informed about the idea of this research.

B.Physical examination and measurements

BMI was calculated by dividing weight in kilograms by the square of height in meters. The formula for BMI is weight (kg) / [height (m)]^2. Additionally, each patient's waist-hip ratio was determined by dividing their waist circumference by their hip circumference, measured at the greater trochanter level. All patients underwent clinical examinations, including blood pressure measurements[15].

C.Laboratory investigations

In this study, all patients were asked to fast 8-12 hours for blood sampling to perform routine investigations, including total cholesterol, triglyceride (TG), fasting blood glucose (FBG), serum creatinine, serum urea, and HbA1c. The samples were sent to the lab using automated KINZA (bio-labo) for analysis.

D.Availability of data and material

This research uses the online eGFR calculator program from the National Institute of Diabetes and Digestive and Kidney Diseases to find the eGFR value and assess the impact of DM on renal function in the (CKD-EPI) method as it is the best measurement of renal function in type 2 diabetic patients[16].

$eGFR_{cr} = 142 \times \min(S_{cr}/\kappa, 1)^{\alpha} \times \max(S_{cr}/\kappa, 1)^{-1.200} \times 0.9938^{Age} \times 1.012$ [if female]

where: S_{cr} = standardized

E.Statistical analyses

Data analysis was done using GraphPad Prism (version 9). The results were expressed as mean ± SD and percentages. The unpaired t-test and the ANOVA test are used to compare the continuous variables between two categories and more than two groups, respectively. The p-value <0.05 is considered significant; p<0.01 is highly significant.

III. RESULTS

A.Sampling and Patient Demographics

800 Type 2 diabetes mellites patients who matched the study's criteria were chosen. 61% (488/800) were females and had a mean age of 56.34 ± 9.36 years; (312/800) 39%were males and had a mean age of 54.22 ± 8.65 years. Weight, height, Waist-to-hip ratio (WHR), and GFR were greater on average among men, while body mass among women was higher. Age, waist circumference, fasting blood glucose, total cholesterol, Triglycerides, serum creatinine, serum urea, HbA1c, and DM duration were variables that did not differ statistically (p>0.05) Table (1).

Table 1: Clinical profile of patients with type 2 diabetes mellitus

Variables	All	Gender		P-Value
		females (N= 488) Mean ± SD	Males (N=312) Mean ± SD	
Age (years)	55.51 ± 9.13	56.34 ± 9.36	54.22 ± 8.65	0.1095*
Weight (Kg)	72.58 ± 9.90	68.46 ± 7.83	79.01 ± 9.38	0.0001***
Height (cm)	161.51 ± 9.02	156.12 ± 6.09	169.94 ± 5.82	0.0001***
BMI (Kg/m²)	27.76 ± 2.52	28.05 ± 2.46	27.32 ± 2.57	0.0457**
WC (cm)	98.60 ± 8.33	98.51 ± 7.95	98.74 ± 8.95	0.8555*
HC (cm)	101.54 ± 7.74	102.24 ± 8.40	100.44 ± 6.49	0.1102*
WHR	0.97 ± 0.06	0.96 ± 0.05	0.98 ± 0.057	0.0223**
FBS (mg/dL)	186.69 ± 72.63	188.56 ± 68.56	183.77 ± 79.63	0.6504*
Total cholesterol (mg/dL)	182.42 ± 39.78	186.57±38.77	175.92 ± 40.71	0.0648 *
Triglycerides (mg/dL)	145.38 ± 74.68	144.66± 70.11	146.51 ± 81.77	0.8643*
Serum creatinine (mg/dL)	0.98 ± 0.31	0.94 ± 0.36	1.02 ± 0.21	0.0821*
Serum urea mg/dL	42.25 ± 13.51	42.26 ± 14.63	42.23 ± 11.62	0.9872*
HbA1c	9.14 ±2.01	9.24± 1.92	8.99± 2.15	0.3959 *
DM duration (years)	7.72 ±6.52	8.10 ± 6.40	7.12±6.70	0.2997*
eGFR (mL/min/1.73 m2)	76.54 ± 18.20	71.5± 17.18	84.35 ± 17.05	0.0001***

***** = extremely significant **= significant *=not significant ;p<0.05; **: p<0.01; ***: p<0.001; M±SD: mean±standard deviation; kg: kilogram; cm: centimeters; Kg/m2: kilograms per square meter;WC: waist circumference; HC: hip circumference; WHR: waist to hip ratio.**

The prevalence of certain biochemical variables in the selected 800 DM patients, categorized by age, such as fasting serum glucose level, serum creatinine, serum urea, and HbA1c, are presented in Table (2).

1. The fasting blood glucose level is correlated positively with age in all the patient's cases and male patients' groups. The female patients' youngest group at the time showed the highest fasting blood glucose levels. The other two age groups showed no significant differences in fasting blood glucose levels.

Table (2): Prevalence of some biochemical variables according to Age.

