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METHODS FOR PREVENTING THE DEVELOPMENT OF TERMINAL RENAL FAILURE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Abstract. Type 2 diabetes mellitus is a global problem of the entire healthcare system, not only in our country, but throughout the world. Diabetic nephropathy remains the most significant in the study among all complications. This article describes the main factors in the progression of diabetic nephropathy. This recommendation makes it possible to effectively plan and target measures for secondary and tertiary prevention of the development of ESRD among patients with type 2 diabetes mellitus. The results of the study on the relationship of the prevalence of CKD with modifiable risk factors allow us to improve preventive approaches aimed at increasing the life expectancy of patients with diabetes.

Keywords: diabetes mellitus, diabetic nephropathy, chronic kidney disease, arterial hypertension.

Diabetes mellitus (DM) remains one of the leading problems of modern medicine and is a highly costly chronic disease for the healthcare system in all countries of the world. In recent years, the number of patients with diabetes in the world has increased tenfold, according to the forecasts of the International Diabetes Federation (IDF), the total number of people with diabetes worldwide will increase from 537 million (8.8%) to 783 million (10.4%) by 2045 [7].

The greatest concern is the development of complications of diabetes against the background of decompensation of glycemia and its negative impact on the vascular endothelium. An important place in this series is occupied by diabetic nephropathy (DN) and chronic kidney disease (CKD), which develop in approximately 20.1% of patients with type 1 DM and 6.3% of patients with type 2 DM [5].

Chronic kidney disease (CKD) is a persistent and progressive decline in kidney function and includes five stages of kidney damage. Stages 3 and 4 of CKD are generally considered to imply moderate or severe kidney damage. Stage 3 is subdivided into two categories of kidney damage: 3a GFR 45 to 59 ml/min/1.73 m2 and 3b GFR 30 to 44 ml/min/1.73 m2. GFR for stage 4 is 15–29 ml/min/1.73 m2.

According to a meta-analysis, the prevalence of stage 3-5 CKD in South Africa, Senegal and Congo is about 7.6%. In China, Taiwan, and Mongolia, the incidence of CKD is about 10.06%, and in Japan, South Korea, and Oceania, it is about 11.73%. In the countries of the European continent, the prevalence of CKD is about 11.86% [10]. In the US and Canada, this figure is about 14.44%. The prevalence of CKD is estimated at about 11.68% in the adult population of Iran, and

it is expected that CKD develop in about 2.9% of Iranian women and 1.3% of Iranian men every year [11].

Patients with stage 3 or 4 CKD are at a much higher risk of progression to end-stage renal disease (ESRD) or death even before the development of ESRD [12]. According to domestic publications in Uzbekistan, the incidence of type 2 diabetes in people over 35 years of age is 7.9%. Approximately 46% are diagnosed late.

People with CKD are at higher risk of drug side effects due to decreased renal excretion, polypharmacy, and multiple comorbidities. For this reason, an individual approach in the treatment of patients with diabetic nephropathy is very important.

Purpose of the study. Optimization of secondary prevention of diabetic nephropathy in patients with type 2 diabetes mellitus.

Materials and research methods. The study was conducted in the Bukhara region on the basis of the Regional Diversified Medical Center. The study participants were 180 patients with various stages of diabetic nephropathy. Of which 65% were men 45% women. During the examination, the following research methods were used: instrumental questionnaire, laboratory and clinical examination. Laboratory methods included complete blood count and ESR, biochemical markers of nephropathy (urea, creatinine), total cholesterol, lipid spectrum and blood glucose.

Results. The development of diabetic nephropathy is more dependent on lifestyle and a large number of risk factors, many of which are modifiable. Thanks to the survey, we were able to identify the most significant progression factors for our region.

- Smoking
- Alcohol abuse
- Poor nutrition
- Irrational pharmacotherapy
- Arterial hypertension
- Experience with diabetes
- Dyslipidemia
- The presence of concomitant cardiovascular diseases

Analysis of risk factors is the theoretical basis for the secondary prevention of diabetic nephropathy, including within the framework of rehabilitation. Knowing the specific risk factors for each patient allows us to develop methods for their correction and prevention, and thereby affect the prognosis.

The development of diabetic nephropathy and mortality from ESRD differ significantly depending on the socioeconomic status of people, which is explained by the distribution of standard risk factors in the population: smoking, increased blood pressure, cholesterol and blood glucose levels, albumin levels, and achieving target levels of glycated hemoglobin (Table 1).

Major risk factors for CKD progression

Parameter	**CKD 3a**	**CKD 3b**	**CKD 4**	**CKD 5**
A\D systolic	144±8,06	150±1,02	153±2,1	160±1,28
A / d diastolic	90,2±1,04	96±0,51	98±1,6	95±1,92
Total cholesterol	6,18±1,9	5,18±0,036	5,5±1,9	5,3±0,12

LDL	3,58±0,176	4,06±0,06	3,1±0,15	3,5±0,2
HDL	0,85±0,04	0,84±0,02	0,98±0,036	1,3±0,064
Triglycerides	1,97±0,077	1,64±0,05	1,8±0,06	1,5±0,064
Urea	12,2±0,68	12,1±0,18	24,9±0,86	29,2±2,3
Creatinine	147±8,1	168,8±5,1	385,7±20,7	854±34,6
Glomerular filtration rate	39,5±0,088	24,2±1,02	19,9±0,52	9,65±0,42
Fasting blood glucose level	13,2±8,3	10,5±0,52	8,7±0,45	5,37±0,1
Glycated hemoglobin	8,9±0,34	8,9±0,32	8,9±0,34	6±0,2
Potassium	3,86±0,052	3,94±0,07	3,81±0,2	4±0,096
Magnesium	0,76±0,02	1,12±0,07	0,76±0,018	0,75±0,018
Calcium	2,1±0,02	2,1±0,036	2,01±0,03	2±0,07
Hemoglobin	103±4,91	93±0,66	80±2,56	76,9±1,92
Albumen	51±0,88	48,5±0,76	37,4±0,84	30,8±0,7

According to the data presented in this table, it can be seen that the target level of blood pressure was not achieved in any of the study groups. A trend towards an increase in the average value of both systolic and diastolic blood pressure was revealed, which is explained by the deterioration of renal function.

The analysis of lipid profile indicators also shows that all parameters do not meet the target levels. The greatest influence on cardiovascular risk has an increase in LDL and triglycerides. The highest LDL-C was found in the group of patients with CKD 3b. The level of triglycerides is the highest in patients with CKD groups 3a and 4. HDL values are low in all groups, except for the group of patients with stage 5 CKD, which may not be sufficiently reliable.

Indicators of kidney function (creatinine, GFR) differ sharply in all groups, changing according to the severity of chronic kidney disease. Thus, the average level of creatinine is minimal in the group of patients with CKD 3a (147 μmol/l) and the highest in the group with CKD stage 5 (854 μmol/l). The glomerular filtration rate correspondingly declines sharply as CKD progresses.

Fasting glycemia did not reach the target levels in the groups of patients with CKD3a, CKD3b and CKD stage 4. Only in groups with stage 5 CKD it is rather low (5.37±0.1 mmol/l), which reflects the tendency to hypoglycemia of varying severity in this category of patients. This trend also corresponds to the level of glycated hemoglobin, which did not reach the target level in the first three groups.

The analysis of microelements reflects the potassium index corresponding to the lower limit of the norm in the groups of CKD3a, CKD3b and CKD 4 stages, slightly increasing in the group with CKD 5. The level of calcium is low in all groups of the studied patients in all the studied groups, which is a manifestation of a violation of phosphorus-calcium metabolism.

The level of albumin in the blood serum decreased depending on the severity of impaired renal function. The lowest rates were observed in the group of patients with CKD stages 4 and 5 (Table 2).

Hypoglycemic therapy.

Preparations	**CKD 3a n-30**	**CKD3b n-30**	**CKD4 n-35**	**CKD 5 n-55**
Biguanides	30%	33%	-	-
Sulfonylurea	3.3%	17%	5.7%	-
iDPP4	26%	17%	-	-
AGPP1	-	-	-	-
Insulin monotherapy (NPH or short acting insulin)	5%	8%	43,4%	54,4%
Combination Therapy (oral hypoglycemic agents and insulin)	45%	25%	25.7%	-
Basis - bolus therapy	-	-	25,2%	45,6%

Metformin monotherapy was received by patients with CKD stages 3a and 3b (30%-33%, respectively), which corresponds to the presence of contraindications (restriction of the use of this group of drugs to GFR 45 ml/min). Sulfonylureas were taken by patients of all study groups, except for stage 5 CKD. From the group of incretins and DPP-4, patients of CKD 3a and CKD 3b groups also received, except for patients with CKD stages 4-5. The study did not include patients receiving drugs from the group of GLP-1 agonists and HHT2 type inhibitors, which may be due to the high cost of these drugs and the presence of contraindications. The largest number of patients receiving only insulin (basal or ICD) were in the groups with CKD stages 4 and 5. Combined hypoglycemic therapy took place in all study groups, except for the group with stage 5 CKD. Basis - bolus insulin therapy was received only by groups with CKD stages 4 and 5 (Table 3).

