

EPIDEMIOLOGY OF CHRONIC KIDNEY DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS IN UKRAINE*

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Chronic kidney disease (CKD) is a supranosological concept encompassing all patients who have signs of kidney injury and/or impaired renal function persisting for 3 months or more and is one of the leading causes of death worldwide. Driven by escalating risk factors such as obesity and diabetes, the number of patients with chronic kidney disease is growing, with 843.6 million people worldwide in 2021, according to Kidney Disease: Improving Global Outcomes (KDIGO) [1]. Albeit with the advent of modern medications such as sodium-glucose cotransporter-2 inhibitors (SGLT2i), glucagon-like peptide-1 (GLP-1) receptor agonists and mineralocorticoid receptor antagonists, the mortality rate of patients with end-stage renal disease has declined, CKD remains one of the leading causes of death worldwide [2, 3].

CKD is easy to diagnose and can be confirmed by laboratory tests to determine the glomerular filtration rate (GFR) based on a filtration marker such as serum creatinine and/or cystatin C using different formulas, or by

urinalysis for albumin or protein and creatinine (ACR) (or a combination of both). Defining these indicators laid the foundation for a classification to systematically identify and monitor CKD worldwide, contributing to a better understanding of the prevalence and outcomes of CKD. Most studies used estimated GFR to diagnose CKD, while some combined albuminuria (usually defined as an albumin-to-creatinine ratio >30 mg/g) and a decrease in GFR. Lastly, to differentiate CKD (which is considered a chronic progressive disease) from conditions such as acute kidney injury or temporary renal impairment not related to kidney injury, the standard definition of CKD includes the so-called «chronicity criterion», whereby low GFR or elevated urinary albumin levels should persist for at least 90 days [3, 4].

According to the International Diabetes Federation, the global diabetes prevalence as of 2021 is 537 million, with further escalation to 784 million people living with diabetes [5]. Estimates suggest that more than 40.0% of

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them will develop CKD, which includes the need for dialysis and transplantation. The prevalence of CKD varies widely around the world [5, 6]. The prevalence of the disease ranges from 6.8% in Western Europe (Spain) to 15.9% in Eastern Europe (Poland), while in the USA it is in the range of 10–17% in different ethnic groups, and in Japan it affects more than 20% of the population. The number of patients on dialysis treatment worldwide is more than 2.5 million, and this number is increasing by 7–8% annually [3]. A 2010 review of 33 population-based representative studies showed a prevalence of CKD of 10.4% in men over 20 years of age and 11.8% in women [4]. A recent meta-analysis of 100 studies involving 6908440 patients reported a prevalence of 13.4% for stage 1–5 CKD and 10.6% for stage 3–5 CKD [7]. As for the stage distribution, the prevalence of stage 3 CKD amounted to 7.6% [7]. Regarding patients with prediabetes and diabetes mellitus (DM), the National Health and Nutrition Examination Survey (NHANES 2001–2020) revealed a predominant prevalence of stage 3–4 CKD. Whereas the prevalence of

stage 3–4 CKD in adults without diabetes was 3.7%, it accounted for 10.0% in those with prediabetes and 18% in adults with undiagnosed diabetes [8]. A national study of US veterans with newly diagnosed type 2 diabetes mellitus (T2D) recorded a prevalence of CKD in 31.6% of cases, half of whom had stage 3–5 CKD [9]. Numerous studies reported a high prevalence of CKD in women without diabetes but a higher rate of progression in men [10–13].

Crucially, as the prevalence of T2D rose, the prevalence of CKD also increased [4, 15]. Timely diagnosis and prevention of disease complications is the most effective strategy in the management of diabetic patients. Investigating the prevalence of CKD in diabetic patients is essential in understanding the disease burden and identifying additional research priorities.

To identify the prevalence of CKD in the Ukrainian population, the Centre for Innovative Medical Technologies of the National Academy of Sciences of Ukraine screened 194 patients seeking an appointment with an endocrinologist.

