RESEARCH ARTICLE

ASSOCIATION OF AGE AND DIABETES DURATION WITH ESTIMATED GLOMERULAR FILTRATION RATE IN PATIENTS WITH DIABETES MELLITUS ATTENDING AL-DOFIAH MARTYR HOSPITAL-BEIHAN, SHABWAH, YEMEN

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Abstract

Chronic kidney disease (CKD) is a common complication of Diabetes Mellitus (DM) and limits treatment options in DM. Estimated glomerular filtration rate (eGFR) is a crucial test for renal assessment. Significant association was found between risk factors and lower eGFR. Ageing is a natural and inevitable biological process that affects all organs. In Yemen, the association between rate of kidney function decline and age or/and duration of diabees has not been well investigated. The current study aimed to determine the association between eGFR and age or/with duration of DM. 177 individuals with DM were studied for the analysis of the association between eGFR rate with age and diabetes duration during the period of February 2022 to February 2023. Results showed high significant differences found in age groups based on eGFR. However, significant difference between the values of eGFR in age groups 25-34, 45-54 and 55-64. Except in the 7 age group, the eGFR of individuals in age groups tended to decreased. In the whole section, prevalence of CKD (high and very high risk) was 16.9% and increased progressively with age. The CKD associated with each 5 year increase in diabetes duration. Of these patients, 11.3% had an eGFR of 15-29 and < 15mL/min/1.73m2, and 5.6% had an eGFR of 30-44 mL/min/1.73m2. In the 4 category (1*5* years), 4% of study subjects were treated with stage 5 of eGFR (very high risk). The shape of the association between age with diabetes duration and risk of CKD was linear. The results of our study and the other kinds of literature indicate that the important of estimated glomerular filtration rate (eGFR) according to age, diabetes duration and degree of renal dysfunction. In conclusion: These results emphasize the importance of assessment of eGFR for CKD risk prediction in diabetes patients. Our findings suggested that early diagnosis and treatment is important for these patients. So, the observation that could guide preventative efforts of efficient glucose-lowering and renal protective strategies are needed in persons with DM.

Keywords: Age, Duration, eGFR, Diabetic Mellitus, Yemen.

Introduction

Diabetes mellitus (DM) is a global health concern affecting millions of individuals worldwide and leads to microvascular complications like diabetic retinopathy (DR) and Chronic kidney disease (CKD) [1]. Chronic diseases now account for the majority of global morbidity and mortality, rather than infectious diseases. The causes of chronic kidney diseases reflect this change and diabetes, together with hypertension, is now the major cause of end stage renal failure worldwide [2].

Estimated glomerular filtration rate (eGFR) is a crucial test for renal assessment. Estimated glomerular filtration rate (eGFR) are independently associated with the worsening of kidney function [3-6]. Significant association was found between Kideny failure and lower eGFR [7].

Blood glucose control targets should be individualized based on life expectancy, renal function, and hypoglycaemia risk. So, management of diabetic elderly patients with CKD involves specific characteristics that affect both metabolic control and therapeutic measures.

Chronic kidney disease (CKD) is a common complication of DM, Increased life expectancy and a higher DM incidence lead to an increase in the number of elderly diabetic individuals with CKD. Renal function in the elderly may be not only due to old age, but also due to the coexistence of DM. Likewise, CKD also limits treatment options in DM [9].

Ageing is a natural and inevitable biological process that affects all organs. Likewise, the diagnostic efficiency of HbA1c for diabetes decreased with aging [8]. As part of this process, in kidneys of healthy elderly people, a series of changes occurs that affect kidney function. Therefore, Age-related macular degeneration (ARMD) and CKD are global health challenges [10-13].

Type 2 diabetes is increasingly being diagnosed in young people [14–16]. People with younger age at diabetes diagnosis, compared with those at older age of diagnosis, are at an increased lifetime risk of microvascular complications [17–20]. Indeed, a number of studies have shown that the risk of end-stage kidney disease (ESKD) is higher in younger-onset (< 40 years) type 2 diabetes than in older-onset (≥ 40 years) type 2 diabetes, and this excess risk is primarily attributable to attainment of a longer duration of diabetes [21-23]. However, it is unclear whether this is fully attributable to longer disease exposure or the inherently aggressive nature of young with diabetes.

