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REVIEW ARTICLE

ALBUMIN/CREATININE RATIO IN A SINGLE URINE SAMPLE (ACR) AS AN EARLY INDICATOR OF KIDNEY DAMAGE IN TYPE 2 DIABETES

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Abstract: Type 2 diabetes mellitus (DM type 2) is associated with numerous organ complications. One of the pathophysiological mechanisms of this disease is damage to the renal filtration barrier, which can lead to increased protein excretion in the urine, an early marker of kidney function impairment.

Detecting albuminuria is crucial in diagnosis and prevention, as its presence, even with normal estimated glomerular filtration rate (eGFR), indicates a higher risk of progression and faster deterioration of kidney function. This approach speeds up the start of treatment and may prevent further kidney damage. According to a review of the available literature, measuring the albumin/creatinine ratio in a single urine sample is a sensitive method for detecting albuminuria and is comparable to the results of 24-hour urine collections, making it a practical tool for risk assessment, diagnosis, and prevention of complications in diabetic kidney disease.

Keywords: diabetic kidney disease, microalbuminuria, urine albumin/creatinine ratio

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INTRODUCTION

Epidemic of type 2 diabetes

Diabetes is one of the most commonly diagnosed diseases of the 21st century. It is characterized by elevated glucose concentrations due to reduced sensitivity of body tissues to endogenous insulin or a deficiency of this hormone. According to data from the World Health Organization, in 2022, 14% of adults had diabetes, which is double the figure of 7% in 1990. The vast majority (95%) of patients were diagnosed with type 2 diabetes mellitus [7]. Chronic exposure to hyperglycemia results in numerous complications, among which we distinguish groups of disorders related to blood vessel dysfunction, divided into macroangiopathic (affecting large and medium-sized vessels) and microangiopathic (affecting small vessels). In 2021, diabetes was the direct cause of 1.6 million deaths, and 47% of all diabetes-related deaths occurred before the age of 70. A further 530,000 deaths from kidney disease were caused by diabetes [7].

Aim of the study

The aim of this article is to present the current results of clinical trials and expert opinions on the determination of proteinuria as a marker of diabetic kidney disease progression and to highlight the benefits of early microalbuminuria.

Hyperglycemia and the kidneys

Carbohydrate metabolism disorders result in excessive production of pro-inflammatory cytokines in the glomeruli, which induce a local inflammatory response. The most sensitive area is the filtration barrier consisting of the basement membranes of the glomeruli, podocytes, and endothelial cells of the nephron capillaries. In people without nephropathy, glomerular filtration involves the passage of water, small molecules, and mineral salts from the blood plasma into the lumen of Bowman's capsule, thus forming primary urine. Damage to the structure of the filtration barrier causes increased permeability, allowing larger molecules, including proteins, to enter the primary urine, which physiologically should not be there[6].

Diabetic nephropathy

Diabetic kidney disease develops in an estimated 20-48% of patients with type 2 DM [2,3,8,12]. In Mogensen's classification, we distinguish five stages of diabetic kidney disease (Tab. 1). The initial stages (I, II, III) are associated with the possibility of reversing or halting the progression of changes. Clinically, we then observe hyperfiltration with increased eGFR of up to 160 ml/min, signs of renal hypertrophy, and transient or persistent albuminuria may occur. Phase IV (overt nephropathy) manifests itself as persistent proteinuria, decreased eGFR, edema, lipid disorders, and hypertension. In phase V (renal failure), we observe a further increase in creatinine, proteinuria, and hypertension.

Clinically apparent stages are associated with a poorer prognosis, which is why screening is very important. The detection of albuminuria in patients with normal or increased glomerular filtration appears to be of particular importance, as it allows for the early implementation of appropriately tailored treatment [3].

Protocol for the detection of diabetic kidney disease

According to clinical guidelines for the management of people with diabetes 2024 (position of the Polish Diabetes Association), albuminuria and reduced eGFR are unfavorable cardiovascular

Tab. 1. The course of diabetic kidney disease according to Mogensen [13].

