ЭПИДЕМИОЛОГИЯ ХРОНИЧЕСКОЙ БОЛЕЗНИ ПОЧЕК В РОССИЙСКОЙ ФЕДЕРАЦИИ ПО ДАННЫМ ФЕДЕРАЛЬНОГО РЕГИСТРА ВЗРОСЛЫХ ПАЦИЕНТОВ С САХАРНЫМ ДИАБЕТОМ (2013–2016 ГГ.)

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ОБОСНОВАНИЕ. Хроническая болезнь почек (ХБП) – одно из наиболее тяжелых осложнений сахарного диабета, что определяет актуальность изучения эпидемиологических характеристик данной патологии.

ЦЕЛЬ. Оценить эпидемиологические характеристики развития ХБП у взрослых пациентов с СД 1 типа (СД1) и СД 2 типа (СД2) в РФ за период 2013–2016 гг.

МЕТОДЫ. Объектом исследования является база данных Федерального регистра СД – 81 региона РФ, включенных в систему онлайн-регистра. Оценивались показатели ХБП на 10 000 взрослых больных СД (>18 лет).

РЕЗУЛЬТАТЫ. В 2016 г. частота регистрации ХБП составила: СД1 – 23%, СД2 – 6,9%, с выраженными межрегиональными различиями от 1,5% до 49,9% и от 0,6% до 23,5% соответственно при СД1 и СД2. Распространенность ХБП в динамике 2013→2016 гг. составила при СД1: 2171,4→2303,0/10 000, СД2: 512,8→687,2/10 000 взрослых. Частота регистрации новых случаев ХБП возросла в 2 раза при СД1 (215,5 против 104,2/10 000 взрослых), в 3,7 раза – при СД2 (190,4 против 51,8/10 000 взрослых). Анализ распределения по стадиям указывает на улучшение диагностики осложнения. В структуре ХБП выявлено увеличение доли пациентов с низким и умеренным риском сердечно-сосудистых событий и терминальной почечной недостаточности по критериям KDIGO (начальные стадии ХБП С1–2, А1–2): СД1 12,0%→46,8%; СД2 10,0%→50,4%. Доля пациентов с очень высоким риском (стадии С–5, А2–3) уменьшилась: СД1 13,4%→6,7%, СД2 11,3→4,4%. Установлена зависимость распространенности ХБП от длительности диагноза СД. При СД1 <5 лет ХБП развивалась у 5,1% пациентов, при СД1 <30 лет – у 48,0%; СД2: 3,5% и 20,3% соответственно. Средний возраст дебюта ХБП у лиц с СД1 увеличился на 4,3 года (36,1→40,4) и 2,4 года при СД2 (64,4→66,8 лет), длительность СД до момента диагностики ХБП увеличилась: СД1 – 11,8→14,2 лет, СД 2 – 7,6→8,2 лет.

ЗАКЛЮЧЕНИЕ. При общем увеличении распространенности ХБП в РФ в динамике 2013–2016 гг. отмечается улучшение качества диагностики осложнения на более ранних стадиях, в более позднем возрасте и при большей длительности СД. Успехи в ведении пациентов с СД в последние годы не снижают риск ХБП, но дают отсрочку в ее развитии. Выраженные межрегиональные различия в частоте регистрации ХБП в регистре указывают на проблемы диагностики ХБП в ряде регионов, где не выполняется стандарт обследования пациентов с СД с обязательной оценкой скорости клубочковой фильтрации (СКФ) и альбуминурии не реже 1 раза в год.

КЛЮЧЕВЫЕ СЛОВА: сахарный диабет; Федеральный регистр сахарного диабета; хроническая болезнь почек; риск сердечно-сосудистых событий

TRENDS IN THE EPIDEMIOLOGY OF CHRONIC KIDNEY DISEASE IN RUSSIAN FEDERATION ACCORDING TO THE FEDERAL DIABETES REGISTER (2013–2016)

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BACKGROUND: Chronic kidney disease (CKD) is one of the most severe complications of diabetes mellitus (DM), this determines the importance of the study of epidemiological characteristics of the disease.

AIMS: To assess the epidemiological characteristics of CKD in adult DM patients with type 1 (T1), 2 (T2) in Russian Federation in 2013–16.

METHODS: We have used the database of the Russian Federal Diabetes register, 81st regions included in online register. Indicators were estimated per 10,000 adult DM patients (>18years).

RESULTS: In 2016, the CKD frequency registration was T1 23%, T2 6.9% with marked interregional differences 1.5-49.9%, 0.6–23.5%, respectively. The CKD prevalence in dynamics 2013→2016 was 2171.4→2303.0 in T1 and 512. →687.2 in T2. The incidence of new CKD cases increased 2 times in T1 (215.5 vs 104.2), and 3.7 times in T2 (190.4 vs 51.8). The analysis of distribution by CKD stages by KDIGO indicates the increase in the proportion of patients with low and moderate cardiovascular risk and end stage renal disease (ESRD) (with the initial stages of CKD, C1/2 A1) - 12.0→46.8% in T1; 10.0→50.4% in T2.

Received: 10.10.2017. Accepted: 10.05.2018.

The proportion of patients with a very high risk (stages C4/5 C3aA3 and C3bA2-3) progressively decreases: 13.4→6.7% in T1, 11.3→4.4% in T2. We observed relation between the CKD prevalence and DM duration. CKD develops in 5.1% patients if T1<5 years and in 48.0% if T1>30years; in T2 3.5% and 20.3%, respectively. The average age of CKD onset in T1 increased for 4,3yr (36,1→40,2), in T2 for 2,4yr (64,4→66,8), DM duration until CKD development increased in T1 11.8→14.2yr, in T2 7.6→8.2yr.

CONCLUSIONS: There is a significant improvement in the quality of CKD diagnostics at the earlier stages, older age and a longer DM duration before CKD onset in both types while we observed the increasing trends in CKD prevalence in Russian Federation in the dynamics of 2013-2016. Advances in the management of patients with DM in recent years do not reduce the risk of CKD, but give us a delay in its development. The marked interregional differences frequency of registration of CKD might indicate some remaining problems in verification in a number of regions where the standard for mandatory assessment of albuminuria and glomerular filtration rate not implemented.

KEYWORDS: diabetes mellitus (DM); the register of diabetes mellitus; chronic kidney disease (CKD); cardiovascular risk

BACKGROUND

Chronic kidney disease (CKD) in patients with diabetes mellitus (DM) remains a primary microvascular complication. Due to the severity, insufficient efficiency and high cost of treatment during the terminal stages of CKD, the epidemiological characteristics of this pathology are of importance.