In Yemen, the association between kidney function decline and age-of-onset or duration of diabetes has not been well investigated. Therefore, the current study aimed to determine the association between estimated glomerular filtration rate (eGFR) decline and age or/with duration of DM.

Subjects and Methods

The study was conducted in the hospital's central laboratory of Al-Dofiah Martyr Hospital-Beihan, during the period of February 2022 to February 2023. The study population consisted of 177 individuals with DM (DM diagnosis was according to WHO diagnostic criteria for DM, 2011) [24]. The study was performed under regulations and monitored by the medical staff of Al-Dofiah Martyr Hospital-Beihan.

For all individuals participated in study, the following parameters were recorded: age, gender, smoking status (never, former, current), and known duration of DM with indication of the class of drug. Participants were also asked to report previous major cardiovascular disease (CVD) event. physical examination was conducted, including measurements of height and weight.

All the required tests, glycosylated hemoglobin (HbA1c) and plasma creatinine level, were carried out automatically in the hospital's central laboratory. HbA1c was measured using i chroma II (Boditech-Korea) and the creatinine parameters were tested with Spectrophotometers (Cyans mart, Belgium).

For the analysis of renal function stages and eGFR, the eGFR was calculated from plasma creatinine levels using Cockcroft-Gault equation [25]. The stages of CKD were based on National Kidney Foundation K/DOQI clinical practice guidelines [26] and Neelamegam *et al.* (2024) [1] and were expressed in ml/min/1.73 m², defined as follows:

Stage 1 (normal) = eGFR ≥90

Stage 2 (Mild limitation) = eGFR 60–89

Stage 3a (Mild to moderate) = eGFR 45–59

Stage 3b (Moderate to severe) = eGFR 30–44

Stage 4 (Severe limitation) = eGFR 15–29

Stage 5 (kidney failure) = eGFR <15

Participants were divided into age groups and diabetes duration categories. The distribution of stages of eGFR category in each age group and diabetes duration category were then calculated. The primary objective of exploring the relationship between eGFR and age as well as diabetes duration within the diabetes patients.

The data are represented as the mean and the standard error (SE). Group comparisons were performed by one-way ANOVA. To evaluate the correlation between the variables (eGFR, age and duration of diabetes), we used reduced major axis (RMA) and the Pearson correlation coefficient. The statistical analysis was performed using the statistical package SPSS version 20 [27] and Software PAST package release 3.25 [28]. *P*-value less than 0.05 were considered as statistically significant.

Results

The basic statistics of eGFR for each age category are summarized in Table 1. One – way analysis of variance (ANOVA) for repeated measures showed high significant differences found in age groups based on eGFR.

Based on least significant difference (LSD) analysis, there were significant changes of eGFR for age groups 1-5 compare to age groups 6 and 7. On the other hand, no important difference was detected among the age groups 1-5. However, significant difference between the values of eGFR in age groups 2, 4 and 5. Except in the 7 age group, the eGFR of individuals in age groups tended to decreased.

Table 1: Basic statistics and LSD of eGFR of diabetic patients in different age groups (n=177)

7	n	Min-Max	Mean±SE	F	P
1 (≤24)	8	43.12±167.07	88.20±13.06$_a$		
2 (25-34)	12	24.12±201.28	96.68±13.10$_b$		
3 (35-44)	20	28.17±157.82	78.39±6.70$_c$		
4 (45-54)	39	18.09±146.03	73.18±3.34$_{b,d}$	7.98	<0.001**
5 (55-64)	52	13.66±123.46	68.35±3.17$_b$		
6 (65-74)	26	7.40±104.17	44.26±6.49$_{a,b,c,d}$		
7 (≥75)	20	7.44±94.38	51.73±4.86$_{a,b,c,d}$		

The mean difference is significant at the 0.001 level. The Means with the same letters in the same column indicate a significant difference (p< 0.05).

