Den Sooluk

HEALTH POLICY ANALYSIS CENTER

Policy Research Paper

Situational Analysis of the Chronic Kidney Disease Incidence and the Main Risk Factors for Its Development and Progression in the Kyrgyz Republic

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ABSTRACT

Currently, world community faces a global problem of not solely medical but also of great socio-economic significance – incidence of chronic non-communicable diseases. These diseases annually claim millions of lives and lead to severe complications related to disability and need in costly treatment. Chronic kidney disease (CKD) takes an important position amongst chronic non-communicable diseases owing to significant incidence, downfall of life quality, high mortality rate and the need to use expensive methods of substitution therapy: hemodialysis and renal transplantation. In recent years, the Kyrgyz Republic has been observing a sharp increase in number of patients with CKD. Both total number of patients with CKD and number of patients with end-stage renal failure who underwent kidney transplant operations and need lifelong provision with required medicines are increasing. This study was aimed at exploring the main causes of growing incidence of the disease which should become the basis for taking preventive measures to decrease the CRD morbidity and mortality.

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ABBREVIATIONS

ACR	Albumin/creatinine ratio
ACE inhibitor	Angiotensin-converting enzyme inhibitor
BP	Blood pressure
AH	Arterial hypertension
HD	Hypertension disease
GN	Glomerulonephritis
CEH	City Endocrinology Center
DN	Diabetic nephropathy
RRT	Renal replacement therapy
UNR	Unified National Registry
BMI	Body mass index
KR	Kyrgyz Republic
CHD	Coronary heart disease
HDL	High density lipoproteins
LDL	Low-density lipoproteins
KR MoH	Ministry of Health of the Kyrgyz Republic
MAU	Microalbuminuria
NH	National Hospital
NSAID	Nonsteroidal anti-inflammatory drugs
NCC&T	National Center of Cardiology & Therapy
NCM&CH	National Center of Maternal and Child Health
HO	Health organization
MIOCH	Merged inter-oblast clinical hospital
RR	Relative risk
PH	Program hemodialysis
GFR	Glomerular filtration rate
CVD	Cardio-vascular diseases
DM	Diabetes mellitus
ESRD	End-stage renal disease
TH	Territorial hospital
CKD	Chronic kidney disease
CG	Chronic glomerulonephritis
CRF	Chronic renal failure
CHF	Chronic heart failure
FMC	Family Medicine Center
KDIGO	Kidney Disease Improving Global Outcomes
KDOQI	Kidney Disease Outcomes Quality Initiative
NICE	National Institute for Health and Care Excellence
NKF	National Kidney Foundation
SIGN	Scottish Intercollegiate Guidelines Network

1. BACKGROUND OF THE STUDY

Chronic kidney disease (CKD) has an important position among chronic non-communicable diseases due to its high prevalence, a drastic deterioration of the quality of life, high mortality, which lead to the need of using expensive renal replacement therapy methods at the end stage, such as hemodialysis and kidney transplantation. Progress of the modern medicine has allowed to develop a series of highly efficient and relatively cheap prevention approaches, allowing to significantly slow down the progression of chronic kidney disease, reduce a risk of complications and treatment costs.

The increased prevalence of CKD is associated with an increase in the number of patients with primary renal disease, diabetes, obesity, aging of population, hypertension, hyperglycemia. Increased number of patients with end-stage renal disease requires a continuous increase of spending for hemodialysis and kidney transplantation, and only a small share of patients with CKD need renal replacement therapy (RRT), which is very costly and burdensome even for advanced economies[1].

Number of patients with CKD has increased drastically in the Kyrgyz Republic in recent years, and there is an increase both in the total number of patients with CKD, and the number of patients with end-stage renal disease (ESRD) taken to the program hemodialysis treatment (PGD) paid from the state budget and patients with a kidney transplantation, requiring lifelong support with immunosuppressants. CKD prevalence indicators are based on services utilization data in healthcare organizations of the Kyrgyz Republic since 2008.

By the beginning of November 2015, 2511 patients with stage 3-5 CKD were seeking care in health organizations and were included into the Unified National Registry (UNR). Since 2008, UNR has shown a steady increase of the registered cases (Table. 1).

Table 1. Number of registered stage 3-5 CKD cases in UNR

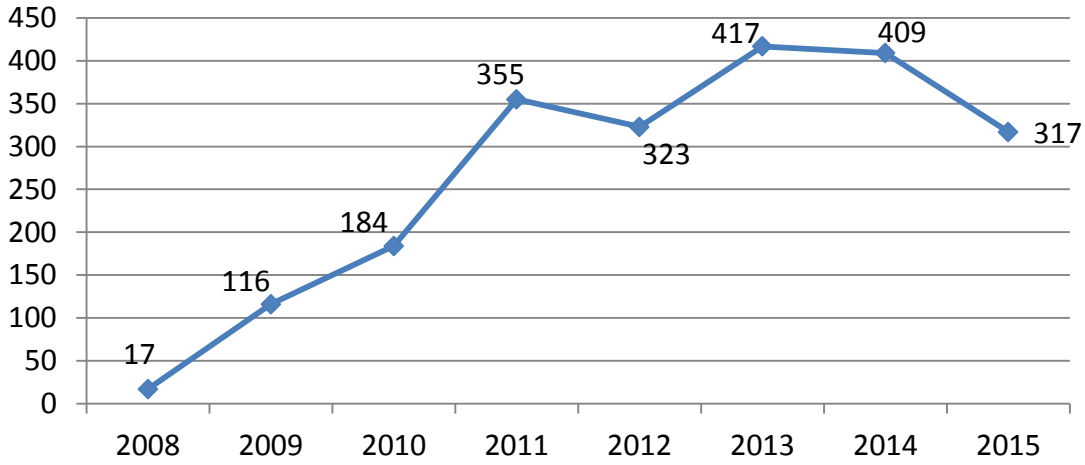
№ п/п	Years	No. of CKD patients		
		Total no. of registered cases	New cases for the year	New cases for 10 months
1	2008 (for 6 months)	17 (for 6 months)	17 (for 6 months)	17 (for 6 months)
2	2009	159	140	116
3	2010	399	242	184
4	2011	809	410	355
5	2012	1213	404	323
6	2013	1702	489	417
7	2014	2194	492	409
8	2015 (for 10 months)	2511	317	317

[1]Fester P. , Ribstein J., du Cailar G., Mimran A. Determinants of cardiorenal damage progression in normotensive and never-treated hypertensive subjects // Kidney Int. — 2005.

An increase in CKD incidence leads to an increase in patients with end-stage renal disease (ESRD) that receive renal replacement therapy (RRT) – hemodialysis, and this burden lies heavily on the state budget.

Data for 10 months of 2015 indicate that CKD incidence in the Kyrgyz Republic had an upward trend, when compared with the number of registered cases for 10 months of the previous year (Figure 1).

Figure 1. Number of CKD cases for 10 months per years (new cases)



It should be noted that additionally more than 1,150 CKD patients at the pre-dialysis stage are registered in the Unified National Registry and followed up by family doctors.