Phase	Clinical picture	Prognosis
I – hyperfiltration, renal hypertrophy	increase in GFR to 160 ml/min, enlargement of the kidneys, transient microalbuminuria in some patients	possibility to undo changes
II – latent nephropathy (onset of histological changes, change in the structure and function of the basement membrane)	thickening of the basement membrane and change in its electrical charge, enlargement of the mesangial matrix, without albuminuria	possibility of partially reversing changes
III – initial clinical nephropathy	albuminuria 30-300 mg/day, decrease in GFR from 160 to 130 ml/min, increase in blood pressure	possibility of halting the progression of changes, sometimes even reversing them
IV – overt nephropathy	persistent proteinuria (using standard methods), reduction in GFR to 70 ml/min, later to 10 ml/min, persistent increase in blood pressure, edema, lipid disorders	possibility of slowing down the course of changes, sometimes stopping them
V – renal failure	increased creatinine levels, hypertension	possibility of slowing down the course of changes, sometimes stopping them

d – day, GFR – glomerular filtration rate

risk factors. In the context of type 2 diabetes, it is recommended that proteinuria be measured annually in patients from the moment of diagnosis [1]. In the comparative analysis, the sensitivity of single urine sample measurements (albumin concentration, albumin/creatinine ratio [ACR, albumin/creatinine ratio]) positively correlated with the results of micro- and macroalbuminuria screening tests in daily urine collections (correlation of results 0.9614 to 0.9868, respectively)[14]. The normal concentration of albumin/creatinine in urine (normoalbuminuria), determined on the basis of ACR, is <30 mg/g (<3 mg/mmol), which corresponds to the amount of albumin excreted as expressed by albumin excretion in a 24-hour urine collection [AER, albumin excretion rate] < 30 mg/24 h. Moderately increased albuminuria (microalbuminuria) refers to a condition in which moderately elevated albumin concentrations in urine are not accompanied by visible symptoms of nephropathy. Moderately increased albuminuria is characterized by an ACR range of 30–300 mg/g (3–30 mg/mmol), which corresponds to an AER in the range of 30–300 mg/24 h. A condition in which ACR > 300 mg/g (>30 mg/mmol) and AER > 300 mg/24 h is defined as significantly increased albuminuria or macroalbuminuria [1]. The presence of microalbuminuria in people with newly diagnosed type 2 diabetes predisposes them to faster deterioration of glomerular filtration and, in general, faster impairment of kidney function compared to people without albuminuria at the time of diagnosis in a five-year follow-up [15]. Classification and risk of progression of chronic kidney disease according to Kidney Disease: Improving Global Outcomes (KDIGO) is shown in Figure 1[4].

DISCUSSION

Stratification of patients based on eGFR and albuminuria (Tab. 2) shows that low-risk patients have the lowest mortality rate (16.44 deaths/1,000 people/year) and cardiovascular disease mortality rate (7.76 deaths/1,000 people/year) [11].

Furthermore, in studies conducted in normoglycemic patients with a family history of type 2 diabetes, higher ACR values (within the

				Categories of albuminuria (description and scope)		
				A1	A2	A3
The PChN classification takes into account: - cause (C) - GFR (G) - Albuminuria (A)				correct to slightly increased	moderately increased	significantly increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
eGFR categories (mL/min/1.73 m²) (description and scope)	G1	normal or increased	≥90	monitor 1	treat 1	treat and refer 3
	G2	slightly reduced	60–89			
	G3a	slightly or moderately reduced	45–59	treat 1	treat 2	treat and refer 3
	G3b	moderately or significantly reduced	30–44	treat 2	treat and refer 3	
	G4	significantly reduced	15–29	treat and refer 3		treat and refer 4+
	G5	renal failure	<15	treat and refer 4+		

low risk (no CKD if there are no other markers of kidney disease)

moderately increased risk

high risk

very high risk

Tab. 2. Risk of chronic kidney disease progression (CKD), frequency of visits, and referral guidelines to a nephrologist based on estimated glomerular filtration rate (eGFR) and albuminuria [4].