In age groups, moderately risk (stage 2) were observed in 7.3% of age group 5, whereas very high risk were detected in 6.2% of age group 6. In the whole cohort, prevalence of CKD (high and very high risk) was 16.9% and increased progressively with age (Table 2).

Table 2: Chronic Kidney Disease incidence by eGFR of diabetic patients in different age groups

Total = 177				1(≤24) n=8	2(25-34) n=12	3(35-44) n=20	4(45-54) n=39	5(55-64) n=52	6(65-74) n=26	7(≥75) n=20
							n(%)			
eGFR (mL/min/1.73m²)	1	Normal	≥90	2 (1.1)	6 (3.4)	5(2.8)	7(4)	8(4.5)	2(1.1)	1(0.6)
	2	Mild limitation	60–89	5 (2.8)	3 (1.7)	11(6.2)	26(14.7)	25(14.1)	6(3.4)	6(3.4)
	3a	Mild to moderate	45–59	0	2 (1.1)	2(1.1)	5(2.8)	13(7.3)	6(3.4)	6(3.4)
	3b	Moderate to severe	30–44	1 (0.6)	0	1(0.6)	0	3(1.7)	1(0.6)	4(2.3)
	4	Severe limitation	15–29	0	1 (0.6)	1(0.6)	1(0.6)	2(1.1)	0	2(1.1)
	5	Kidney failure	<15	0	0	0	0	1(0.6)	11(6.2)	1(0.6)

*Green, low risk (if no other markers of kidney disease, no CKD); yellow, moderately increased risk; orange, high risk; red, very high risk.

Comparison of eGFR parameters of 177 diabetes patients with duration of diabetes has been presented in Table 3. Results showed significant differences between the 4 categories. A statistically significant difference in values of eGFR was observed between 2, 3 and 4 categories. The value of eGFR in category 4 was slightly lower than in category 2.

Table 3: Basic statistics and LSD of eGFR of diabetic patients in different duration of disease (n=177)

Duration of diabetes (years)	n	Min-Max	Mean±SE	F	P
1 (1 years)	14	35.42±125.28	76.16±6.80		
2 (5 years)	59	7.40±201.28	75.77±4.73$_a$		
3 (10 years)	42	7.44±111.04	63.06±3.71$_a$	2.85	0.04*
4 (15 years)	62	7.67±140.68	61.97±3.59$_a$		

The mean difference is significant at the 0.05 level. The Means with the same letters in the same column indicate a significant difference (p< 0.05).

The information on duration of disease and the level of eGFR was available allowing the grouping of these patients into different CKD stages (Table 4). From table 4, the CKD associated with each 5 year increase in diabetes duration. Of these patients, 11.3% had an eGFR of 15-29 and < 15 mL/min/1.73m2, and 5.6% had an eGFR of 30-44 mL/min/1.73m2. In the 4 category (15 years), 4% of study subjects were treated with stage 5 of eGFR (very high risk).

| EJUA | **Electronic Journal of University of Aden for Basic and Applied Sciences**
Vol. 5, No. 2, June 2024 | **Duwihan and Al Hered** | **Pages 163-172** |

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Table 4: Chronic Kidney Disease incidence by eGFR of diabetic patients according duration of disease.

Total = 177				1 (1years) n=14	2(5years) n=59	3 (10 years) n=42	4 (15 years) n=62
				n (%)			
eGFR (mL/min/1.73m²)	1	Normal	≥90	3 (1.7)	16 (9)	3(1.7)	9(5.1)
	2	Mild limitation	60–89	8 (4.5)	25(14.1)	24(13.6)	25(14.1)
	3a	Mild to moderate	45–59	1(0.6)	10(5.6)	9(5.1)	14(7.9)
	3b	Moderate to severe	30–44	2 (1.1)	2(1.1)	1(0.6)	5(2.8)
	4	Severe limitation	15–29	0	3 (1.7)	2(1.1)	2(1.1)
	5	Kidney failure	<15	0	3(1.7)	3(1.7)	7(4)

*Green, low risk (if no other markers of kidney disease, no CKD); yellow, moderately increased risk; orange, high risk; red, very high risk.