Currently, eight hemodialysis units are open and have been operating in public healthcare facilities of the Kyrgyz Republic to treat stage 5 CKD cases. These units are located in the National Center of Cardiology and Therapy (NCC&T), the National Center for Maternal and Child Health (NCMCH), National Hospital (NH), as well as in all regional healthcare organizations, except Naryn and Batken oblasts.

All artificial kidney units have been operating in three shifts. 349 patients, paid by the government, receive hemodialysis in these units. Currently, the Ministry of Health pays for this service at a rate of $ 100 for one hemodialysis session.

However, the continuous growth of CKD cases leads to a drastic shortage of dialysis beds in public healthcare organizations and **the state budget cannot fully cover the needs of all those patients.**

Due to the lack of available budget-funded beds in healthcare organizations, the government has to buy the dialysis services from private providers. And, the government provides treatment to another 200 patients under the contract with private providers for dialysis service. **Therefore, some patients have to receive dialysis in private medical centers at their own expense, and the price varies from 5200 to 6000 KGS** for one hemodialysis session.

So, as of 10/12/2015, about 70 patients receive program hemodialysis treatment in private centers at their own expense.

One patient should receive in average about 12-13 sessions on a monthly basis, or about 144 - 156 sessions a year.

Rapidly growing number of patients with CKD of stage 5 (ESRD) requires a constant increase in the number of dialysis beds by increasing workload on operating dialysis units or opening new units with all working infrastructure, which entails an increase in maintenance and supplies expenses of the state in order to provide hemodialysis to patients.

It should be noted that maintenance of hemodialysis units is quite an expensive thing for the state; they considered to be complex and high-cost units in terms of organization and process operating conditions that require qualified engineering service, regular inspection and repair, replacement of expensive parts of dialysis equipment and water treatment systems, as well as training and support of skilled personnel in providing specialized care.

One way to reduce CKD incidence in the Kyrgyz Republic is to detect CKD root causes and identify causes of renal failure progression to the end stage, which should become a basis for preventive measures to reduce CKD morbidity and mortality.

At present, there is a long-felt need to carry out a situational analysis of CKD morbidity and the structure of CKD development risk factors in the Kyrgyz Republic, in order to plan preventive interventions. In this regard, it is necessary to examine what has caused increased CKD incidence in the country, as well as what are the most common factors contribute to the rapid progression of kidney disease from the 1st to the 5th stage (ESRD).

2. THE GOAL OF THE STUDY

To review the causes of CKD incidence increase and the factors that affect rapid progression of CKD end-stage to take preventive measures in order to reduce the growing prevalence of end-stage renal disease (ESRD), disability and premature death from CKD complications in population of the Kyrgyz Republic.

3. OBJECTIVES

1. To examine CKD development causes and determinants of CKD progression based on data of registered CKD patients
    - development of electronic Unified National Registry (UNR) database of CKD patients, entering all CKD patients registered in logbooks from 2008 to the present time into statistical program;
    - to carry out statistical analysis of UNR trends in CKD patients change since July 2008 to the present time (October 2015) by comparing data;
    - to identify populations at higher risk of CKD development, causes and rate of progression of chronic renal failure.

2. To determine predictors structure of CKD development and progression in patients with cardiovascular disease (CVD), diabetes mellitus (DM) and the primary glomerular kidney disease - glomerulonephritis (GN).
3. To clarify values of the known and potential risk factors for CKD development and progression, and to define diagnostic criteria of early (reversible or controlled) CKD stages.

4. To develop preventive measures for CKD development in the Kyrgyz Republic population and CKD progression to ESRD.

4. METHODOLOGY

The evaluation methodology is based on a review of international literature and international evidence-based clinical practice guidelines related to CKD and analysis "of health care seeking patterns" (utilization of healthcare services) of CKD patients registered in the Unified National Registry (UNR).

4.1. Desk review

1) Review of the international literature on CKD and international practice for diagnosis and prevention of CKD, based on evidence-based medicine.
2) Review of existing practice in the Kyrgyz Republic related to diagnosis and prevention of CKD, or diseases that lead to CKD.

4.2. Review of registration of CKD patients in UNR

1) Policies and procedures, documentation list, responsible personnel;
2) Evaluation of activities related to the Registry of CKD patients (strengths and weaknesses, recommendations);
3) Development of database of patients with chronic renal failure based on service utilization data of the Registry of patients with CRF (database shall include details from medical records and reporting logs of patients with chronic renal failure).

4.3. Analysis of UNR data on utilization of services by CKD patients

1) To carry out data analysis based on UNR database (on service utilization) to identify the most common CKD causes;
2) To identify the main factors contributing to CKD development and progression in 3 conditions (HD, diabetes and GN)
    - Retrospective review of medical records and statistical reporting data of the NH, NCC&T, City Endocrinology Center (CEC).
    - To carry out semi-structured qualitative interviews with health professionals in the field of nephrology, representatives of the Ministry of Health and others.

5. THE FINDINGS OF THE STUDY

5.1. Classification and definition of CKD

Until the recent times, the medicine lacked not only conventional classification of various progression stages of renal pathological process leading to abnormalities of the kidney' function, but also a universal terminology.

US National Kidney Foundation has reviewed many publications related to diagnosis and treatment, assessment of significance of a number of indicators in determining the rate of kidney disease progression, concepts and terminology and proposed the concept of **chronic kidney disease (CKD)**. In order to align approaches to assess CKD stages, Associations of Nephrologists, Transplant Surgeons, and Dialysis Physicians (NKF/KDOQI) in Europe and the United States adopted CKD classification in 2002, developed CKD concept, which includes the definition of CKD and its stages, the choice of laboratory parameters, adequately characterizing

CKD; studied the relationship between the degree of renal damage and CKD complications; stratified risk factors of CKD progression and cardiovascular diseases. And in 2005, KGIGO (Kidney Disease Improving Global Outcomes) confirmed KDOQI initiative related to common use of the term 'CKD'. ICD-10 does not include CKD. But the international classification ICD-9-CM had assigned codes to all five CKD stages since October 1, 2005. Criteria for CKD definition in adults and children are identical. Use of the CKD term implies the exclusion of the term CRF.

Chronic kidney disease is the kidney damage for 3 or more months, as defined by structural or functional abnormalities, irrespective of diagnosis. And also use of the term "end-stage renal disease", ESRD, which means stage 5 CKD, requiring dialysis therapy or kidney transplantation irrespective of kidney function level[2].

5.2. Data of existing CKD-related international clinical practice guidelines

At this stage, not all risk factors, which modification would allow reducing CKD progression rate, are studied properly. Approaches of forecasting unfavorable course of chronic kidney disease at early stages are not developed properly yet. In this regard, examination of risk factors, development and progression of chronic kidney disease in various pathologies, including comorbidities have a great importance. At the same time CKD progression is the main criteria, which determines a quality and length of a patient's life, the fight against this disease has not only medical, but also social and economic importance. Focus has to be made on the risk factors that could be modified, since they can reduce the risk of CKD development. At the same time, both approaches to analysis of the roles of non-modifiable (eg, genetic) and modifiable risk factors for progression of chronic kidney disease have to be actively developed (Table 2).