Table 3

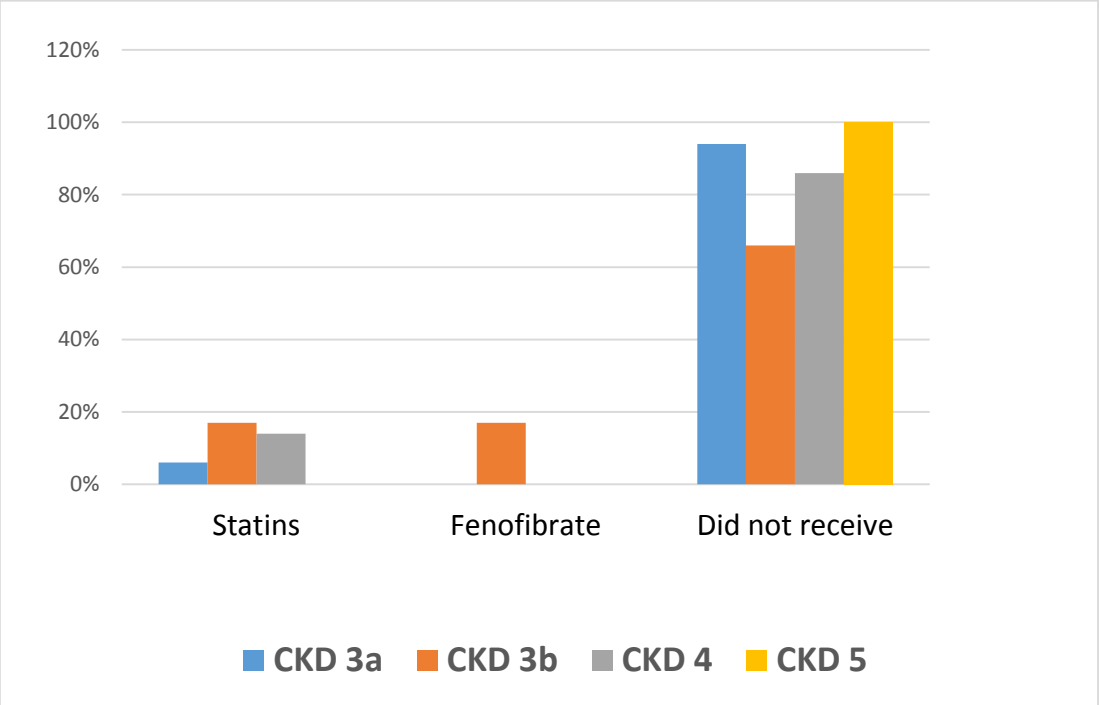
Antihypertensive therapy.

Preparations	**CKD 3a n-30**	**CKD3b n-30**	**CKD4 n-35**	**CKD 5 n-55**
B-blockers	-	-	20%	-
Ca antagonists	39%	17%	-	36%
ACE inhibitors	20%	-	18%	36%
Angiotensin receptor blockers	6	66%	11%	11%
Ca + ACE antagonists	35%	17%	51%	17%

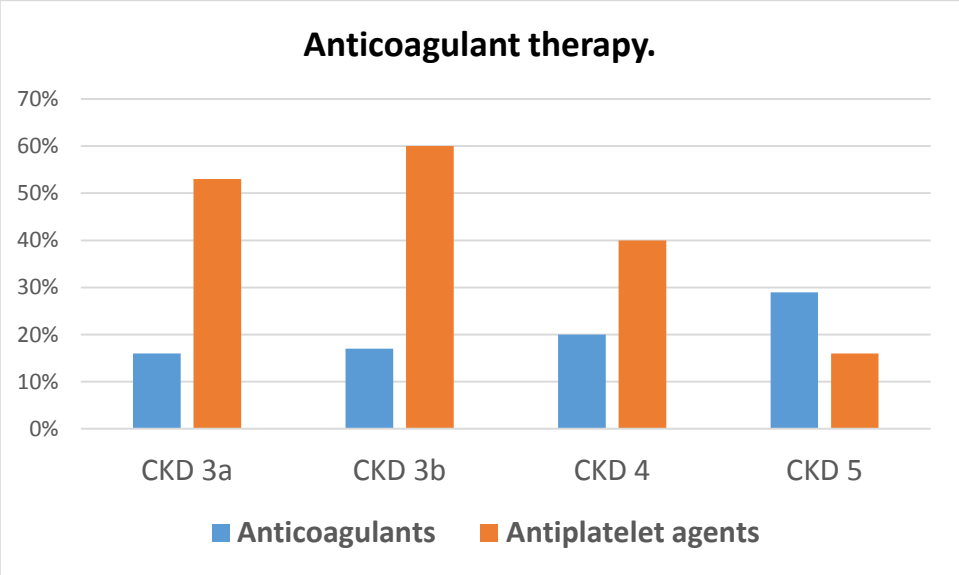
The study of the intake of antihypertensive drugs showed that the main part of patients with CKD 3a received drugs from the group of Ca antagonists (39%), and ACE antagonists (20%) and ARBs (6%) and 35% of patients received a fixed

combination of calcium antagonists and ACE inhibitors. Despite the pronounced nephroprotective effect of ACE inhibitors, there were no patients who received monotherapy with these drugs in the group of patients with CKD 3b. Most of the patients took ARBs (66%), 17% received a fixed combination of drugs (calcium antagonists and ACE inhibitors), 17% took only drugs from the Ca antagonist group. In the group of patients with CKD4, the number of patients receiving combination therapy with ACE and Ca antagonists was 51%, β-blockers received 18% and 11% of ARBs. The number of patients taking only Ca antagonists or ACE inhibitors in the CKD 5 group was 36% each, 11% were taking ARBs and 17% were receiving combination therapy (diagram 1).

Lipid-lowering therapy.



A review of lipid-lowering therapy showed that the frequency of statin and fenafibrite use was unsatisfactory in all groups. Despite the need for mandatory intake of drugs that affect dyslipidemia as a key pathogenetic factor in complications of diabetes mellitus, the use of drugs in this group in all groups was quite low.



Analysis of anticoagulant therapy shows that the majority of patients in all study groups, except for patients with CKD 5, received antiplatelet drugs, mainly acetylsolecylic acid. Anticoagulant therapy (heparin, or low molecular weight heparin) was received, by approximately the same number of patients in all study groups, in the group of patients with CKD 5 this indicator was the highest. Unfortunately, a significant percentage of patients in all study groups did not receive the necessary anticoagulant therapy (diagram 2).

Table 4.

Criteria for target levels in the treatment of patients with diabetes mellitus and the presence of complications.

	Indicators	**Achievement of target levels**
1	Arterial pressure	Systolic BP <140 mmHg Diastolic BP<90 mmHg
2	Glucose	<7.5-8 mmol/l
3	Glucose after eating	After 2 hours of food <11mmol/l
4	Glycated hemoglobin	<7,5-8%
5	Total cholesterol	<5 mmol/l
6	Triglycerides	<1,77 mmol/l
7	LDL	<3,5 mmol/l
8	LDL	Men >1.0 mmol/l Women >1.2 mmol/l

Comparing the recommended target levels of glycemia, lipids and blood pressure (ADA, EASD, 2019) with the results obtained in the examination of patients with various stages of CKD, it can be concluded that the majority of patients do not achieve the desired indicators. This is due to unsatisfactory therapy that does not meet accepted standards for the administration of patients with type 2 diabetes

This threatens with an increase in complications, an increase in disability and mortality rates, and the cost of treatment and, of course, a decrease in the quality of life of patients with diabetes mellitus.

Conclusion. The conducted studies have identified some features of the management of patients with diabetes mellitus complicated by chronic kidney disease. Data have been obtained on the shortcomings in the management of this category of patients, which is fraught with rapid progression of CKD to end-stage renal failure, a decrease in the quality of life of patients, and, accordingly, an increase in the cost of direct and indirect costs for the treatment of this complication. For the first time, a study was conducted on the study of the incidence and prevention of nephropathy in the Bukhara region. The results, which allow, firstly, to optimize the treatment process and, secondly, to predict the rate of progression of CKD.

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