The youngest age with longer duration of diabetes had eGFR more declines compared to those diagnosed at middle age or those with shorter duration of diabetes. In eGFR of age at 45–54 and 65-74 years with diabetes duration 5, 10 and 15 years. However, The states of CKD based on eGFR decline were greater in those with age at ≥ 65 years with duration of diabetes > 10 years compared to those diagnosed at ≤65 years or those with duration of diabetes = 5 years (Table 5).

Table 5: Clinical Characteristics of kidney in diabetes patients according to eGFR according to duration of diabetes and age

				1 (1years)*				
Kidney stage				**n (%)**				**Total**
	1(≤24)	2(25-34)	3(35-44)	4(45-54)	5(55-64)	6(65-74)	7(≥75)	
1(≥90)	1(7.14%)		1(7.14%)	1(7.14%)				14(7.91)
2(60–89)	2(14.28)		1(7.14%)	3(21.42)	1(7.14%)	1(7.14%)		
3a(45–59)							1(7.14%)	
3b(30–44)	1(7.14%)						1(7.14%)	
4(15–29)								
5(<15)								
				2(5years)				
1(≥90)	1(1.60)	4(6.78)	4(6.78)	3(5.08)	4(6.78)			59(33.33)
2(60–89)	1(1.60)		7(11.86)	10(16.95)	6(10.17)	1(1.60)	1(1.60)	
3a(45–59)		1(1.60)	1(1.60)	1(1.60)	4(6.78)	3(5.08)		
3b(30–44)					1(1.60)	1(1.60)		
4(15–29)			1(1.60)	1(1.60)	1(1.60)			
5(<15)						3(5.08)		
				3(10years)				
1(≥90)		1(2.38)		1(2.38)	1(2.38)			42(23.73)
2(60–89)	2(4.76)	2(4.76)	2(4.76)	8(19.05)	6(14.29)	2(4.76)	2(4.76)	
3a(45–59)		1(2.38)		4(9.52)	1(2.38)	1(2.38)	2(4.76)	
3b(30–44)							1(2.38)	
4(15–29)					1(2.38)		1(2.38)	
5(<15)					1(2.38)	1(2.38)	1(2.38)	
				4(15years)				
1(≥90)		1(1.61)		2(3.23)	3(4.84)	2(3.23)	1(1.61)	62(35.03)
2(60–89)		1(1.61)	1(1.61)	5(8.06)	12(19.35)	3(4.84)	3(4.84)	
3a(45–59)			1(1.61)		8(12.90)	2(3.23)	3(4.84)	
3b(30–44)			1(1.61)		2(3.23)		2(3.23)	
4(15–29)		1(1.61)						
5(<15)						7(11.29)	1(1.61)	

*Green, low risk (if no other markers of kidney disease, no CKD); yellow, moderately increased risk; orange, high risk; red, very high risk.

The effects of age and duration of disease on eGFR were analyzed using the reduced major axis (RMA) regression. The shape of the association between age and risk of CKD was linear. Table 6 and Figures 1&2 indicates that there is a high negative significant correlation between age and eGFR as well as negative significant correlation between duration of diabetes and eGFR was also observed. Person correlation illustrates a significant relationship between age and duration of diabetes with eGFR (Fig. 3).

Table 6: The y-intercept (a) and the regression coefficient (b) of reduced major axis (RMA) that describes the relationship between the age and the Period of disease and eGFR (n=177)

Equation	eGFR	b±SE	a	r	*p-value*
RMA regression	Age	-1.93 ± 0.13	172.44	-0.4	<0.001**
	Duration of diabetes	-9.22 ± 0.68	141.45	-0.2	0.006*