Table 2. Classification and Characteristics of the Main CKD Risk Factors [Levey A.S. at all., 2005]:

Types	Definition	Description
Susceptibility factors	Increased susceptibility to kidney damage	Old age, family history of CKD, weight reduction of renal parenchyma, low birth weight, racial and ethnic minority status, low levels of income or education
Initiation factors	Cause direct kidney damage	Diabetes mellitus, high blood pressure, autoimmune diseases, systemic infections, urinary tract infections, cystic calculi, obstruction of lower urinary tract, drug toxicity, hereditary diseases
Progression factors	Cause worsening kidney damage or faster decline in GFR	High levels of proteinuria, high blood pressure, poor control of blood glucose levels in diabetes, dyslipidemia, smoking
End-stage CKD factors	Increase of morbidity and mortality in kidney failure	Lower dialysis dose, temporary vascular access, lower serum albumin level, high levels of phosphorus, late referral to nephrologists

[2]NKF: Clinical practice guidelines for chronic kidney disease: Evalution, classification and stratification/ - Am.J.kidney Dis., 2002. – 39 [suppl. 1]: S1-S266.

According to this classification, it is difficult to draw a clear line between the factors of CKD initiation and progression. From a practical point of view, gradation of risk factors is used: risk factors for CKD development and progression, highlighting non-modifiable and modifiable factors (Table. 3, 4).

Table 3. Risk Factors for CKD Development

Non-modifiable	Modifiable
Old age	Diabetes
Male	Arterial hypertension
Low initial number of nephrons (low birth weight)	Autoimmune diseases
Racial and ethnic characteristics	Chronic inflammation / systemic infection
Hereditary factors (including family history of CKD)	Urinary tract infections and calculus
	Obstruction of lower urinary tract
	Drug toxicity
	High protein intake
	Dislipoproteinemia
	Smoking
	Obesity / Metabolic Syndrome
	Hyperhomocysteinemia
	Pregnancy

Table 4. Risk Factors for the Progression of CKD

Non-modifiable	Modifiable
Old age	Persistent activity of the main pathological process
Male	High levels of systemic blood pressure, proteinuria
Low initial number of nephrons (low birth weight)	Poor metabolic control of diabetes
Racial and ethnic characteristics	Obesity / Metabolic Syndrome
	Dyslipoproteinemia
	Smoking
	Anemia
	Metabolic Syndrome
	Pregnancy
	Abnormal calcium-phosphorus metabolism (hyperparathyroidism)
	High-protein diet and an increased intake of sodium with food

We made a search for clinical practice guidelines for chronic kidney disease in national and international electronic databases on the Internet.

Search for clinical guidelines and the results of meta-analyzes, systematic reviews, randomized clinical trials, cohort studies, etc., in relation to diagnosis, treatment and prevention of chronic kidney disease was carried out in the Cochrane Library, *Medline* database (MEDLINE), and in

English (*Yahoo, AltaVista, Google, DoctorGuide*) and Russian search engines (*Yandex, Ra*mbler) using certain keywords.

5.2.1. Key words

We searched information for chronic kidney disease in MEDLINE for the time period from 2000 to 2015. By using MeSH we entered such terms as “chronic kidney disease”. We used the following sub-headlines: complication, diagnosis, epidemiology, etiology, mortality, prevention and control, therapy, risk factor. As far as prevention and control is concerned, we limited our search by randomized controlled clinical trials, cohort trials or reviews. We used different word combinations during the search.

Preferred publications for the final report were selected on the websites NICE, KDIGO, SIGN for the period of 2008-2015. The review was made based on these data.

We found the following CPG, during our search:

- SIGN-103 – Diagnosis and management of chronic kidney disease, 2008;
- KDIGO, 2013 - Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease [8];
- NICE: CG182, 2014 – Chronic kidney disease in adults: assessment and management [9];
- NICE (CMG37) – Early identification and management of chronic kidney disease in adults. – July, 2012 [10];
- NICE quality standard (QS5) – Chronic kidney disease in adults. – March, 2011.

According to KDIGO, NICE, SIGN, **chronic kidney disease** – is an abnormality of kidney structure or function for more than 3 months, and classified according to the glomerular filtration rate (GFR) and proteinuria at the stage 1-5. Stage 5 of the disease with a loss of renal function (GFR <15 ml / min per 1.73 m^2), when the patient needs a dialysis is called as an end-stage renal disease (ESRD).

Chronic kidney disease (CKD) is described as a damage of kidney function/ or structure. It is common condition; it is often not detected and can be a comorbid condition (e.g., to cardiovascular disease and diabetes mellitus). Moderate and severe CKD is related to an increased risk of other significant adverse outcomes such as acute renal failure, disability and lethality.

CKD is usually asymptomatic, but can be detected, and tests for CKD are simple and readily available. There is evidence that treatment can prevent or delay the progression of CKD, reduce or prevent the development of complications and reduce the risk of cardiovascular diseases.

Nevertheless, CKD often is not detected because there are no specific symptoms, and it is often not diagnosed or diagnosed at a late stage.

5.2.2. Prognosis of chronic kidney disease (CKD)

The following parameters have to be evaluated in order to predict the development of CKD:

1) The cause of chronic renal failure;
2) GFR (glomerular filtration rate) data;
3) The degree of albuminuria;
4) Other risk factors and comorbidities.

CKD classification by the level of albuminuria is based on evidence which indicates that the risks of total and cardiovascular lethality, transition to the end-stage renal failure, acute kidney injury and progression of CKD could be different depending on level of urinary albumin excretion in any GFR range.

Diagnostic criteria of CKD include signs of kidney damage detected by lab and/or instrumental tests, and/or a decrease in GFR less than 60 mL/min /1,73m^2.

5.2.3. International recommendations according to NICE, KDIGO, SIGN[3]

CKD is determined by estimating glomerular filtration rate (GFR) and by measurement of albumin/creatinine ratio (ACO), according to GFR (G1-G5) and ACH (A1-A3) categories.

For example:

- glomerular filtration rate –is 25 mL / min / 1,73m2 and the albumin/creatinine ratio is 15 mg / mmol – means that this is G4A2 CKD.
- GFR of 50 mL / min / 1,73m^2 and albumin/creatinine ratio is 35 mg / mmol – means that this is G3aA3 CKD.
- GFR is less than 15 mL/min/1,73м^2, this is G5 category, which is renal failure.

CKD is usually associated with a reduction in glomerular filtration rate, but other important functions can be depressed without GFR reduction.