Variables (c)	Gender	Group 1 (30-39 years)	Group 2 (40-49 years)	Group 3 (≥ 50 years)
Fasting blood glucose	All	178.12 ± 64.74	180.61 ± 70.05	188.73 ± 74.04
	F	203.00 ± 70.13	180.55 ± 60.51	189.18 ± 69.84
	M	134.50 ± 13.45	180.68 ± 82.52	188.00 ± 81.08
Serum Creatinine	All	0.91 ± 0.08	0.90 ± 0.15	0.99 ± 0.35
	F	0.93 ± 0.09	0.90 ± 0.15	0.97 ± 0.40
	M	0.87 ± 0.05	0.98 ± 0.16	1.03 ± 0.26
Serum Urea	All	37.91 ± 8.22	38.02 ± 8.04	42.98 ± 14.82
	F	36.28 ± 9.37	35.15 ± 7.05	44.20 ± 15.57
	M	40.75 ± 5.73	41.62 ± 7.95	40.98 ± 13.39
HbA1c	All	8.70 ± 1.10	8.88 ± 1.80	9.24 ± 2.10
	F	8.88 ± 0.99	9.45 ± 1.89	9.22 ± 1.99
	M	8.37 ± 1.35	8.16 ± 1.44	9.26 ± 2.30

2. Serum Creatinine is correlated positively with age in male patients' groups in the time that female patients' group 2 showed the lowest level, and group 3 showed the highest level. No significant difference between female and male patients' groups was noticed.

3. Serum urea is correlated positively with age in all patients' groups; female patients in group 2 showed the lowest value, and group 3 showed the highest value. The male patients' group showed the highest value, and the group showed the lowest value.

The previous result indicates that hyperglycemia does not affect serum urea level, so it may not be useful in evaluating renal function for DM at the time that the result shows that group 3 (⩾ 50 years) presents the highest value of both creatinine and urea, which may be a result of renal function disorders. There is no significant difference between male and female patients in all groups.

4. This study also concluded a Positive relationship between HbA1c and age in all patient groups. Female patients in group 2 showed the highest levels, and group 1 showed the lowest value. The lowest HbA1c value was in the male patients' group. There is no significant difference between male and female patients in all groups.

B.Distribution of eGFR Values According to the study variables

Table (3) summarizes the relationship of eGFR values with fasting blood glucose levels, HbA1c, DM duration, and age. As the previous clinical and biochemical variables increase, the eGFR decreases, increasing the CKD risk factor.

Regarding fasting blood glucose levels, male patients in the third group recorded the lowest eGFR value.

An extremely high significant correlation was recorded in the first group, which shows that renal impairment in female patients is more prevalent than in male patients. HbA1c in the fourth group recorded the same correlation.

Table (3): Distribution of eGFR values According to blood glucose levels, HbA1c, DM duration, serum creatinine, serum urea, and age.

Variables	Groups	eGFR			P value
		All	M	F	
Fasting blood glucose	GroupI <200 mg/dl	78.60± 18.40	71.41±17.53	87.71±15.28	0.0001 ***
	GroupII 200-300 mg/dl	73.81±16.84	73.13±16.29	76.00 ± 18.99	0.5821 *
	GroupIII >300 mg/dl	63.29±19.74	61.17±18.81	65.38±19.29	0.1459 *
HbA1c	6.5-7.0	77.03±19.76	67.06±18.55	87.00±15.81	0.002**
	7.1-7.5	78.32±18.06	72.25±18.35	88.71±12.72	0.0522*
	7.6-8.0	76.50±15.40	72.13±12.17	82.33±18.37	0.2339 *
	>8.0	76.16±18.25	72.28±17.28	83.02±18.08	0.0009 ***
DM duration	<5years	80.56± 18.97	73.63 ± 18.64	88.91 ± 15.94	0.0003***
	5 – 10years	77.06 ± 16.72	74.04 ± 15.32	82.27 ± 18.27	0.0450 **
	>10years	70.26 ± 17.57	66.03 ±16.85	78.72 ± 16.25	0.0109**
Age	Group 1 (30-39 years)	91.64± 17.24	80.57 ± 9.91	111.00 ± 2.94	0.0002***
	Group 2 (40-49 years)	87.58 ± 13.18	84.70 ± 11.35	91.19 ± 14.74	0.1446*
	Group 3 (≥ 50 years)	72.85 ± 17.75	68.11 ±17.11	80.62 ±16.06	0.0001 ***

***= extremely significant **=very significant *=not significant

The DM duration in the first group recorded an extremely high significant correlation between the prevalence of renal impairment in female patients and a very significant

correlation in the second and third groups of the same prevalence. Male patients in the third group recorded the lowest eGFR value.

An extremely high significant correlation was recorded in the first and third age groups, which also showed that renal impairment in female patients is more prevalent than in male patients. Male patients in the third age group also recorded the lowest eGFR value.

C.Evaluate renal function based on CKD stage

The majority of patients (60%) are in the CKD stage-2 category (kidney damage with mildly reduced GFR), 23.5%arein stage-1 category (kidney damage with normal GFR), 15.5% in the stage-3 category (moderately reduced GFR),and1% in stage-4 category (severely decreased GFR). Male patients had a higher percentage in the stage-1 category, while female patients had higher percentages in all the other stage categories (Table 4).