The mean difference is significant at the 0.001 level
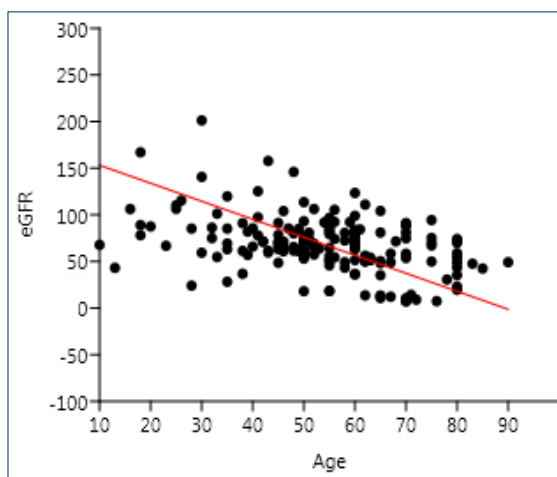
Fig. 1: The relationship between age and eGFR of diabetic patients
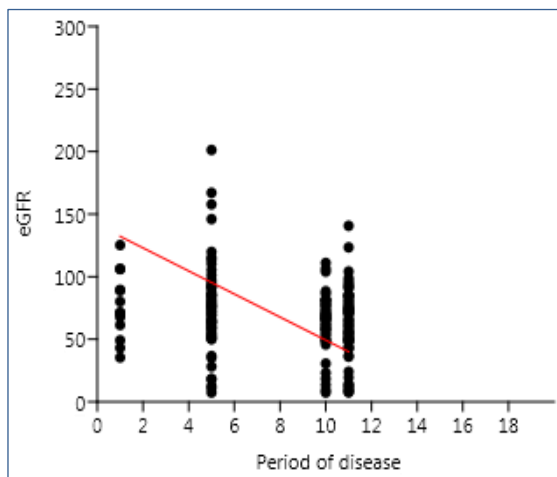
Fig. 2: The relationship between duration of diabetes and eGFR of diabetic patients
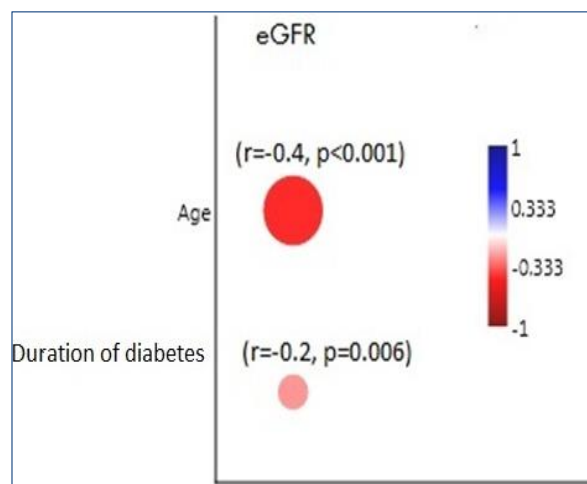

Fig. 3: The correlation between the age and the duration of disease and eGFR

Discussion

Chronic kidney disease (CKD) is highly prevalent in patients with T2DM, the GFR decline in T2DM patients is almost twice as high as in patients without diabetes [29,30]. Previous studies confirmed that both the amount of urinary albumin and eGFR value are useful to predict the outcome of kidney function in subjects with type 2 diabetes [4,5,31]. Various risk factors that cause the decline of eGFR, such as albuminuria, glycemic control, blood pressure, obesity, diabetes, blood urea nitrogen, high blood lipids, and smoking are associated with lower GFR [5,6,7, 31-34].

DKD has a multifactorial pathogenesis due to microenvironmental changes in the diabetic kidney. Pathological glomerular changes are one of the most important signs of DKD that appear in many cases within 0–3 years after diabetes diagnosis. Changes such as thickening of the glomerular basement membrane (GBM), podocyte injury, mesangial matrix expansion and loss of glomerular endothelium fenestrations, damage the glomerular filtration barrier and microvascular permeability and are clinically expressed as micro- and macroalbuminuria [35,36].

| EJUA | Electronic Journal of University of Aden for Basic and Applied Sciences **Vol. 5, No. 2, June 2024** | Duwihan and Al Hered | Pages 163-172 |

https://ejua.net

The present study suggested that, in the general adult population, there associations between disorder in kidney function and age and duration of diabetes in diabetes patients. This association differs for different measures of eGFR and among different age groups and diabetes duration. The associations of lower eGFR were consistent nearly within categories of age and duration of diabetes. Older age and duration of diabetes were associated with increased risk in kidney function, but associations were attenuated in the lower range of eGFR. These results stratification with Grams et al. [37]. Across age quartiles, eGFR declined progressively at a time-linear rate, with older adults [38].