According to the definition originally formulated by KDOQI (National Kidney Foundation, 2002) [1] and subsequently supplemented by Kidney Disease Improving Global Outcomes (2012) [2], CKD is summarised as renal damage or reduced glomerular filtration rate (GFR; < 60 ml/min/1.73 m2) persistent for >3 months regardless of the initial diagnosis. The definition of CKD requires a two-fold measurement of GFR or albuminuria (AU) or the both indicators for at least 3 months. For monitoring CKD in the healthcare setting, single measurements of creatinine and AU in patients under stable outpatient settings are acceptable and provide a realistic assessment. However, there is variability in these indicators due to factors such as nutrition, physical activity and hydration status. Special attention should be given to the fact that popular formulae for calculating GFR (Cockroft-Gault, MDRD and CKD-EPI) have limitations when used in the elderly and in those with low muscle mass or extreme body size (body mass index < 18 kg/m2 and > 40 kg/m2).

To stabilise the number of patients with severe stages of CKD, early detection of patients in initial stages and using modern methods of nephro-protection in their treatment practices are essential. This will reduce the large burden of renal replacement therapy (RRT) required at the terminal stage of CKD.

Table 1. CKD stages according to the GFR level [2]

Stage	Definition	GFR, ml/min/1.73 m²
1	High and optimal	>90
2	Slightly reduced	60–89
3a	Moderately reduced	45–59
3b	Significantly reduced	30–44
4	Severely reduced	15–29
5	Terminal renal failure	<15

AIM

This study aimed to assess the epidemiological characteristics of CKD development in adult patients with type 1 diabetes mellitus (DM1) and type 2 diabetes mellitus (DM2) from 2013 to 2016.

METHODS

STUDY DESIGN

The data used in this study were obtained from the database of the Federal Register of DM (FRDM) of 81 regions of the Russian Federation included in the online register system. The prevalence and incidence rates (new cases/year) per 10,000 adult patients with DM (age, >18 years) from 2013 to 2016 were estimated.

Analysis of the structure of therapy for CKD was conducted for 2017 (after the inclusion of CKD in 2015) according to the data of the top 10 regions on the quality of register maintenance. This approach was used to reduce the influence of the register management factor on the results because the field of anti-hypertensive and other concomitant therapy was not mandatory and filled qualitatively in only some regions.

The data of the register enabled the assessment of albuminuria and automatic calculation of GFR using the CKD-EPI formula. Thus, the diagnosis of CKD was made according to modern diagnostic standards based on the GFR level which reflects the number and total volume of nephron work, including those associated with non-excretory functions (Table 1).

Table 2. Classification of CKD according to albuminuria [2]

Category	A/Cr ratio of urine		DAE (mg/24 h)	Description
	mg/mmol	mg/l		
A1	<3	<30	<30	Norm or slightly increased
A2	3–30	30–300	30–300	Moderately increased
A3	>30	>300	>300	Significantly increased#

#including nephrotic syndrome [Daily albumin exrection (DAE) >2200 mg/24 h (A/Cr ratio >2200 mg/g > 220 mg/mmol)]

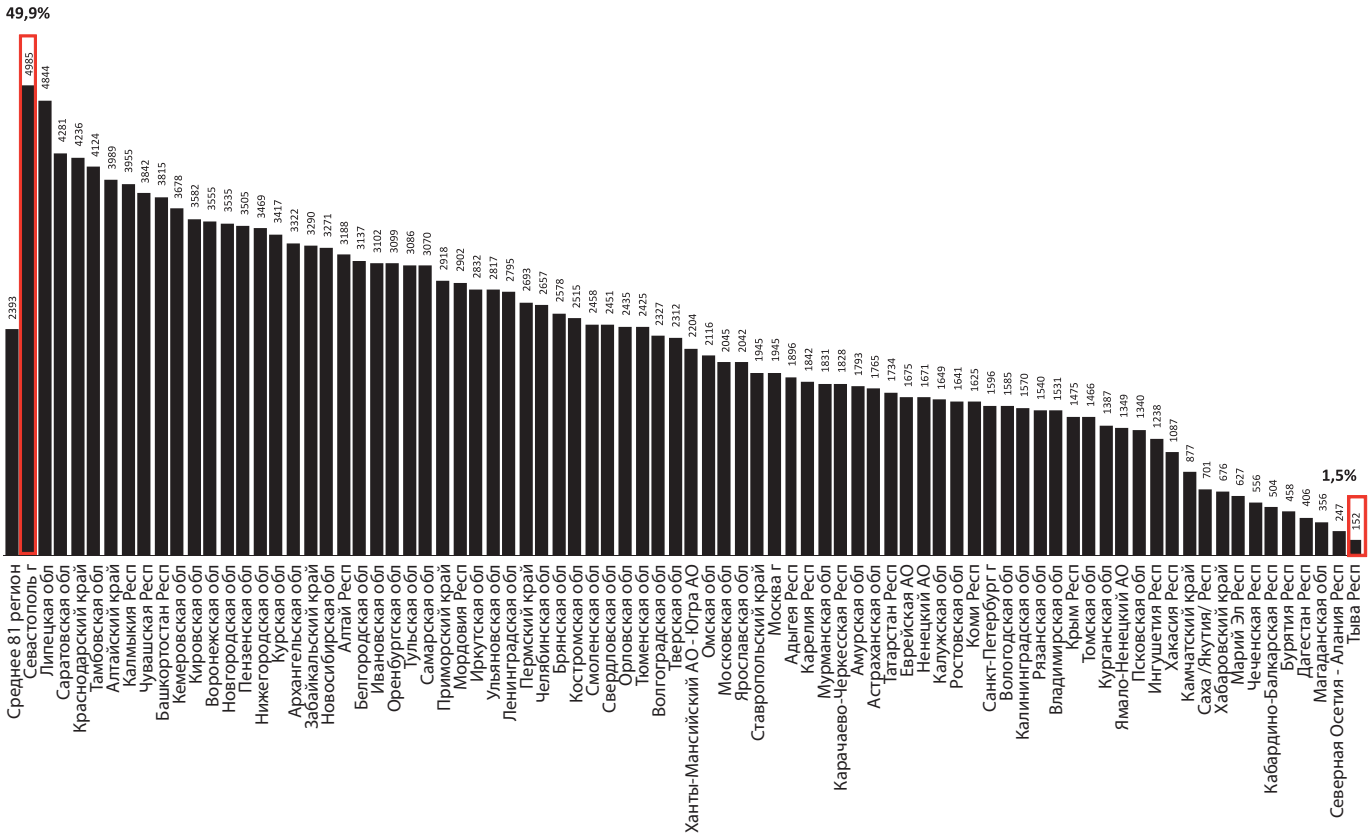

Fig. 1. The prevalence of CKD in regions of the Russian Federation (per 10,000 adult patients with DM1) according to the data from FRDM in 81 regions of the Russian Federation in 2016.