Table (4): Renal function assessment according to CKD stages

	Stage	Gender	Total no.(%)	eGFR
CKD	Stage 1 ≥ 90 mL/min/1.73 m^2	All	188(23.5%)	100.21 ± 6.40
		F	68(36.2%)	98.71± 5.68
		M	120(63.8%)	101.07± 6.72
	Stage 2 (60-89) ml/min/1.73m^2	All	480(60%)	74.83±8.75
		F	316(65.8%)	73.24±8.48
		M	164(34.2%)	77.88±7.88
	Stage 3 (30-59) ml/min/1.73m^2	All	124(15.5%)	50.94 ±7.40
		F	96(77.4%)	51.04 ± 7.04
		M	28(22.6%)	50.57 ± 9.14
	Stage 4 (15-29) ml/min/1.73m^2	All	8(1%)	19.50 ± 13.44
		F	8(1%)	19.50 ± 13.44
		M	0 (0%)	-

IV. Discussion

Diabetic kidney disease DKD is a condition marked by chronic albuminuria and a gradual loss of renal function. The term DN denotes the presence of a characteristic glomerular disease pattern [17, 18]. The DN affects (20–40%) of people with diabetes [5, 19], making it one of the most prevalent complications associated with the disease[18, 20]. To slow down its progression, screening for DN, early intervention, and proper glycemic control are crucial[21]. Pecoits-Filho R et al. [22] confirmed the optimum glycemic management with HbA1C at 6-7, indicating a considerably low risk of compromised GFR. Our investigation revealed a connection between reduced renal function and a low HA1C of 6%. This was most likely brought on by decreased red blood cell production, which causes anaemia, and the severe disruption of glucose homeostasis that occurs in T2DM patients with chronic kidney disease (CKD), who are very susceptible to hyper- and hypoglycemia[23, 24]. The duration of diabetes is a significant factor that can contribute to the development of diabetic kidney damage. Many studies have found a link between the duration of diabetes and the severity of nephropathy, particularly when it initially presents 5-10 years in T2DM patients and 10-15 years after T1DM starts [25, 26]. This result is consistent with the findings of Harita et. a [27]. who discovered a link between lower creatinine and an increased risk of type 2 diabetes, which might be due to a reduced skeletal muscle volume. Skeletal muscle is a vital insulin target tissue, and a decreased amount of skeletal muscle means fewer insulin target sites, leading to increased insulin resistance and the development of type 2 diabetes. This might help to explain why type 2 diabetes is linked to decreased serum creatinine levels. However, our findings differ from those of similar research in the past [28, 29].

To preserve homeostasis, the kidneys can control the amount and make-up of fluid in the body. Filtration, reabsorption, and secretion are among the renal functions that support the maintenance of the body's internal environment [26, 30].

The GFR is the gold standard for DKD diagnosis, as GFR screening helps current kidney damage to be detected [31]. In patients with T2DM and hypertension, the severity of DKD increases with declining GFR and increasing albuminuria [32]. In type and type diabetic patients, decreased kidney filtering capability will lead to the accumulation of waste products and, hence, to an increase in serum creatinine and urea levels; impaired nephron activity in patients with diabetes contributes to elevated serum creatinine levels [33,34]. This research observed that the average serum eGFR levels were significantly lower in individuals with type 2 DM. The estimated glomerular filtration rate (eGFR) is a crucial measure of the kidney's effectiveness in filtering waste from the body. As a result, the reduction in eGFR in the current study's participants implies a higher risk of renal disease in diabetics. This outcome agreed with the study of Skupien et al.[35], who found a substantial linear decrease in eGFR in those with type 2 diabetes. Our findings demonstrate that as blood glucose levels rise, the eGFR decreases. Females have a greater eGFR than males, which is a risk factor for Diabetic Kidney Disease (CKD). Additionally, our findings are consistent with the report of Belguith H [28, 36], who had previously discovered a reduction in eGFR in diabetic individuals. It is essential to proactively address the disease process leading to gradual eGFR reduction once it has commenced, as the linear decline in eGFR is associated with an increased risk of end-stage kidney disease.

V. Conclusions

The glomerular filtration rate (GFR) ~~is~~ the cornerstone for many of the kidney's regulatory functions and is widely regarded as the most comprehensive indicator of renal function. We suggest that laboratories calculate and provide an estimated GFR (eGFR) using the Modification of Diet in Renal Disease (MDRD) method whenever adult blood creatinine levels are measured. Automatic reporting of eGFR alongside serum creatinine results could greatly enhance the early detection of chronic kidney disease (CKD). This will aid in reducing the risk of kidney failure progression in diabetic patients.

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ETHICAL CONSIDERATION

The study was conducted according to the Declaration of the National Diabetes Center / Mustansiriyah University and was approved by the local ethics committee of the College of Authors in October 2021. Before enrolling in this study, all subjects provided informed written consent.

CONFLICT OF INTEREST

The authors assert that they possess no conflicts of interest.

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