[3]KDIGO - Kidney Disease Improving Global Outcomes, NICE – National Institute for Health and Care Excellence, SIGN – Scottish Intercollegiate Guidelines Network

Table 5. CKD Classification Based on ACR and GFR Data, and Risks' Stratification for Development of Complications

GFR and ACR			ACR category (mg/mmol)		
			<3 Normal to mildly increased	3-30 moderately increased	>30 Severely increased
			A1	A2	A3
GFR Ml/min/ 1,73m2	≥90 normal or high	G1	No CKD		
	60-89 mildly decreased	G2			
	45-59 moderately decreased	G3a			
	30-44 moderately to severely decreased	G3b			
	15-29 severely decreased	G4			
	<15 end-stage renal disease	G5			

5.2.4. Tests to define CKD

Measurement of kidney function:

- Creatinine measurement for estimating glomerular filtration rate (enzymatic assay compared with isotope dilution mass spectrometry) or by using the Cockcroft-Gault, MDRD (Modification of Diet in Renal Disease);
- Cystatin C - with GFR 45-59 ml / min / 1,73m2, longer than 90 days without proteinuria (ratio of albumin/creatinine less than 3 mg/mmol) or another marker of the kidney disease. In patients with hypothyroidism it can be increased and, on contrary, it can be decreased in patients with hyperthyroidism.
- Measurement of GFR and albumin/creatinine ratio in patients with such risk factors as diabetes mellitus, hypertension, acute renal failure, cardiovascular disease (ischemic heart disease, heart failure, peripheral vascular disease, or cerebrovascular disease), structural kidney disease, recurrent urolithiasis or hypertrophy prostate, multisystem disease (SLE), positive family history, opportunistic hematuria.

Monitoring of patients – in order to assess development and progression of CKD, GFR and ACR have to be measured within 2-3 years after the acute kidney failure, even if serum creatinine has returned to normal.

Diagnostic criteria for CKD:

- Albuminuria (greater than 30 mg per day, albumin/creatinine ratio - 30 mg / mmol).
- Urinary sediment abnormalities;
- Tubular disorders;
- Abnormalities detected by histology;
- Structural abnormalities detected by imaging (ultrasound);
- History of kidney transplantation
- GFR - less than 60 ml/ min/ 1,73m^2

Table 6. Frequency of Monitoring by GFR and ACR Category

GFR and ACR			ACR category (mg/mmol)		
			<3 Normal to mildly increased	3-30 Moderately increased	>30 Severely increased
			A1	A2	A3
GFR Ml/min/ 1,73m2	≥90 normal or high	G1	≤1	1	≥1
	60-89 mildly decreased	G2		1	≥1
	45-59 mildly to moderately decreased	G3a	1	1	2
	30-44 moderately to severely decreased	G3b	≤2	2	≥2
	15-29 severely decreased	G4	2	2	3
	<15 end-stage renal disease	G5	4	≥4	≥4

5.2.5. Prevention of CKD progression

Risk factors for development of chronic kidney disease include:

- Diabetes - development of diabetic nephropathy. All patients with diabetes should have their renal function measured regularly (level D).
- Hypertension - kidney function has to be measured in all patients receiving antihypertensive and lipid-lowering therapy (level D).
- Smoking is a risk factor for development of chronic kidney disease (level C). With 16-30 years of smoking history, the relative risk is 1.32, with more than 30 years - RR = is 1.52 (positive associations between smoking and CKD development).
- Cardiovascular diseases – development of CKD is 1.5 times higher in patients with atherosclerosis than without it, in patients with chronic heart failure is twice higher.
- Age: the risk is higher in patients older than 65 years than in patients younger 65 years (RR = 101.5, a positive correlation between age and CKD development).
- Prolonged use of non-steroidal anti-inflammatory drugs (NSAID);
- Obesity (body mass index greater than 30).
- Low socioeconomic status (level C).

Risk factors for the progression of CKD:

- Cardiovascular diseases;
- Proteinuria;
- Acute renal failure;
- Arterial hypertension;
- Diabetes;
- Smoking;
- Long-term use of NSAID;
- Lack of treatment for urinary tract obstruction.

Prevention methods for CKD progression:

- Active lifestyle and physical activity compatible with diseases;
- Reduce body weight (BMI 20-25 kg/m^2);
- Stop smoking;
- Reduce high protein intake (41,3 g/kg/a day) (Level C);
- Reduce intake of salt (<2 г/сутки), phosphates, potassium;
- Glycemic control - glycated hemoglobin HbA1c <7.0%;
- Control of the lipoproteins level;
- Adjustment of medication dosage used to treat comorbidities;
- Withdrawal of nephrotoxic medications (angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers II, aldosterone inhibitors, direct renin inhibitors, diuretics, NSAIDs, metformin, lithium medications, digoxin and others.

5.3. Review of the practice of prevention and diagnosis of CKD and conditions that lead to CKD in the Kyrgyz Republic

Clinical practice guidelines and clinical protocols (CPG/CP)for CKD are not developed in the Kyrgyz Republic. The country has only approved clinical protocols for pyelonephritis, cystitis, and asymptomatic bacteriuria in pregnant women.

These clinical protocols have antibiotic therapy schemes, but contain no information related to the consequences of lack of treatment of these diseases.

The CKD structure of the Kyrgyz Republic suggests that such diseases as glomerulonephritis, diabetes and hypertension most frequently progress to the end-stage.

There are no developed and approved CPG and CP for diagnosis, treatment and prevention of glomerulonephritis.

For diabetes there is an approved clinical guidelines and clinical protocols *Diagnosis and Treatment of Type 2 Diabetes at the PHC Level* (MOH Order №325 of 08.06.2009). Clinical practice guidelines have a section dedicated to diabetic nephropathy (DN). The clinical protocol for diabetic nephropathy provides information about necessary **diagnostic tests, screening, monitoring and frequency of tests to be done for patients with diabetes, depending on DN stage**.

However, this CKD classification is outdated and needs to be updated. GFR estimation is recommended to be done once every 6-12 months in patients with proteinuria, and once a month in patients with CRF. Albumin/creatinine ratio is also outdated and need to be updated too. According to this clinical protocol patients with diabetes are recommended to undergo annual screening for microalbuminuria, and to have their glycated hemoglobin HbA1c checked at least 2 times a year. According to diabetic nephropathy screening it is recommended to measure albumin/creatinine ratio in single urine test, creatinine in blood plasma, and GFR annually. GFR is recommended to be measured annually irrespective of level of albumin discharged in the urine (level B). It is recommended to estimate microalbuminuria and glomerular filtration rate (level C) by screening tests. Recommendations also provided for control of blood pressure, and lipid profile.

To assess implementation of the recommendations provided in the approved clinical protocol *Diagnosis and Treatment of Type 2 Diabetes at PHC Level,* indicators have to be developed, which requires retrospective review of outpatient medical records of diabetics.

There are no clinical practice guidelines and clinical protocols for type 1 diabetes. For assessment of monitoring of patients with type 1 diabetes, retrospective review of outpatient medical records of diabetics is also required at PHC level.