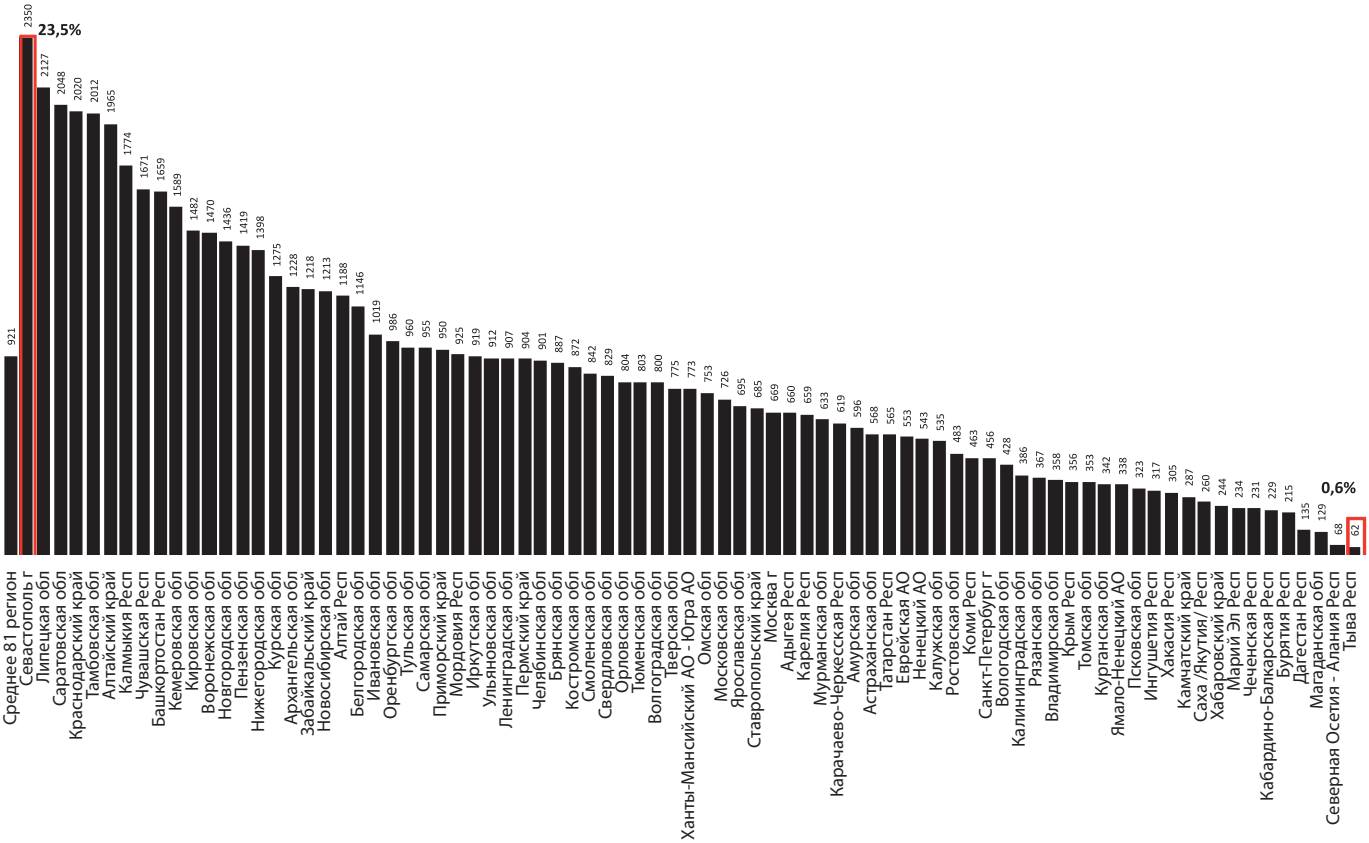

Fig. 2. Prevalence of CKD in the regions of the Russian Federation (per 10,000 adult patients with DM1) according to the data from FRDM in 81 regions of the Russian Federation in 2016.

The quantitative estimation of AU, which is not affected by the hydration status, includes the albumin/creatinine (A/Cr) ratio in urine sample collected randomly. However, the first urine collected in the morning is preferred because it shows the best correlation with 24-h protein excretion. There are three categories of albuminuria (Table 2).

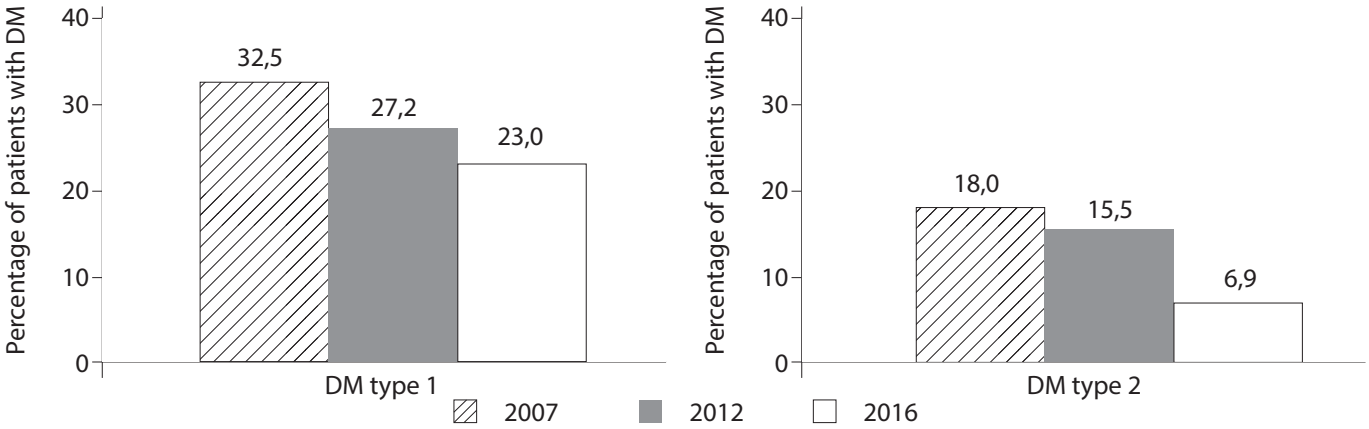

Fig. 3. Dynamics of the prevalence of diabetic nephropathy and CKD (%) in patients with DM1 and DM2 according to FTP in 2007 and 2012 and FRDM in 2016.