The decline of eGFR that occurred in men and women after age 65 associated with duration of T2DM, probably reflects the superimposition of diabetic kidney disease onto age-related loss of nephron units [39,40]. Russo et al. [41] recorded that in T2DM patients, the prevalence of both eGFR and Albuminuria increase with age.

The previous studies showed that metformin and particularly sulphonylureas in subjects with an eGFR greater than 60 mL/min per 1.73 m2 increases with aging, despite the fact that age and age-related comorbidities confer a greater risk of adverse effects such as lactic acidosis and hypoglycemia [38].

Grams et al. [37] suggested that reduced eGFR is consistent strong risk factors for acute kidney injury (AKI), whereas associations of AKI with age, sex, and race may be weaker in more advanced stages of chronic kidney disease (CKD).

Age-related macular degeneration (ARMD) and CKD are global health challenges [42-45]. Neelamegam et al. [1], found that the reduced eGFR values were associated with an increase in the severity of ARMD and the risk factors associated with CKD were age, gender and duration of diabetes.

The study of Bruno et al. [46] suggests that in type 2 diabetes macroalbuminuria is the main predictor of mortality, independently of both eGFR and cardiovascular risk factors. Wang et al. [47] showed that the family history of diabetes is independently associated with a rapid decline in eGFR in the current relatively young studied patients. The analyses of Zoppini et al. [48] revealed that annual eGFR decline is strongest predictor in older age patients with type 2 diabetes and preserved kidney function. The study of Jiang et al. [49] highlights that substantial heterogeneity in the patterns of eGFR decline among patients with diabetic kidney disease.

Islam et al. [50] showed that the diabetes mellitus and hypertension are associated with CKD and age and this associated was with stage 3 or 4 CKD. However, this association was statistically significantly stronger at younger age groupings. The low overall prevalence of stage 3 or 4 CKD among adults <50 years of age may mask the increased risk of CKD among individuals with hypertension or diabetes mellitus. Furthermore, van der Velde et al. [51] showed that significantly associated between eGFR and risk of Cardiovascular events (CV) in individuals <60 years of age than in elderly people (>60 years of age). Those with youngest age or longer duration of diabetes had more rapid declines in eGFR compared to those diagnosed at middle age or those with shorter duration of diabetes. eGFR decline was the slowest in those with age at 50–59 years. The rates of eGFR decline were significantly greater in those with age onset < 40 years compared to those diagnosed at 50–59 [52]. In general, these findings agree with current study.

Araumi et al. [53] showed that the renal function slowly declined with age in a healthy population, and that decline in renal function often observed in the elderly does not attribute to aging alone. It is possible that some features of obesity, including increased levels of fatty acids and leptin, may contribute to greater decline in kidney function in those who develop diabetes at younger age. The elevated levels of fatty acids is accompanied by increased oxidative stress which, together may result in premature kidney damage [54-56]. Young age at diabetes diagnosis amplified the effect of increasing diabetes duration on increased risk of CKD [57].

The proportion of persons with type 1 diabetes (T1D) have renal complications at<20 years after diagnosis as diabetic patient [58]. Overall in the total cohort of present study, 4% had severely impaired renal function (eGFR<30ml/min). The risk of renal complications increased with longer diabetes duration, and 13 out of 177 patients with diabetes duration ≥5 years had Kidney state in very high risk (eGFR<15 ml/min). These findings on duration of disease and the level of eGFR are agreement with that findings of Dena et al. [58].

The influence of age with diabetes duration on eGFR was studied by Buyadaa et al. [52], they found that the youngest age with/ or longer duration of diabetes had more rapid declines in eGFR compared to those diagnosed at middle age or those with shorter duration of diabetes. eGFR decline was the slowest in those with age at 50–59 years or those with duration of diabetes < 5 years. The rates of eGFR decline were significantly greater in those with known age-of-onset < 40 years or those with duration of diabetes > 20 years compared to those diagnosed at 50–59 or those with duration of diabetes < 5 years.