There are approved CPG and CP for hypertensive disease (Ministry of Health Order №839 from 25.12.2009). These documents indicate recommended laboratory tests, including measurement of cholesterol, daily proteinuria or the ratio of urine albumin (mg) to urine creatinine (mmol) in randomly taken urinalysis, serum creatinine, high-density lipoprotein (HDL), low density lipoprotein (LDL), but do not indicate their frequency.

The recommendations for arterial hypertension treatment with ACE inhibitors, angiotensin receptor blockers are provided, since these groups are more effective and safe for nephropathy treatment. But at the same time, these documents do not contain any data on monitoring treatment by these groups of medications, as they are not so safe in nephropathies and in some cases may enhance the progression of CKD.

Both clinical guidelines do not contain a separate section, dedicated to prevention of CKD development.

It should be noted that clinical guidelines adopted in the Kyrgyz Republic use the term ‘chronic renal failure’, although this term is not used any longer in international practice, as it was noted above.

5.4. Organization of activities related to the registry of patients with CKD – the Unified National Registry (UNR)

A log for patients with kidney disease at different stages of chronic kidney failure, called the *Unified Waiting List* for hemodialysis, was started for the first time in the NCC&T in 2008. The purpose of this log was to count the total number of patients with chronic renal failure, in order to identify the number of people in need of dialysis by region and to forecast demand for dialysis beds in the country.

Registration list of patients with CKD in the UNR seek care is currently maintained by the Artificial Kidney Unit of the National Hospital by the KR MoH. At present, UNR includes six (6) different registries, initiated in 2008 and continued to the present. These logs are numbered and laced in accordance with the requirements for maintaining reporting documents of the Kyrgyz Republic.

One of the UNR strengths is that patients with CKD were registered there after referral of physicians of specialized healthcare units (cardiology, nephrology, endocrinology, urology, and others.), where patients were supervised and treated after nephrologist’s consultations and recommendations. Most often, their referral was included into their hospital discharge summary provided by the Department of Nephrology of the NCC&T, NH and MICH. Thus, it can be concluded that persons with questionable or unsubstantiated diagnoses were not included into the Registry. When registering a patient with CKD in UNR, the staff of the NH Artificial Kidney

Unit responsible for maintaining the records, retain a copy of outpatient records or hospital discharge summary with indication of a patient's primary diagnosis, CKD stage, indications on hemodialysis and the full name of the doctor, that have referred this patient for registration.

However, UNR has some weaknesses, alongside with its strengths. Thus, one of the UNR weaknesses is that it does not include patients with stages 1-2 CKD, when the disease has no laboratory signs of severe filtration dysfunction and elevated level of creatinine and urea. Another important UNR drawback is the lack of patients referred to the registration by health providers of primary and secondary levels (FMC, TH), where there is no suspicion of doctors on the possible development of CKD due to hypertension, CHD, diabetes, obesity and other chronic diseases, which early manifestation is microalbuminuria (MAU). As a result, for example, patients with diabetic nephropathy (DN) at the stage of hyperfiltration and MAU, without an increase in serum creatinine, were not included into this Registry. And MAU is one of the indicators of early diagnostic intervention that can indicate CKD development in patients with diabetes mellitus, which then will transit to ESRD.

In addition, this Registry does not include patients with CKD under 18 years, which does not give a picture of CKD prevalence among the pediatric population.

These drawback of the Registry do not allow assess the true CKD prevalence in the Kyrgyz Republic. But, by taking into account the number of requests for registration, one can make a tentative analysis of causes of CKD development of the adult population and to make preliminary conclusions concerning the fact, in which region, and in which age group, and due to which reasons CKD is more likely to be developed and progresses to end-stage renal failure.

5.5. Analysis of CKD incidence based on UNR data

5.5.1. Criteria for inclusion of patients into the general UNR database

As part of the implemented assessment on the basis of available hard copies (logbooks) of the Unified National Registry (UNR) of patients with CKD, electronic database was developed in format of EXCEL statistical program.

Personal data of all patients with CKD were entered into this UNR base, in a chronological order of their registration. As a result, after the exclusion of repeated registration of the same patients at the time of their readmission, UNR database had 2511 registered patients since 17.07.2008 (the date of the start of the log no.1) to 10/24/15.

According to **criteria for CKD diagnosis**, adopted by international associations of nephrologists and dialysis physicians (KDIGO, ERA, EDTA), patients with CKD were included into the National Registry of the Kyrgyz Republic on the basis of the presence of the established kidney disease markers:

- biochemical changes in blood tests (increase in urea, creatinine, electrolyte abnormalities);
- decrease in glomerular filtration rate (GFR);
- changes in urine tests (albuminuria, proteinuria, decreased urine specific gravity, etc.);
- kidneys' structural abnormalities detected by imaging;
- an established fact of kidney damage of any etiology, duration of 3 or more months, accompanied by functional disorders.

Staging of CKD was done according to KDIGO classification for CKD, which has 5 stages, based on GFR category and 3 categories based on proteinuria (Tables 7, 8).

Table 7. GFR Categories in CKD

Stages	Terms	GFR (ml/min/1,73m^2)
1	Normal or high	>90
2	Mildly decreased	60-89
3а	Mildly to moderately decreased	45-59
3б	Moderately to severely decreased	30-44
4	Severely decreased	15-29
5	End-stage renal disease	<15

Table 8. CKD classification on the level of albuminuria/proteinuria

	ACR		AER[4]	Terms
	mg/mmol	mg/g	(mg/24 hours)	
A1	<3	<30	<30	Normal or high
A2	3-30	30-300	30-300	Mildly increased
A3	>30	>300	>300	Severely increased[5]

CKD diagnosis with indication of proteinuria stage and category is established after specifying the main condition, which was associated with kidneys damage. Stage of CKD was established based on the measurement of GFR in serum creatinine, body surface area, taking into account age, sex, race based on Cockcroft-Gault, MDRD, CKD-EPI formulas or by a standard measurement of endogenous creatinine clearance (Rehberg Tareeva-test).

If a patient has signs of nephropathy (abnormalities in urinalysis, or structural abnormalities for 3 or more months), and GFR was a normal, then a patient is assigned stage 1 CKD. In case nephropathy combined with moderate decrease in GFR – from 60 to 90 mL/min, stage 2 is assigned. In both cases, patients with normal GFR and normal serum creatinine level shall not be referred for registration in the UNR.

If the patient has a decreased GFR, ranging from 30 to 60 ml/min, then this patient was assigned stage 3 CKD, irrespective of his/her nephropathy signs. In case the glomerular filtration rate is 15 to 30 ml/min – the 4th stage is assigned. Finally, at a rate of less than 15 ml/min - stage 5 or ESRD is assigned. As part of the early (well-known in the Kyrgyz Republic) classifications, CKD stages from 3 to 5 correspond to the three stages of chronic renal failure (CRF): sub-clinical, clinical, and end-stage.

All registered patients have CKD stage from 3 to 5 by the time of their registration. UNR database was developed on the Excel basis, and include the following details:

- personal details of all patients with 3-5 CKD stage that seek registration,
- patient's place of residence (province),

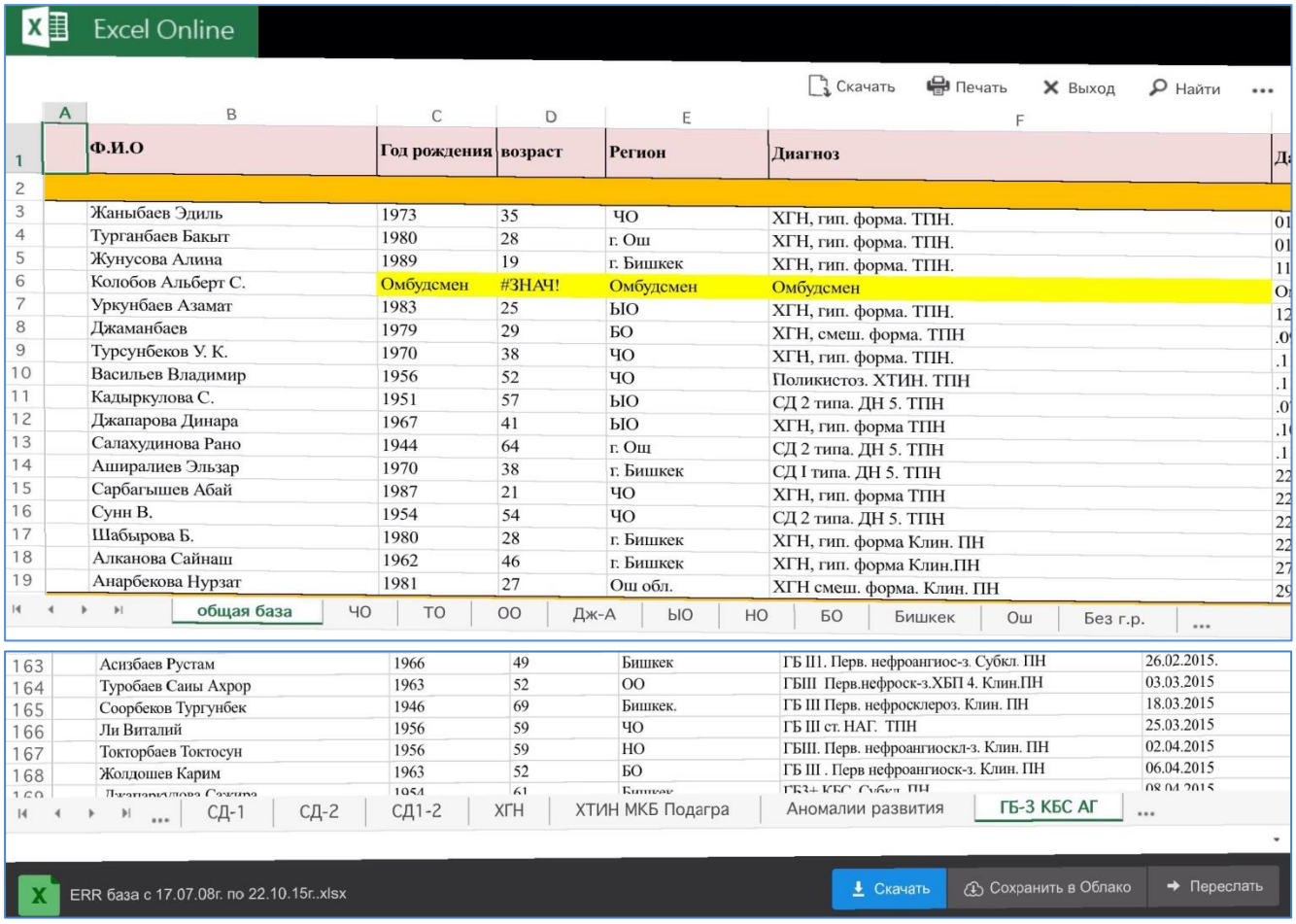
[4]AER – albumin excretion rate, ACR – albumin to creatinine ratio,

[5]including nephrotic syndrome (albumin excretion usually 42200 mg/24 hours [ACR >2200 mg/g; >220 mg/mmol])

- principle diagnosis,
- stage of CKD complication,
- date of registration in UNR,
- levels of creatinine and GFR at the time of registration,
- type of RRT,
- date of RRT initiation,
- location of RRT,
- the date of death (in case of lethal outcome),
- the cause of death (if established).

After entry of details of all patients into the base spreadsheet of UNR, the number of all patients, registered in UNR as of 24.10.15 was 2511.

Figure 2. Screenshot of electronic database of patients registered with different conditions



Excel Online

Скачать | Печать | Выход | Найти

	A	B	C	D	E	F
1		Ф.И.О	Год рождения	возраст	Регион	Диагноз
2						
3		Жаныбаев Эдиль	1973	35	ЧО	ХГН, гип. форма. ТПН.
4		Турганбаев Бакыт	1980	28	г. Ош	ХГН, гип. форма. ТПН.
5		Жунусова Алина	1989	19	г. Бишкек	ХГН, гип. форма. ТПН.
6		Колобов Альберт С.	Омбудсмен	#ЗНАЧ!	Омбудсмен	Омбудсмен
7		Уркунбаев Азамат	1983	25	ЫО	ХГН, гип. форма. ТПН.
8		Джаманбаев	1979	29	БО	ХГН, смеш. форма. ТПН
9		Турсунбеков У. К.	1970	38	ЧО	ХГН, гип. форма. ТПН.
10		Васильев Владимир	1956	52	ЧО	Поликистоз. ХТИН. ТПН
11		Кадыркулова С.	1951	57	ЫО	СД 2 типа. ДН 5. ТПН
12		Джапарова Динара	1967	41	ЫО	ХГН, гип. форма ТПН
13		Салахудинова Рано	1944	64	г. Ош	СД 2 типа. ДН 5. ТПН
14		Аширалиев Эльзар	1970	38	г. Бишкек	СД I типа. ДН 5. ТПН
15		Сарбагышев Абай	1987	21	ЧО	ХГН, гип. форма ТПН
16		Сунн В.	1954	54	ЧО	СД 2 типа. ДН 5. ТПН
17		Шабырова Б.	1980	28	г. Бишкек	ХГН, гип. форма Клин. ПН
18		Алканова Сайнаш	1962	46	г. Бишкек	ХГН, гип. форма Клин.ПН
19		Анарбекова Нурзат	1981	27	Ош обл.	ХГН смеш. форма. Клин. ПН

общая база | ЧО | ТО | ОО | Дж-А | ЫО | НО | БО | Бишкек | Ош | Без г.р.

163		Асизбаев Рустам	1966	49	Бишкек	ГБ II1. Перв. нефроангиос-з. Субкл. ПН	26.02.2015.
164		Туробаев Саны Ахрор	1963	52	ОО	ГБII Перв.нефроск-з.ХБП 4. Клин.ПН	03.03.2015
165		Соорбеков Тургунбек	1946	69	Бишкек.	ГБ III Перв. нефросклероз. Клин. ПН	18.03.2015
166		Ли Виталий	1956	59	ЧО	ГБ III ст. НАГ. ТПН	25.03.2015
167		Токторбаев Токтосун	1956	59	НО	ГБII. Перв. нефроангиоскл-з. Клин. ПН	02.04.2015
168		Жолдошев Карим	1963	52	БО	ГБ III . Перв нефроангиоск-з. Клин. ПН	06.04.2015

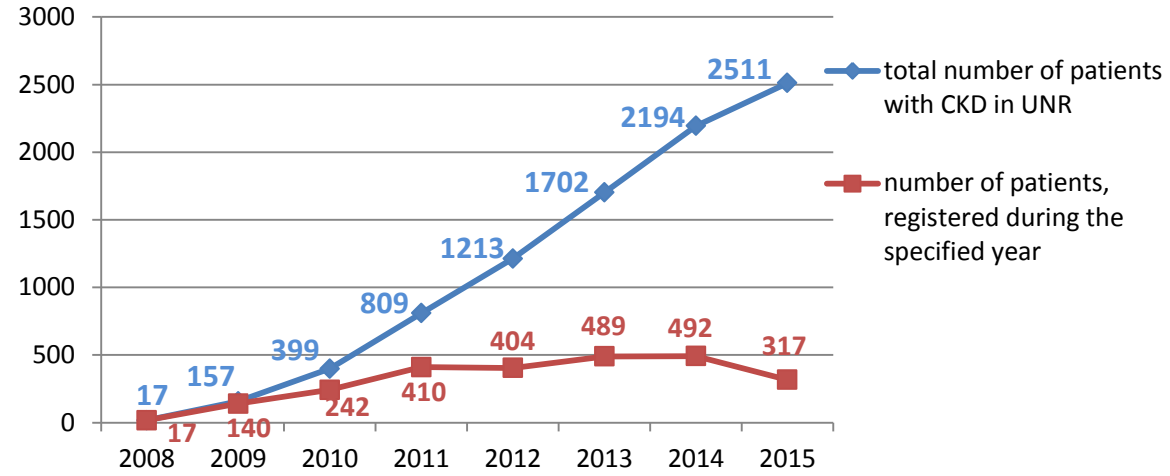
СД-1 | СД-2 | СД1-2 | ХГН | ХТИН МКБ Подагра | Аномалии развития | ГБ-3 КБС АГ

ERR база с 17.07.08г. по 22.10.15г..xlsx | Скачать | Сохранить в Облако | Переслать

5.5.2. Analysis of registered CKD cases, based on UNR.

The total number of patients with CKD requested registration was 2,511 at the beginning of November 2015. This number, compared with the number of patients registered by December 31, 2010 (399 patients), has increased in more than 6 times. There is a steady increase in both the total number of requests for registration, as well as in the number of initially registered patients within one year.

Figure 3. Trends of registration of patients with stages 3-5 CKD for 2008-2015



The number of registrations of new CKD cases in UNR has been gradually reduced. At the same time, the number of dialysis patients and patients after transplantation has been steadily increasing. High-tech methods and intensive replacement therapy provide a chance to save a patient's life, but not always - to maintain life's quality, working ability and active involvement into the social life. Therefore, it is very important to identify the most vulnerable groups exposed to diseases leading to ESRD, identify factors of CKD development and progression.

Figure 4. Dynamics of number of patients on hemodialysis and after transplantation

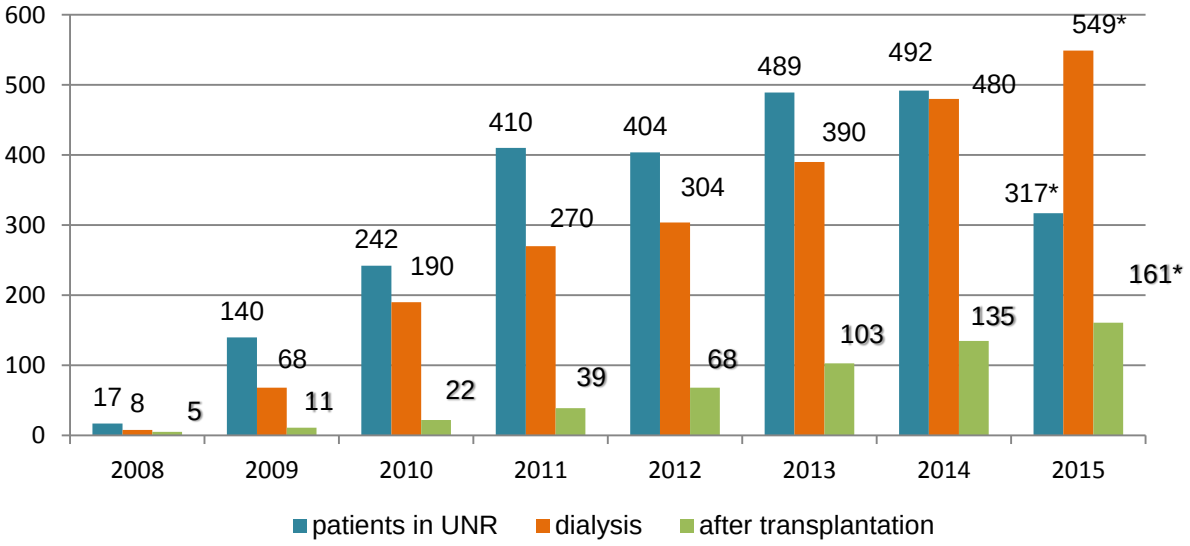


Table 9 demonstrates analysis of patients' requests for registration in UNR from different regions of the country.

Table 9. A number of requests by regions

Regions	2008	2009	2010	2011	2012	2013	2014	2015	Total (people)	%
Chui oblast	5	32	56	93	90	91	97	51	**515**	**20,5%**
Talas oblast	0	7	6	21	11	24	20	15	**104**	**4,1%**
Osh oblast	1	8	23	54	55	92	90	42	**365**	**14,5%**
Jalalabad oblast	0	3	25	42	44	55	60	34	**263**	**10,5%**
Issyk-Kul oblast	3	15	28	36	41	54	44	30	**251**	**10%**
Naryn oblast	0	15	11	32	16	39	33	14	**160**	**6,4%**
Batken oblast	1	7	15	15	21	16	22	13	**110**	**4,4%**
Bishkek	4	45	69	99	108	113	105	92	**635**	**25,3%**
Osh	2	6	9	18	17	3	21	10	**86**	**3,4%**
Patients without identified address	1	2	0	0	1	2	0	16	**22**	**0,88%**
Total:	17	140	242	410	404	489	492	317	**2511**	**100**

According to the Table 9, there is a high percentage of patients with CKD who had been registered, and resided in Bishkek (25.3%), Chui oblast (20.5%), Osh oblast (14.5%). In Jalal-Abad and Issyk-Kul oblasts the numbers of requests were 10.5% and 10%, respectively.