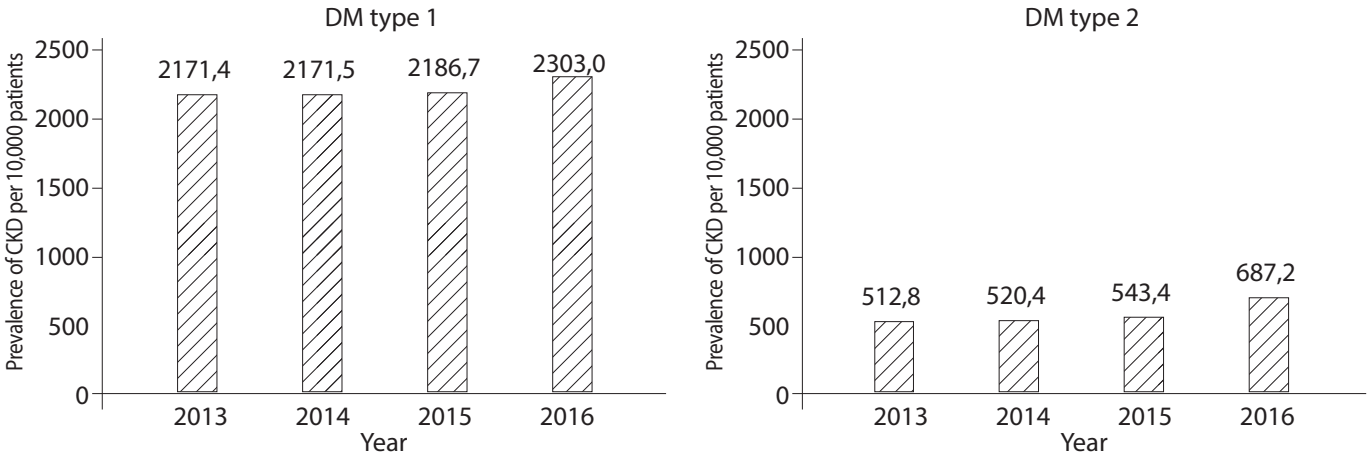

Fig. 4. Prevalence of CKD per 10,000 adult patients with DM1 and DM2 from 2013 to 2016 according to FRDM in 81 regions of the Russian Federation.

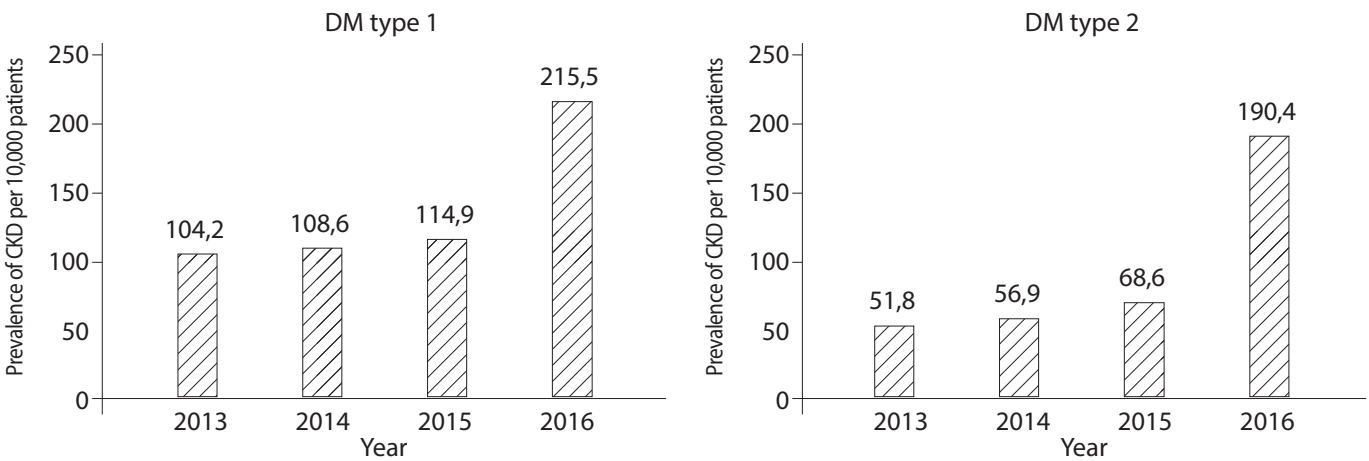

Fig. 5. Frequency of new CKD cases per year per 10,000 adult patients with DM1 and DM2 from 2013 to 2016 according to the data from FRDM in 81 regions of the Russian Federation.

ETHICAL EXPERTISE

The study protocol No. 20 from 14 December 2016 was reviewed and approved by the ethical committee of the Federal State Budgetary Institution National Medical Research Centre of Endocrinology, Ministry of Health of the Russian Federation.

RESULTS

In 2016, the average frequency of CKD registration (all stages) in the FRDM database in Russia was 23% for DM1 and 6.9% for DM2, with marked inter-regional differences from 1.5%–49.9% for DM1 and 0.6%–23.5% for DM2 (Figs. 1 and 2).

The dynamics of the prevalence of diabetic nephropathy and CKD according to FRDM for 2016 compared with the data obtained during the sub-programme 'Diabetes Mellitus' from the Federal Target Programme 'Prevention and Control of Socially Significant Diseases 2007-2012' (FTP) is presented in Figure 3.

The dynamics of the complication is shown in Figure 4. There was an increase in the prevalence of CKD in the Russian Federation with DM1 (1.1-fold) and DM2 (1.3-fold) over the past 4 years according to FRDM data.

The frequency of registration of new cases (morbidity) of CKD in FRDM significantly increased in 2016 compared with 2013 for DM1 (2-fold) and DM2 (3.7-fold; Fig. 5).

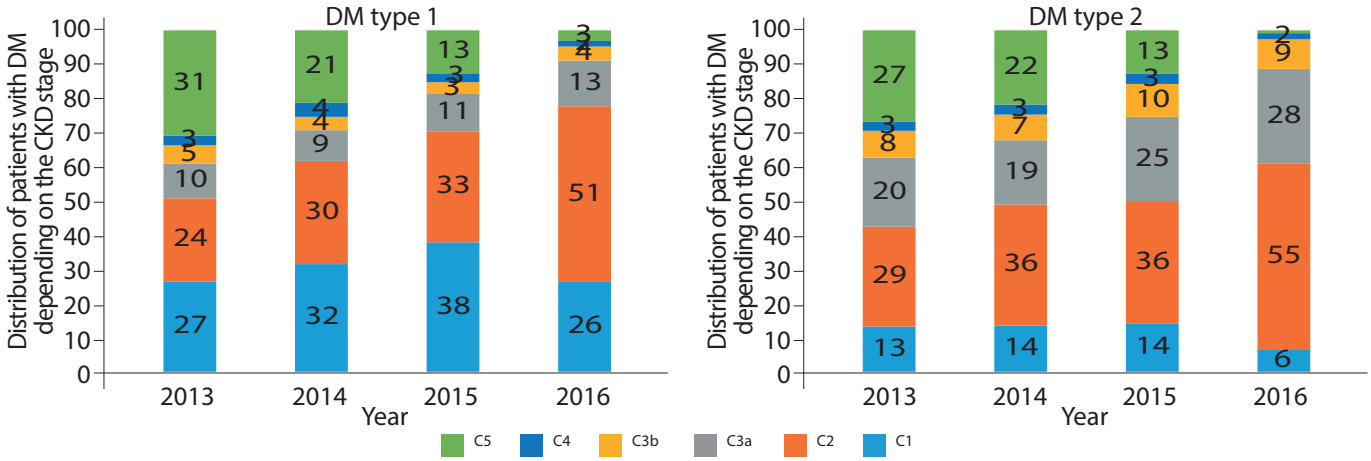

Fig. 6. Distribution of adult patients with DM1 and DM2 from 2013 to 2016 according to CKD stages (new cases/year, percentage of patients) reported in FRDM in 81 regions of the Russian Federation.

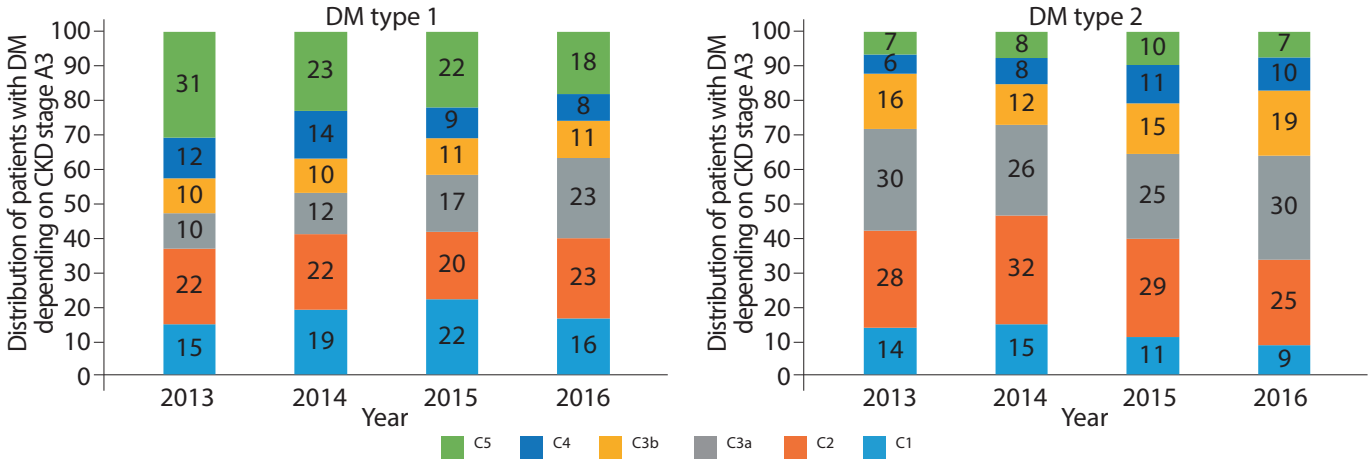

Fig. 7. Ratio of different stages in new cases of CKD in patients with albuminuria A3 during 2013-2016 according to FRDM in 81 regions of the Russian Federation.

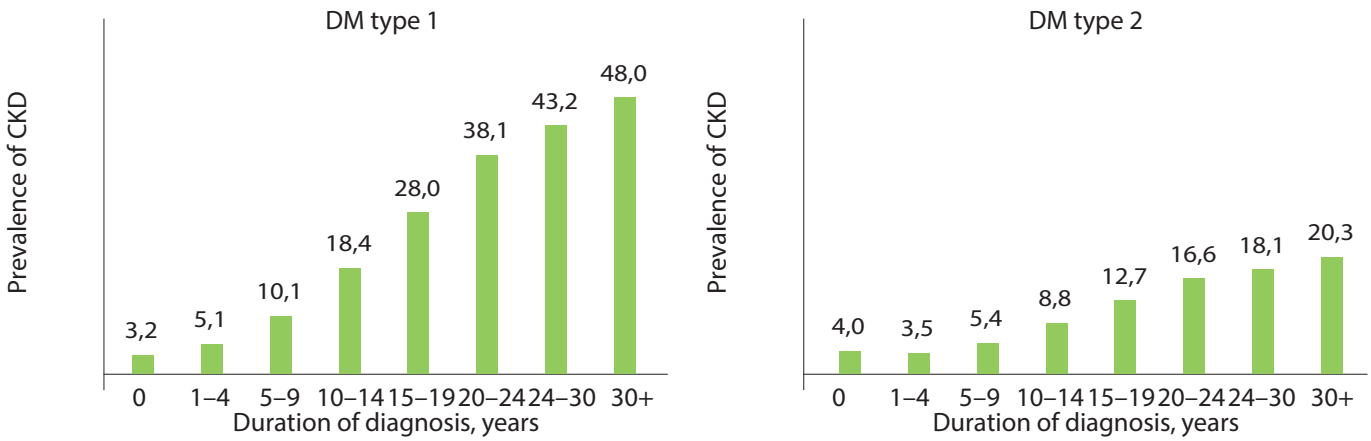

Fig. 8. The prevalence of CKD depending on the duration of DM1 and DM2 according to FRDM in 81 regions of the Russian Federation.

Due to an increase in the prevalence of CKD, the analysis of the distribution according to CKD stages indicated an improvement in the diagnosis of complications, such as earlier detection of C1-2 CKD in the early stages (almost 2-fold) and significantly less in the terminal stage (Fig. 6).

The distribution of CKD according to stages in patients with A3 AU (proteinuria > 0.2 g/L, albuminuria > 300 mg/day or 200 mg/L or A/Cr ratio in the urine sample >300 mg/g) is shown in Figure 7. It indicated a significant reduction in the terminal stage of C5 over the last 4 years.

The prevalence of CKD over time for the diagnosis of DM was established. With the DM1 duration of <5 years, CKD developed in 5.1% of patients; however, with the DM duration of >30 years, CKD prevalence increased to 48%. For patients with DM2, this increase in CKD prevalence for <5 and >30 years was 3.5% and 20.3%, respectively (Fig. 8).

The average age of CKD onset in patients with DM1 increased from 4.3 to 40.4 years (36.1 years in 2013), whereas in patients with DM2, it increased from 2.4 to 66.9 years (i.e. 64.5–66.9 years). The average duration of DM1 before the development of CKD increased from 11.8 to 14.2 years and that of DM2 increased from 7.6 to 8.2 years (Fig. 9).

The pathogenesis of CKD from 2013 to 2016 revealed an increase in the proportion of patients with a low and

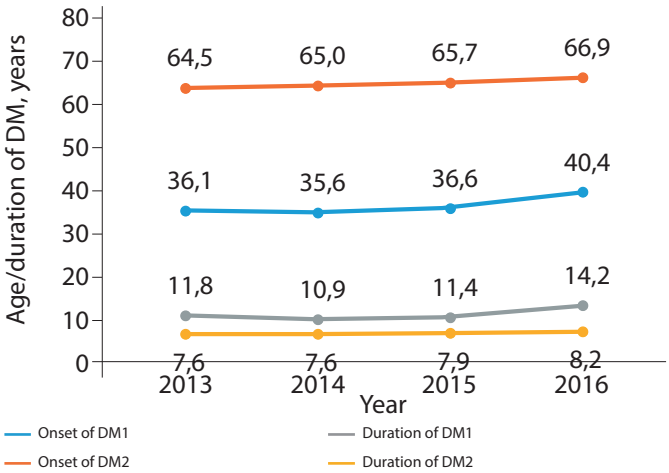

Fig. 9. The mean age and duration of DM in patients before the development of CKD from 2013 to 2016 according to FRDM in 81 regions of the Russian Federation.

moderate combined risk of cardiovascular events and terminal renal failure (TRF) for initial stages of CKD C1-2 and A1-2 according to KDIGO (from 12.0% to 46.8% for DM1 and from 10.0% to 50.4% for DM2) [2]. Conversely, the proportion of patients with very high risk (CKD stages C3-5 and A2-3) progressively decreased from 13.4% to 6.7% for DM1 and 11.3 to 4.4% for DM2 (Fig. 10).

The register contains information on the use of nephro-protective drugs for the treatment of arterial hypertension (AH), dyslipidemia and correction of anaemia (Table 3). Currently, these fields in the register are not to be mandatorily filled; hence, the analysis included data from 10 regions of the Russian Federation, which were the best in data entry in FRDM.

AH is the most significant complication of CKD and the primary factor in its progression. The distribution of patients with DM1 and DM2 according to BP level in the presence of CKD in 81 regions according to FRDM from 2013 to 2017 is presented in Table 4. BP gradation was performed in accordance with the recommended target level for patients with CKD (<130/85 mm Hg), standard target level in patients with DM (<140/85 mm Hg) and level for unsatisfactory AH control (≥ 140/85 mmHg).

DISCUSSION

When analysing the prevalence of CKD from 2013 to 2016, several factors should be considered, the most important factor being the change in the diagnosis paradigm. During this period, there was a transition from the assessment of AU as a classic marker for diabetic nephropathy to that of GFR for the verification of CKD as a supranosological state [3]. A large pool of patients had decreased GFR and normoalbuminuria, which was not considered in the diagnostics of diabetic nephropathy, which led to the increase in the number of patients with this complication according to the CKD criteria. This may be associated with a significant increase in the prevalence of CKD over the past 4 years without an actual increase in the incidence of complication, as indicated by a comparative analysis of FTP data of 2007–2012 [4].

In addition, the change in many technical parameters of the register, such as the introduction of GFR calculation using the CKD-EPI formula instead of the Cockroft-Gault formula (overestimating the result), which occurred in 2015 enabled a more accurate assessment of the presence and stage of CKD. For some individuals, the evaluation of GFR by computational methods could be affected by limitations such as morbid obesity, age of >85 years, body weight deficit or kidney transplantation because the estimated GFR level is generally below the actual level.

Nevertheless, pronounced inter-regional differences in the frequency of complication diagnostics indicated the persistent problem of CKD screening in many regions where the standard for examining patients with DM with a mandatory assessment of GFR and AU is performed less than once a year [5, 6]. This also indicated the underestimated diagnostics of CKD in DM2 (average 6.3% in the RF), especially compared with results of clinical epidemiological studies with active screening in which this indicator is 40%–60% [4, 7].

Normoalbuminuria with reduced GFR in many patients, especially those with DM2, is of particular importance. The 'face' of diabetic nephropathy has evolved, and we are moving away from albumin-centric concepts that view AU as an indicator for the pathological process leading to proteinuria, subsequent

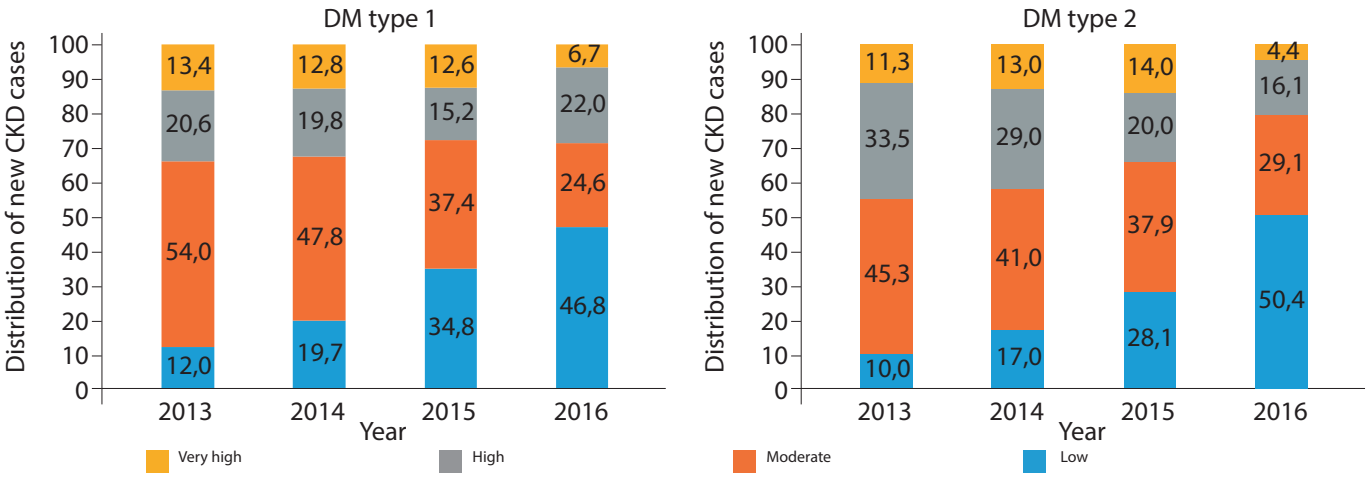

Fig. 10. Distribution of CKD (new cases/year, percentage of patients) based on the KDIGO criteria of cardiovascular events risk and TFR in adult patients with DM1 and DM2 from 2013 to 2016 according to FRDM in 81 regions of the Russian Federation.

Table 3. Structure of anti-hypertensive, lipid-lowering, anti-platelet and anti-anaemic therapies in 2017 in 10 regions of the Russian Federation.

DM type	DM1				DM2			
Presence of CKD	No CKD		CKD*		No CKD		CKD*	
Groups of medications	% of group without CKD	% of group with therapy	% of group with CKD	% of group with therapy	% of group without CKD	% of group with therapy	% of group with CKD	% of group with therapy
Anti-hypertensive drugs	8,4		24,7		23,6		45,6	
ACE Inhibitors	5,9	69,5	18,0	72,9	15,8	66,9	32,9	72,2
Angiotensin II receptor blockers (ARBs)	1,2	13,8	4,3	17,5	4,6	19,2	14,8	32,4
Diuretics	2,9	34,1	8,6	34,9	11,2	47,3	26,2	57,5
Beta-blockers (BBs)	2,4	28,4	8,7	35,4	8,6	36,5	22,4	49,1
Alpha-blockers	0,0	0,4	0,2	0,7	0,1	0,4	0,2	0,4
Calcium channel blockers	0,7	8,1	3,8	15,5	3,8	15,9	14,3	31,5
Preparations of the central action	0,1	0,6	0,4	1,8	0,2	1,0	1,1	2,4
Direct inhibitors of renin	0,0	0,4	0,0	0,1	0,0	0,2	0,0	0,1
Lipid-lowering drugs	3,9		12,8		10,4		28,4	
Statins	3,6	94,4	10,9	85,1	10,1	97,2	27,1	95,5
Fibrates	0,2	5,6	2,2	17,2	0,1	1,4	2,0	6,9
Anti-platelet agents	2,8		9,2		10,1		26,1	
Anti-anaemic drugs	0,1		1,8		0,2		1,0	

*CBC of high gradation, A2 or A3 and/or C3-5

Table 4. Distribution according to BP level (mmHg) in the presence or absence of CKD for patients with DM1 and DM2 (%) in 81 regions according to FRDM.