The results of current study illustrated excellent correlation between age with diabetes duration and eGFR level. So, this study emphasized the association between eGFR and DM in terms of age and diabetes duration in area that has received less attention in Yemen. Furthermore, the findings reveal significant correlations between kidney stages based on eGFR. These results

align with previous international studies that have reported associations between impaired renal function and DM. This underscores the need for interdisciplinary collaboration among ophthalmologists, nephrologists, endocrinologists, and primary care providers in managing diabetes patients. Because the aim of this study was not to answer a question about health and disease. Therefore, this study is not categorized as medical scientific research.

In conclusion, an important finding of this study is the distribution of estimated glomerular filtration rate (eGFR) according to age, diabetes duration and degree of renal dysfunction. in individuals ≥55 years of age with diabetes duration ≥ 5 years, all measures of eGFR are associated with risk of CKD events. These results emphasize the importance of assessment of eGFR for CKD risk prediction in diabetes patients. Our findings suggested that early diagnosis and treatment is important for these patients. So, the observation that could guide preventative efforts of efficient glucose-lowering and renal protective strategies are needed in persons with DM.

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مقالة بحثية

لارتباط بين العمر و فترة المرض بالسكري مع مقدار الترشيح الكبيبي في مرضى السكري المراجعين مستشفى الدفيعة العام- بيحان، شبوة – اليمن

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المُلخّص

المرض الكلوي المزمن أصبح شائعًا ارتباطه مع داء السكري، والذي استدعى عند معالجة داء السكري الانتباه لأمراض الكلى. يملك تحليل معدل الترشيح الكبيبي أهمية، حيث أصبح انخفاضه مرتبط مع عوامل الخطورة. ان الكبر في العمر يعتبر عملية حيوية طبيعية حتمية تؤثر على كل الأعضاء بالإضافة لفترة الإصابة بالسكري. في اليمن لم يتم بشكل جيد دراسة الارتباط بين الانخفاض في وظيفة الكلى والعمر من جهة وفترة المرض بالسكري من جهة أخرى، كذلك بين العمر مع فترة المرض بداء السكري والانخفاض في وظيفة الكلى. لذلك هدفنا في العمل الحالي الى دراسة ما أذا الانخفاض في معدل الترشيح الكبيبي يختلف مع العمر أو فترة المرض بالسكري أو مع كليهما. لغرض ذلك تمت الدراسة على 177 مريض بداء السكري في الفترة من فبراير 2022 الى فبراير 2023م. أوضحت النتائج وجود اختلافات ذات أهمية عالية المعنوية بين المجموعات العمرية بالنسبة لمعدل الترشيح الكبيبي والذي كان واضح في المجموعات العمرية 25-34و45-54 و 55-64. بشكل عام الانتشار لمرض الكلى المزمن كان بنسبة 16.9 % ويزيد مع العمر. من جهة أخرى يزيد كل 5 سنين زيادة في الإصابة بمرض السكري. 11.3% من المرضى معدل الترشيح الكبيبي لهم من 15-29 وأقل من 15 $mL/min/1.73\ m^2$ بالنسبة لفترة المرض بالسكري، و5.6% من المرضى كان معدل الترشيح الكبيبي لهم من 30-44 $mL/min/1.73\ m^2$ بالنسبة لفترة المرض بالسكري، 4% من المرضى الذين ينتمون للمجموعة الرابعة من مرض الكلى المزمن CKD. ارتباط خطي ظهر بين العمر مع فترة المرض بالسكري ومرض الكلى المزمن CKD. مقارنة نتائج الدراسة الحالية مع نتائج دراسات سابقة لمؤلفين آخرين أكدت على أهمية تقدير معدل الترشيح الكبيبي وفقا للعمر وفترة المرض بالسكري ودرجة الاختلال الكلوي .

الكلمات المفتاحية: العمر، فترة الاصابة، مرضى السكري، معدل الترشيح الكبيبي، اليمن.

How to cite this article: