

Features Of The Course Of Chronic Kidney Disease According To The Degree Of Nephriuria In A Comorbid State With Hypertension And Diabetes Mellitus.

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Abstract: According to diabetes incidence statistics for 2011, 360 million patients were registered, and by 2030 their number will reach 552 million. In recent years, when talking about comorbidity, the most discussed area in the field of internal medicine is the cardiorenal continuum. Cardiovascular diseases, obesity, type II diabetes and renal dysfunction are becoming more and more pandemics of the 21st century. In recent years, the main cause of kidney dysfunction is not its primary disease, but hypertension, that is, essential arterial hypertension (AH) and diabetes. Earlier detection of changes in podocytes and nephropathy makes it possible to diagnose and stop the process of kidney damage before the appearance of clinical signs.

Key words: nephrin, podocyte, diabetes mellitus, arterial hypertension, microalbuminuria.

Introduction. Diabetic nephropathy is the most common cause of chronic kidney disease and represents a large and ominous public health problem. Patients with diabetic kidney disease have exceptionally high rates of cardiovascular morbidity and mortality. In fact, the excess mortality among patients with diabetes appears to be largely limited to the subgroup with kidney disease and explained by their high burden of cardiovascular disease. The mechanisms underlying the strong association between diabetic kidney disease and various forms of cardiovascular disease are poorly understood [4,9].

Traditional risk factors for cardiovascular disease, although prevalent among those with diabetes, do not fully account for the heightened risk observed. Despite their susceptibility to cardiovascular disease, patients with chronic kidney disease are less likely to receive appropriate risk factor modification than the general population. Moreover, as patients with chronic kidney disease have commonly been excluded from major cardiovascular trials, the evidence for potential treatments remains limited. Currently, mainstays of treatment for diabetic kidney disease include blockade of the renin-angiotensin-aldosterone system, and control of hypertension, hyperglycemia and dyslipidemia. Increased awareness of the vulnerability of this patient population and more timely interventions are likely to improve outcomes, while large evidence gaps are filled with newer studies [9].

Almost all studies reported that a high level of concomitant pathology reduces the quality of life, disrupts social adaptation and increases mortality [3,7].

In the last 10 years, when talking about comorbidity, the most discussed area in the field of internal medicine is the cardiorenal continuum. Cardiovascular diseases, obesity, type II diabetes and renal dysfunction are becoming more and more pandemics of the 21st century. In recent years, the main cause of renal dysfunction is not its primary disease, but hypertension, that is, essential arterial hypertension (AH) and diabetes [4].

The combination of diabetes mellitus and AH is detected in 60% of cases and is a serious risk factor for cardiovascular diseases [5].

AH accounts for 75% of cardiovascular diseases diagnosed in patients with diabetes mellitus [9]. Only the presence of type II diabetes increases the risk of cardiovascular diseases by 2 times in men and 3 times in women, which increases by 4 times with the addition of hypertension [2,8].

According to diabetes incidence statistics for 2011, 360 million patients were registered, and by 2030 their number will reach 552 million [8].

It is known that irreversible severe changes in target organs occur in type II diabetes mellitus. Their number increases sharply in comorbid cases, including when accompanied by AH. The combination of diabetes mellitus and AH is detected in 60% of cases and is a serious risk factor for cardiovascular diseases [5,9].

Podocytes are a complex structural structure that provides its broad functions and adaptive processes in physiological conditions. This also makes the cells very sensitive to damage [1,7].

In recent years, the existence of an organic link between albuminuria and ultrastructural and functional disorders of podocytes has been confirmed in a number of experimental and clinical studies [6,7]. It has been shown that these changes occur long before the appearance of microalbuminuria [4,8].

The data obtained confirmed that podocytes were involved in the processes much earlier and increased interest in them. This is due to the fact that the detection of changes in this cell and nephropathy allows you to diagnose and stop the process of kidney damage before the appearance of clinical signs.

The purpose of the study. Comparison of the difference in the degree of nephrinuria by the duration of the disease in combination with hypertension, diabetes mellitus.

Materials and methods of research. The study included 58 patients diagnosed with DM, including 21 with type 1 diabetes and 37 with type 2 diabetes, of which 28 (48%) men, 30 (52%) women aged 18 to 60 years. The average age of patients with type 1 diabetes was 29.7 ± 17 years, the duration of the underlying disease was 13.5 ± 11 years. The average age of the subjects with type 2 diabetes was 52.5 ± 10 years, the duration of the disease was 10.7 ± 7.5 years. The patients were examined and treated at the Bukhara Regional Multidisciplinary Medical Center, in the Department of Nephrology and Endocrinology. The control group included 10 healthy volunteers (5 men, 5 women aged 19 to 55 years).

Diabetes is a strong risk factor not only for CVD, but also for the development of CKD. The risk of ESRD is increased 12-fold in patients with diabetes. Roughly 40% of patients with diabetes have evidence of CKD upon screening for decreased eGFR and albuminuria [9].

The development of albuminuria has long been recognized as a poor prognostic indicator in patients with diabetes. Numerous studies examining the association of decreased eGFR and/or increased albuminuria with CV endpoints in patients with diabetes have made similar observations as those in general population cohorts; both eGFR and albuminuria independently predict increased CV morbidity and mortality.

Indicators of nephrinuria (NU) exceeding the 75th percentile in the control group (i.e. practically not found in healthy people), we took as "positive" values ($NU+ > 5.78$ ng/ml/g). $NU+$ was detected, on average, in 69% (40 out of 58) patients with DM: in 63% (23 out of 37) patients with AU < 30 mg/g (A1), in 77% (7 out of 9) - with AU 30-300 mg/g (A2) and in 80% (9 out of 12) - with PU

The average level of well in the subgroups of patients with A1 and A2 albuminuria did not differ between types 1 and 2 DM ($8.01 [5.98;7.22]$ and $8.05 [6.07;7.82]$ ng/ml/g - DM1 and DM2 with A1 albuminuria, respectively, $p > 0.05$; $9.56 [7.66;9.56]$ and $6.91 [6.73;7.06]$ ng/ml/g - DM1 and DM2 with albuminuria A2, respectively, $p > 0.05$), which apparently reflects the common mechanisms of podocyte damage in diabetes. With clinically obvious DN occurring with PU, urinary nephrin excretion was significantly higher than in the subgroup with albuminuria.

In patients with a duration of DM1 and DM2 of less than 5 years, well directly correlated with the index of glycosylated hemoglobin HbA1c ($R=0.78$, $p < 0.01$).

The value of the NU indicator for different duration of diabetes was influenced by hypertension. This was more clearly observed in patients with type 2 diabetes, in whom hypertension was detected not only during the development of DN, but often preceded the development of kidney pathology. In this category of patients, we found a direct reliable relationship between systolic blood pressure and the severity of urinary nephrine excretion ($R=0.33$, $p < 0.05$).

Type 1 and was detected by immunoblotting in 23% of DM patients with normalalbuminuria, in 18% - with MAU, in 28% - with PU, while nephrin was not detected in the urine of healthy individuals. In the work of V. Jim [6], NU was detected in 54% of patients with normoalbuminuria and in all patients with type 2 diabetes with PU and MAU. As in our study, the average urinary excretion of nephrin in patients with MAU and especially with PU significantly exceeded that in patients with lower AU.

Conclusion. The prevalence of diabetes and chronic kidney disease, which has already reached epidemic proportions in Western societies, continues to increase. Given the substantial morbidity and mortality associated with these conditions, the rising prevalence represents a daunting problem. In light of data demonstrating that cardiovascular disease disproportionately affects patients with diabetic nephropathy, early and aggressive interventions are needed to lessen their risk of adverse outcomes. Alarming, patients with chronic kidney disease, including diabetic nephropathy, are underdiagnosed, undertreated and underrepresented in cardiovascular disease trials. Increased awareness of the tremendously high risk for cardiovascular disease in the setting of diabetic kidney disease, addressing known risk factors, as well as a focus on filling evidence gaps is critical to improving outcomes.

Moreover, in the majority (from 28 to 56%) of patients with DM, a high urinary excretion of markers of podocyte damage (nephrin, podocin) is detected, preceding the development of clinically significant albuminuria and PU, which allows using these urinary tests for early preclinical diagnosis of glomerular damage in DM.

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