MATERIALS AND METHODS

We diagnosed CKD by calculating the estimated GFR based on the creatinine level using the CKD-EPI Creatinine formula and determining albuminuria as the albumin-to-creatinine ratio. The 2022 KDIGO guidelines classify patients according to GFR and ACR [2]. Based on GFR, patients were divided into the following categories: stage 1 CKD — GFR ≥ 90 mL/min/1.73 m², stage 2 — GFR = 89–60 mL/min/1.73 m², stage 3a — GFR = 59–45 mL/min/1.73 m², stage 3b — GFR = 44–30 mL/min/1.73 m², stage 4 — GFR = 29–15 mL/min/1.73 m² and stage 5 — GFR ≤ 15 mL/min/1.73 m². The albuminuria category was A1 when ACR amounted to < 30 mg/g, A2 — 30–300 mg/g, and A3 > 300 mg/g, respectively. The degree of obesity was assessed by body mass index (BMI). The normal weight was defined as a BMI of 20–24.9 kg/m², overweight — BMI 25–29.9 kg/m², Obesity Class 1 — BMI 30–34.9 kg/m², Obesity Class 2 — BMI 35–39.9 kg/m², Obesity Class 3 — BMI > 40 kg/m². CKD was diagnosed if the GFR was confirmed to decrease after 3 months.

The mean age of the patients was 64.82 ± 0.88 years, and the duration of diabetes mellitus amounted to 9.29 ± 0.60 years. Of these, 53.1% were female and 46.9% were male. Out of the screened patients, 79.4% had type 2 diabetes mellitus, 3.6% had type 1 diabetes mellitus, 9.3% had prediabetes, and 7.7% had other types of diabetes.

The albumin-to-creatinine ratio (ACR) was determined using the URISCAN Optima system (YD Diagnostic, Yongin-si, South Korea). Those devices are among the most widely used urine analysers proven accurate in studies [16]. This study used fresh urine samples collected from outpatients and inpatients between December 2022 and June 2023. The samples were preservative-free. A minimum of 10 mL sample was taken for urine dipstick test. The samples were tested within 1 hour of collection and delivery to the laboratory.

The study results were statistically processed using SPSS version 26 for Windows. Descriptive statistics were performed to obtain demographic data. The demographic data are

reported as mean \pm standard deviation, standard error or percentage. We used linear regression analysis to determine the relationship between the measures and presented the data as an unstandardised coefficient (beta, B) and 95 % confidence interval for the B (95 % CI). The difference was considered statistically significant at $p < 0.05$. We employed a General Linear Model (UNIANOVA) to compare the groups. Also, we used T-test to compare data between groups. The sample parameters are

given in the following tables and text with the following designations: M = sample mean, m = standard deviation, n = sample size (size of the analysed group), p = level of statistical significance.

The study was authorised by the Medical Ethics Committee at the State Scientific Institution «Centre for Innovative Medical Technologies of the National Academy of Sciences of Ukraine».

RESULTS AND THEIR DISCUSSION

Among diabetic patients, 26.8 % had stage 1 CKD, 42.3 % had stage 2, 21.6 % had stage 3a, 8.2 % had stage 3c, and 0.5 % had each of stage 4 and 5. 70.6 %, 21.6 %, and 7.7 % of the entire study population were found to have ACR corresponding to category A1, A2, and A3 albuminuria, respectively.

In diabetic women, 24.3 % had stage 1 CKD, 40.8 % had stage 2, 21.4 % had stage 3a, 12.6 % had stage 3c, and 1.0 % had stage 4. 74.8 %, 19.4 %, and 5.8 % of female patients were found to have ACR corresponding to category A1, A2, and A3 albuminuria, respectively. In diabetic men, 29.7 % had stage 1 CKD, 42.9 % had stage 2, 22.0 % had stage 3a, 4.4 % had stage 3b, and 1.0 % had stage 5. 64.8 %, 25.3 %, and 9.9 % of male patients were found to have ACR corresponding to category A1, A2, and A3 albuminuria, respectively. Hence, we observed no gender differences in prevalence. Overweight

and obesity constitute some of the negative risk factors for CKD (KDIGO).

As can be seen, patients with category A3 albuminuria were mainly those with a BMI of more than 35.0 kg/m², while overweight and obese patients of class 1 dominated categories A1 and A2. Furthermore, the first two categories had twice as many patients of normal weight compared to A3 category (Fig. 1).

The group of patients with ACR over 300 mg/g is dominated by those with stage 3a and 3c CKD, while the category A1 and A2 groups consist mainly of patients with stage 2 CKD (Fig. 2).

The regression analysis revealed a negative correlation between the duration of diabetes mellitus and the level of GFR, B (95 % CI) = - 0.102 (- 0.179/-0.26), $p = 0.009$, and a positive correlation with ACR, B (95 % CI) = 2.87 (0.089/5.605), $p = 0.043$. Therefore, the longer

Distribution of the degree of obesity by the level of albuminuria.

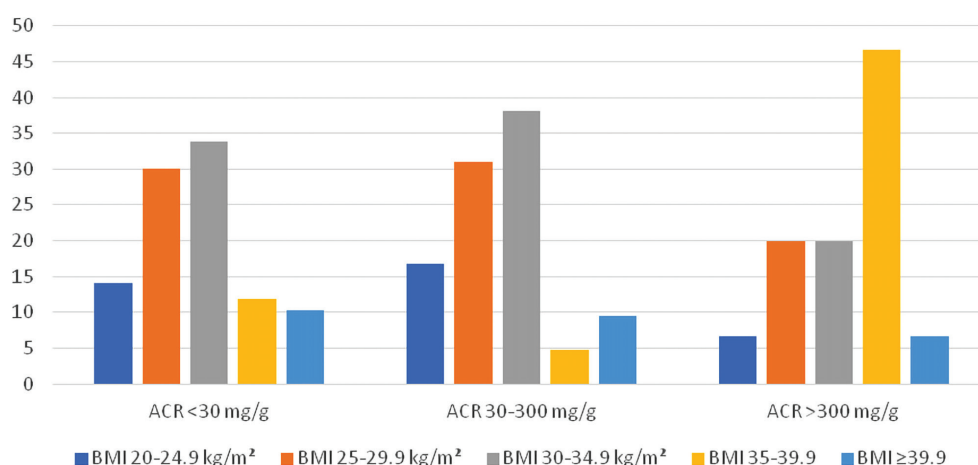


Fig. 1. Distribution of the degree of obesity by the level of albuminuria according to the urine albumin-to-creatinine ratio (ACR).

Distribution of diabetic patients with CKD depending on ACR

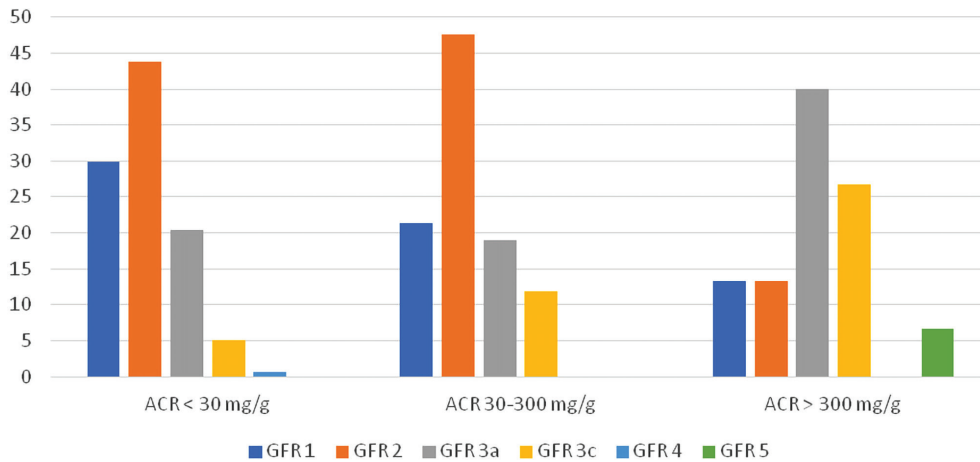


Fig. 2. Distribution of diabetic patients with CKD by albuminuria category.

CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A)				Albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased < 30 mg/g < 3 mg/mmol	Moderately increased 30-299 mg/g 3-29 mg/mmol	Severely increased ≥ 300 mg/g ≥ 30 mg/mmol
GFR categories (ml/min/1.73 m ²) Description and range	G1	Normal or high	≥ 90	Screen 1	Treat 1	Treat 3
	G2	Mildly decreased	60-89	Screen 1	Treat 1	Treat 3
	G3a	Mildly to moderately decreased	45-59	Treat 1	Treat 2	Treat 3
	G3b	Moderately to severely decreased	30-44	Treat 2	Treat 3	Treat 3
	G4	Severely decreased	15-29	Treat* 3	Treat* 3	Treat 4+
	G5	Kidney failure	< 15	Treat 4+	Treat 4+	Treat 4+

■ Low risk (if no other markers of kidney disease, no CKD) ■ High risk
■ Moderately increased risk ■ Very high risk

Fig. 3. Utility of GFR and ACR determination in CKD patients.

the duration of diabetes mellitus, the lower the GFR and the higher ACR.

Moreover, we found a negative correlation between lower GFR and increased albuminuria in our patients, B (95 % CI) = 8.879 (- 14.826/ - 2.926), p = 0.04.

Notably, we did not detect an effect of BMI on GFR, B (95 % CI) = - 0.029 (- 0.53/0.47), p = 0.90, and albuminuria category, B (95 % CI) = - 0.009 (- 0.005/0.024), p = 0.19.

Identifying the risk of developing end-stage renal disease is a crucial component of the diagnosis and prevention of CKD for timely monitoring and initiating treatment of this life-threatening disease. According to KDIGO data, green indicates a low risk of developing end-stage CKD and annual screening is recommended, yellow indicates a moderate risk with annual monitoring and treatment recommended, orange indicates a high risk with biannual

monitoring and treatment recommended, and red and dark red indicates a very high risk with mandatory treatment and monitoring 3–4 times a year recommended (Fig. 3).

Our study found that 52.1 % of the patients had a low risk of developing end-stage CKD, 28.9% had a moderate risk, and 8.2 % and 10.8% had a high and very high risk, respectively. This means that 30.0 % of diabetic patients have a high risk of developing end-stage CKD. Regrettably, none of the patients screened consulted a nephrologist. International KDIGO guidelines recommend that patients with pre-existing CKD should be treated with an angiotensin receptor blocker (ARB) or angiotensin converting enzyme inhibitor (ACEi) and sodium-glucose cotransporter-2 inhibitor (SGLT2i);

12.9 % of patients enrolled in our study were taking an ACEi or ARB, and 10.3 % were taking a SGLT2i. The issue of managing diabetes mellitus and CKD is complex and demands the engagement of physicians of different specialties as part of a multidisciplinary team. This is how a certain channel of communication should be established between endocrinologists, nephrologists, and general practitioners. Unfortunately, the real-world data point to the neglect in detecting such a grave disease as CKD, resulting in erroneous management and monitoring of patients, potentially leading to early disability, poor quality of life, reduced life expectancy, and not only the decompensation of diabetes mellitus but also to further progression to CKD.

CONCLUSIONS

1. Of diabetic patients, 73.2 % had stage 2-5 chronic kidney disease, and 29.3 % had stage A2 and A3 albuminuria.
2. 28.9% of patients were at moderate risk of developing end-stage renal disease, and 30 % had high and very high risk, requiring conservative treatment and regular monitoring of glomerular filtration rate and albuminuria.
3. The duration of diabetes mellitus is a negative factor affecting glomerular filtration rate and albumin-to-creatinine ratio.
4. All diabetic patients, regardless of the duration of the disease, diabetes compensation, or obesity, should undergo screening for chronic kidney disease for early diagnosis, prevention, and treatment of this life-threatening complication engaging physicians of various specialties.

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The article reports on the prevalence of chronic kidney disease (CKD) in Ukrainian diabetic patients. A total of 194 patients who seeking an appointment with an endocrinologist underwent CKD screening.

Materials and methods. The mean age of the patients was 64.82 ± 0.88 years, and the duration of diabetes mellitus amounted to 9.29 ± 0.60 years. Of these, 53.1 % were female and 46.9 % were male. Out of the screened patients, 79.4 % had type 2 diabetes mellitus, 3.6 % had type 1 diabetes mellitus, 9.3 % had prediabetes, and 7.7 % had other types of diabetes. We diagnosed CKD by calculating the estimated glomerular filtration rate (GFR) based on the creatinine level using the CKD-EPI Creatinine formula and determining albuminuria as the albumin-to-creatinine ratio.

Results. Among diabetic patients, 26.8 % had stage 1 CKD, 42.3 % had stage 2, 21.6 % had stage 3a, 8.2 % had stage 3c, and 0.5 % had each of stage 4 and 5. 70.6 % of patients were found to have albumin-to-creatinine ratio (ACR) A1, 21.6 % — A2, and 7.7 % — A3. Of these, 30.0 % were at high and very high risk of developing end-stage CKD. The regression analysis revealed a negative correlation between the duration of diabetes mellitus and the level of GFR, B (95 % CI) = -0.102 ($-0.179/-0.26$), $p = 0.009$, and a positive correlation with ACR, B (95 % CI) = 2.87 ($0.089/5.605$), $p = 0.043$.

Conclusions. Among the examined patients with diabetes mellitus, 73.2 % had stage 2–5 chronic kidney disease, and 29.3 % had stage A2 and A3 albuminuria. Of these, 30 % belong to the high- and very high-risk group for developing end-stage chronic kidney disease, requiring regular monitoring of glomerular filtration rate and albuminuria at least 3–4 times a year and conservative treatment. The duration of diabetes is a negative risk factor for chronic kidney disease. Hence, chronic kidney disease screening should be performed in all patients with diabetes with no exception.

Key words: chronic kidney disease, diabetes mellitus, risk of end-stage renal disease, albuminuria.

ЕПІДЕМІОЛОГІЯ ХРОНІЧНОЇ ХВОРОБИ НИРОК У ПАЦІЄНТІВ З ЦУКРОВИМ ДІАБЕТОМ 2 ТИПУ В УКРАЇНІ

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В статті наведено дані щодо частоти виявлення хронічної хвороби нирок (ХХН) у пацієнтів з цукровим діабетом в Україні. Було проведено скринінг ХХН у 194 пацієнтів, які приходили на консультативний огляд до ендокринологів.

Матеріали та методи. Середній вік пацієнтів становив $64,82 \pm 0,88$ років, тривалість цукрового діабету — $9,29 \pm 0,60$ років, серед них жінок — 53,1 %, чоловіків — 46,9 %. Серед обстежених на цукровий діабет 2 типу хворіли 79,4 % пацієнтів, на цукровий діабет 1 типу — 3,6 % осіб, предіабет — 9,3 %, інші типи діабету — 7,7 %. Наявність ХХН визначали за допомогою розрахункової швидкості клубочкової фільтрації (ШКФ) за рівнем креатиніну за формулою СКД-EPI Creatinine, а також визначення альбумінурії як співвідношення альбуміну до креатиніну (САК).

Результати. Серед хворих на цукровий діабет ХХН 1 ст. виявлялась у 26,8 %, 2 ст. — 42,3 %, 3а ст. — 21,6 %, 3в ст. — 8,2 %, 4 та 5 ст. по 0,5 %. САК А1 виявлялась у 70,6 % випадків, А2 — 21,6 % та А3 у 7,7 % обстежених. З них високий та дуже високий ризик розвитку термінальної стадії ХХН мали 30,0 % обстежених. Знайдено негативний взаємозв'язок за даними регресійного аналізу між тривалістю цукрового діабету та рівнем ШКФ B (ДІ 95 %) = $-0,102$ ($-0,179/-0,26$), $p = 0,009$; позитивний зі співвідношенням альбумін-креатинін B (ДІ 95 %) = $2,87$ ($0,089/5,605$), $p = 0,043$.

Висновки. Серед обстежених хворих на цукровий діабет виявляється 73,2 % з хронічною хворобою нирок 2–5 ст., з альбумінурією стадії А2 та А3 — 29,3 % осіб. З них 30 % осіб, відносяться до групи високого та дуже високого ризику термінальної стадії хронічної хвороби нирок, яким вже необхідно проводити регулярний моніторинг швидкості клубочкової фільтрації та альбумінурії не менше ніж 3–4 рази на рік та консервативне лікування. Тривалість цукрового діабету є негативним фактором ризику розвитку хронічної хвороби нирок, тому скринінг на наявність хронічної хвороби нирок необхідно проводити всім без винятку пацієнтам з цукровим діабетом.

Ключові слова: хронічна хвороба нирок, цукровий діабет, ризик термінальної стадії хронічної ниркової недостатності, альбумінурія.