DM type	DM1, patients (%)					DM2, patients (%)				
BP, mm Hg	2013	2014	2015	2016	2017	2013	2014	2015	2016	2017
No CKD										
<130/85	86,1	87,0	84,9	85,3	87,1	24,1	25,2	28,0	32,3	36,7
<140/85	90,2	90,9	89,7	90,6	92,3	35,2	37,3	41,9	48,0	53,5
≥140/85	9,8	9,1	10,3	9,4	7,7	64,8	62,7	58,1	52,0	46,5
CKD (any stage)										
<130/85	72,5	72,9	70,0	71,5	73,8	16,3	18,6	20,4	27,3	32,1
<140/85	78,4	78,7	77,3	79,8	82,1	24,5	28,2	32,3%	41,1	48,0
≥140/85	21,6	21,3	22,7	20,2	17,9	75,5	71,8	67,7	58,9	52,0
CKD at high gradations (A2 or A3 and/or C3-5)										
<130/85	69,7	69,4	69,4	70,0	71,8	16,1	18,4	20,1	26,1	29,3
<140/85	75,5	75,5	76,5	78,4	80,2	23,4	27,6	32,2	40,0	44,6
≥140/85	24,5	24,5	23,5	21,6	19,8	76,6	72,4	67,8	60,0	55,4

decrease in GFR and ultimately TRF. Data are available from the United States from 1988 to 2014 for 6,251 adult patients with DM aged >20 years as participants in the National Health and Nutrition Examination Survey (NHAES); these patients had AU and reduced GFR (<60 and <30 ml/min/1.73 m2) [8]. The prevalence of CKD did not change significantly (from 28% to 26%). The prevalence of AU decreased progressively over the years from 20% to 15.9% ($p < 0.001$), whereas the decrease in GFR increased from 9% to 14%, especially for GFR <30 ml/min. The decrease in AU frequency was characteristic for individuals aged <65 years and Caucasians; however, GFR was not dependent on age or race. Regarding AU, these results could be explained by an improvement in the control of glycaemia, BP and lipids and the widespread use of the renin–angiotensin–aldosterone system (RAAS) blockade. With decreased GFR, these factors were not sufficiently influential. The age of patients did not change significantly, but the duration of DM increased. To a certain extent, an increase in the life expectancy of

patients, reduced mortality from cardiovascular diseases and other complications of diabetes could also result in the development of progressive damage of the kidneys.

Given the current trends, it is important to assess average GFR according to age, especially in patients aged >60 years because this age group has the highest prevalence of CKD. Thus, the average GFR for individuals aged >60 years in the United States according to the United States Renal Data System (USRDS) is 25 ml/min/1.73 m2, which is lower than the mean GFR for the entire population with CKD [9].

Data from FRDM revealed that successful management of patients with DM in recent years has not reduced the risk of CKD but has delayed its development. An increase in the age and duration of the disease at the time of diagnosis is a significant feature. Unfortunately, we do not have accurate data on the treatment of CKD in terminal stages; therefore, it is difficult to estimate the parameters of the Russian register of RRT. According to the register, in TRF cases receiving treatment with programme haemodialysis, peritoneal dialysis and functioning kidney transplantation, DM cases account for 13.8%, 14.6% and 5.8%, respectively [10].

The epidemiological study of the Pittsburgh Epidemiology of Diabetes Complications (Pittsburgh EDC), which evaluated the 50-year risk of developing kidney complications in 932 patients with an onset of DM1 in childhood in 1950–1980, showed that this risk does not decrease regardless of sex in those who develop these complications in early childhood (up to 6 years) [11]. The results of the study showed the effect of a prolonged course of DM1 on the risks of the expressed stages of CKD. With DM1 for >40 years, encouraging data on the reduction in the frequency of the terminal stage of CKD by 45% are shown by a 3% growth in and stable frequency of micro-albuminuria. According to experts, these results reflect an improvement in the treatment approaches and a slower progression of the disease. However, it does not prevent disease development. Thus, an increase in the life expectancy of patients with DM1 and kidney pathology shifts the focus on the glycaemic control and also on the management of other risk factors (dyslipidemia and hypertension). The search for additional therapeutic modalities is therefore essential.

Data from the national Norwegian register of paediatric diabetes indicated an increasing incidence of TRF among 7,871 patients with DM1 onset in childhood: 0.7%, 2.9% and 5.3% with disease duration of 20, 30 and 40 years, respectively. The risk of development was lower in women than in men (0.62; 95% CI, 0.41–0.91) [12].

Similar data were obtained in a cohort study in Finland involving 29,906 patients with a diagnosis of DM1 before the age of 30 from 1965 to 2011 and before the onset of RRT, death or study completion in 2013. TRF developed in patients after 20 (2.2%) and 30 years (7%) of disease onset [13].

Monitoring of DM onset during puberty is also essential. According to the Norwegian registry, there is a higher risk of TRF development in patients with DM onset between 10 and 14 years of age than in those with DM onset at 10 years of age (1.29; 95% CI, 1.06–1.56) [12].

Puberty is a period when the task of achieving compensation is extremely difficult. During this time, numerous factors compete for attention, and control issues of DM occupy a very insignificant place in the list of priorities [14], which can contribute to the early development of complications to the standard time of primary diagnostics.

In 5.1% of adult patients, CKD development is seen in patients who have DM1 for <5 years according to FRDM. Therefore, there is a need to change the conventional examination for CKD examination to 5 years from the onset of DM1, so that these 5.1% of patients are not overlooked. Conversely, under the influence of diabetic kidney disease, other kidney pathology, primarily a urinary infection, may be masked.

The registration of the incidence of CKD in adult patients according to FRDM significantly increased in 2016 compared with 2013, primarily 2-fold for DM1 and 3.7-fold for DM2. With a general increase in the prevalence of CKD, the analysis of the distribution by stages indicated an improvement in the diagnosis. CKD is a 'silent' disease in the initial stages, and few patients are aware before it progresses to stages 1–3. More number of patients become aware of the disease only after the symptoms of stage 4 manifest. It is extremely important to identify patients with initial stages and to introduce nephro-protection techniques to reduce the number of patients progressing to advanced stages of CKD. Earlier diagnosis of stage 2 (almost 2-fold) in the regions should be recorded. This occurs less often at the terminal stage of CKD. These positive dynamics will affect the number of patients with DM who start dialysis with a late diagnosis of TRF after undergoing life-saving therapy in an intensive care unit [10].

Morbidity with AU level A3, which is indicative of the development of severe CKD and its late diagnosis in individuals with a lower renal function, did not decrease from 2013 to 2016 in 81 regions of the Russian Federation. This requires further attention and analysis. On the contrary, it may reflect the proportion of true diabetic nephropathy with a predominant lesion of the renal filter in the CKD structure diagnosed according to new standards.

The register receives information on the use of nephro-protective drugs for the treatment of AH, dyslipidemia and anaemia. There is no information about medications used for the treatment of mineral and bone disorders in CKD. The register has only generalised data, but data on drug therapy enable the collection of further information on the current treatments of these clinical syndromes. The data show that anti-hypertensive therapy is more frequently prescribed in CKD cases, along with the predominance of nephro-protective drugs [angiotensin-converting enzyme (ACE) inhibitors] and angiotensin II receptor blockers (ARBs) in its structure. ACE inhibitors and ARBs are the mainstay of nephro-protective therapy. However, their use, especially in cases of CKD of high grades (A2 or A3 and/or C3-5), is not standard and does not exceed 50% for DM2 and 22.3% for DM1 (Table 3). The same trend is seen for other organ-protective therapies (lipid-lowering, anti-anaemia). Tracking pharmacologic treatments only began in 2015,

after they were included in the online register. However, data on nephro-protective treatments have not been included in the register. Therefore, the data presented on the frequency of medications may not reflect the actual clinical practice.

AH, being the most significant complication of CKD, plays a key role in its progression and in the development of macrovascular pathology, which requires the optimisation of AH control. With CKD progression, the role of metabolic factors decreases and that of haemodynamic factors increases. Analysis of BP distribution data (target for patients with CKD, standard for those with DM and unsatisfactory) showed positive trends: an increase in the number of patients with CKD, including high grades reaching BP levels of <130/85 mm Hg, recognised as safe [5] for further progression of kidney damage. Nevertheless, the majority of patients remain beyond the target range, especially those with DM2. Furthermore, KDIGO recommends individualising the target level of BP for patients with CKD depending on age, existing cardiovascular pathology, concomitant diseases, risk of CKD progression, presence or absence of retinopathy and tolerance to the current therapy [2]. Nevertheless, the classically safe BP threshold for patients with CKD is <130/85 mm Hg [5].

According to previously published FRDM data, the leading causes of death in patients with DM in the Russian Federation are cardiovascular pathologies for both DM types. Total chronic cardiovascular insufficiency, cerebral circulation disorders, myocardial infarction and acute cardiovascular disorders led to the death of 31.9% of patients with DM1 and 49.5% with DM2. This confirmed the necessity of early diagnosis and therapeutic approaches aimed at correcting cardiovascular risks in patients with DM [15].

CKD was defined as an independent risk factor for cardiovascular disease, which remains the primary cause of death in both DM1 and DM2. Among CKD patients, death from cardiovascular pathology occurs more often than due to progression to the terminal stage of renal failure [16]. The complex relationship between cardiovascular pathology and kidney disease is based on the generalisation of population risk factors. These include the traditional risk factors such as decreased renal function and non-traditional factors such as anaemia, hyperparathyroidism, vitamin D deficiency, hypoalbuminemia, hyperphosphataemia, decreased GFR and AU that accelerate the development of cardiovascular diseases. Therefore, the pathophysiology of the latter is multifaceted and unique in conditions with progressive renal dysfunction.

Regarding CKD incidence from 2013 to 2016, there was an increase in the proportion of patients with a low and moderate combined risk of cardiovascular events and TRF according to the KDIGO criteria, i.e. with the initial stages of CKD (C1-2 and A1-2) and a progressive decrease in the proportion of patients with very high risk (CKD stages C3-5 and A2-3). However, doctors should remain vigilant in assessing the symptoms of cardiovascular dysfunction and use modern methods of diagnosis and treatment.

What else can the FRDM present in the future?

1. Epidemiology of cardiovascular diseases and cardiovascular mortality in a population of patients with CKD.
2. Assessment of all cases of mortality and hospitalisation depending on the presence or absence of CKD.
3. Calculation of mean GFR for patients with CKD aged >60 years.
4. Complete pharmacotherapy of patients with CKD, including erythropoiesis-stimulating drugs, iron preparations, vitamin D and its analogues and phosphate binders.
5. Determination of the number of patients with CKD who achieve the target level of glycaemic control for HbA1c, BP, lipid spectrum, Hb and bone mineral abnormalities.
6. Evaluation of the dynamics of CKD progression including TRF and its complications (AH, anaemia and electrolyte and bone mineral disorders), initiation of RRT and the frequency of urgent hospitalisation.
7. Collection of information about treating patients on dialysis by endocrinologists after kidney transplantation and simultaneous pancreas–kidney transplantation.

CONCLUSION

With a general increase in the prevalence of CKD in the Russian Federation from 2013 to 2016, there was an improvement in the quality of diagnosing complications in the earlier stages with a low risk of cardiovascular events and TRF with increasing age and longer DM duration. Successful management of patients with DM in recent years does not reduce the risk of CKD but delays its development. The pronounced inter-regional differences in the frequency of CKD registration in FRDM indicated diagnostic problems in many regions where the standard for examining patients with DM with a compulsory evaluation of GFR and albuminuria is performed not less than once a year. Constant monitoring of regional databases and improvement in the quality of filling the register will improve the quality of the information received, thereby improving not only the diagnostics but also the prospects of treating patients with this pathology.

ADDITIONAL INFORMATION

Funding. The work was conducted within the State task of the Ministry of Health of the Russian Federation No AAAA-A18-118051590061-9.

Conflict of interest. The authors declare no obvious and potential conflicts of interest related to the publication of this article.

Acknowledgements. CJSC Aston Consulting for technical support of the online DM register.

All medical specialists (doctors, nurses and data recorders) who are actively working to fill the database of the DM register.

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ЦИТИРОВАТЬ:

Шамхалова М.Ш., Викулова О.К., Железнякова А.В., Исаков М.А., Шестакова М.В., Дедов И.И. Эпидемиология хронической болезни почек в Российской Федерации по данным Федерального регистра взрослых пациентов с сахарным диабетом (2013-2016 гг.) // *Сахарный диабет*. — 2018. — Т. 21. — №3. — С. 160-169. doi: 10.14341/DM9687

TO CITE THIS ARTICLE:

Shamkhalova MS, Vikulova OK, Zheleznyakova AV, Isakov MA, Shestakova MV, Dedov II. Trends in the epidemiology of chronic kidney disease in Russian Federation according to the Federal Diabetes Register (2013–2016). *Diabetes Mellitus*. 2018;21(3):160-169. doi: 10.14341/DM9687