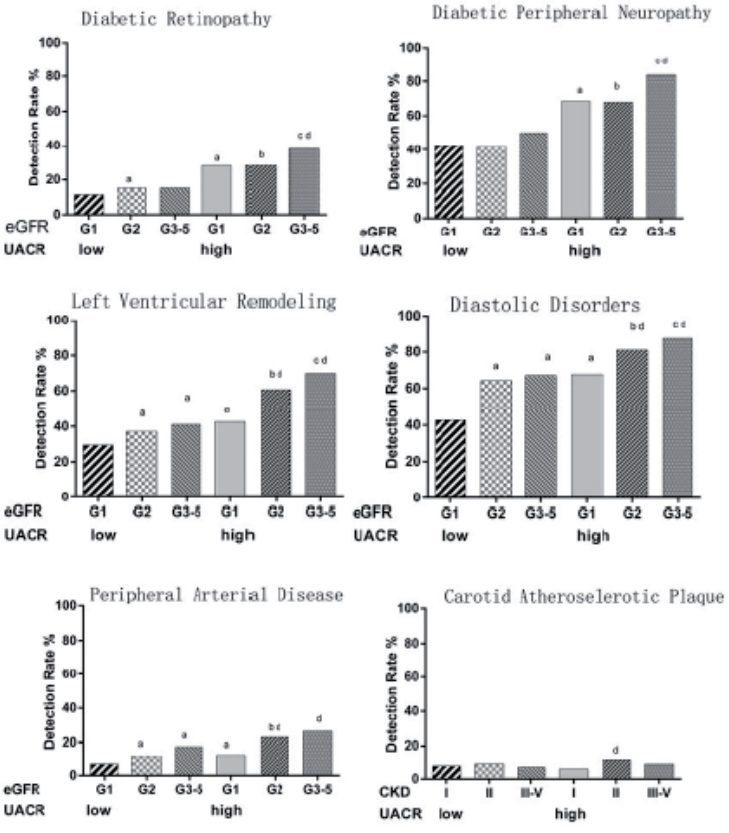
range of normoalbuminuria) were associated with a higher risk of progression to prediabetes during a 5.5-year follow-up period [5]. In turn, the presence of albuminuria in patients with newly diagnosed type 2 diabetes is associated with a faster decline in the estimated glomerular filtration rate over time than in patients with normoalbuminuria (-2.6 ml/min/1.73 m²/year compared to -1.5 ml/min/1.73 m²/year) [10].

Furthermore, ACR in patients showed seasonal variability, being higher in winter and lower in spring, early summer, and fall, particularly in the ACR ≥ 30 mg/g subgroup, whereas eGFR did not show seasonal variability [10]. Compared with the control group, patients with higher albuminuria and lower eGFR had higher adjusted odds ratios (OR) for organ complications, particularly in the high ACR 5 + G3-5 (according to eGFR) group. OR values of 2.010, 3.444, 1.633, 2.742, and 3.014 were obtained for diabetic retinopathy (DR) and diabetic peripheral neuropathy DPN), peripheral arterial disease (PAD), remodeling and diastolic dysfunction of the left ventricle (Fig. 1). After grouping according to eGFR, regression analysis of urine protein levels at each stage showed that most complications had a statistically significant difference, and a higher risk of complications was observed in the group of patients with progressive albuminuria [9].

CONCLUSIONS

1. The occurrence of microalbuminuria, resulting from damage to the renal filtration barrier, is an early marker of kidney damage.
2. Identifying microalbuminuria in the early stages of type 2 diabetes allows for faster treatment and can prevent further kidney damage and other complications, such as retinopathy and polyneuropathy.
3. ACR measurement in a single urine sample is a sensitive method for detecting albuminuria and is comparable to the results of 24-hour urine collection, making it a practical tool for risk stratification in diabetic kidney disease.

Fig. 1. Vascular complication detection rate [9].



High ACR ≥ 30 mg/g or low ACR < 30 mg/g; G1: eGFR ≥ 90 mL[min x 1.73 m²]; G2: eGFR = 60-89 mL/[min x 1.73 m²]; G3-5: eGFR < 60 mL/[min x 1.73 m²]

AUTHORS' DECLARATION

Study Design: Szymon Nazar. **Data Collection:** Szymon Nazar. **Manuscript preparation:** Szymon Nazar. The Author declares that they have no conflicts of interest.

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