Analysis of CKD patients' age structure indicated that the largest number of patients with stages 3-5 CKD was in the age range of 50-69, average age was - 58.3. Patients with stages 3-5 CKD in the age of 30-49 years (average age - 40.8) were at the second position.

Table 10. Age groups of patients with CKD

Age groups	2008	2009	2010	2011	2012	2013	2014	2015	Total
18-29	7	30	44	84	71	78	73	53	440
30-49	5	58	99	136	139	162	156	78	833
50-69	4	46	89	170	184	218	241	160	1112
70 and above	0	3	5	19	10	28	22	23	110

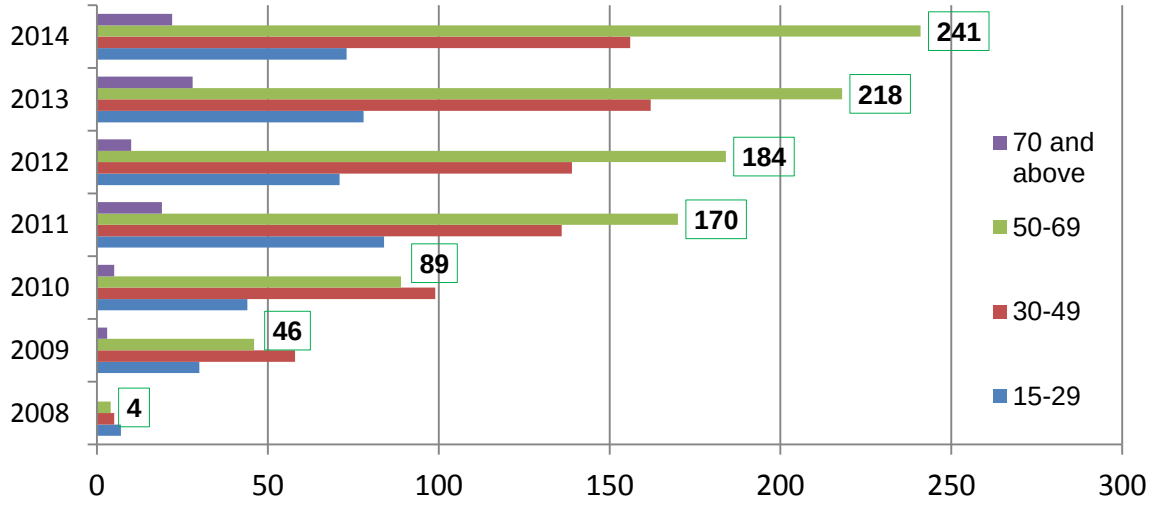
Table 10 suggests that 44.5% of patients with CKD were in the age group of 50-69 years, 33.4% - in the age of 30-49 years, 17.6% - 18-29, and besides, CKD has a tendency of development in patients older than 70 years (4.4% cases).

Dynamics of the number of registered patients with CKD by age in Kyrgyz Republic shows increase in the number of patients with CKD among people of active working age from 30 to 65 years, with average age - 40.8 - 58.3 years.

In addition, there is an upward trend of CKD prevalence among patients above 70, the average age is 74.1 years.

Increased number of CKD patients of employable age (socially active), that loose their chance to be an active member of a family and the society, and have to live on their disability benefits, should become a basis for decisions related to CKD prevention.

Figure 5. Dynamics of registered patients with CKD by age groups



Data analysis of patients with CKD according to nosology cause that led to the development of chronic renal failure indicated that **primary glomerular diseases (45.2%) have the leading position among the causes of CKD development**. This group of diseases includes all clinical forms of glomerulonephritis.

It should be noted that glomerulonephritis (GN) should be established based on the presence of combination of clinical signs and structural abnormalities in kidney tissues, detected by kidney biopsy. Currently, glomerulonephritis diagnosis in KR is not based on renal biopsy due to lack of access to this test. This diagnosis is usually based on empirical data and there is a chance of overdiagnosis.

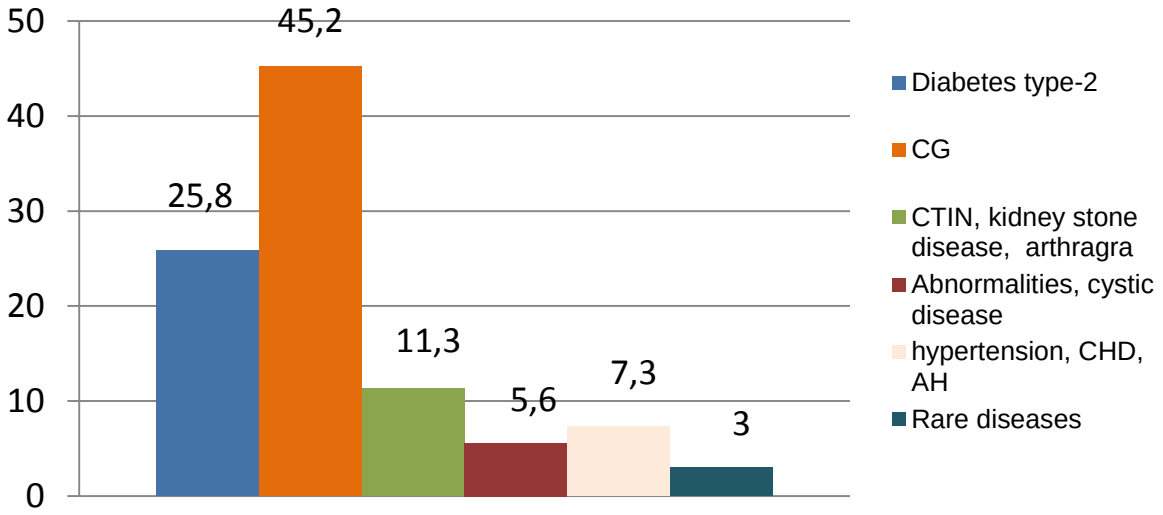
The second largest group of patients with CKD includes people with diabetes mellitus (type 1 and 2) as a cause of CKD development - (25.8%). The majority of these patients have type 2 diabetes - 23.5% of cases.

The share of patients with CKD who had chronic primary and secondary tubulointerstitial nephritis (CTIN) as a result of communicable diseases of the urinary system and metabolic disorders leading to renal dysfunction (kidney stones, gouty nephropathy) was 11.3%.

According to UNR, cardiovascular diseases, including hypertension, coronary heart disease, atherosclerotic cardiosclerosis, became the main CKD causes, and made - 7.3% of the total number of registered patients.

8.6% of the cases fall on congenital and hereditary abnormalities of the urinary system (polycystic kidney disease, aplasia, stricture, neurogenic bladder atony, etc.), secondary nephropathy (alcohol-, or heroin-associated) nephropathy, and acute nephropathy in pregnancy, which transitioned to ESRD.

Figure 6. Main nosologies caused CKD, %

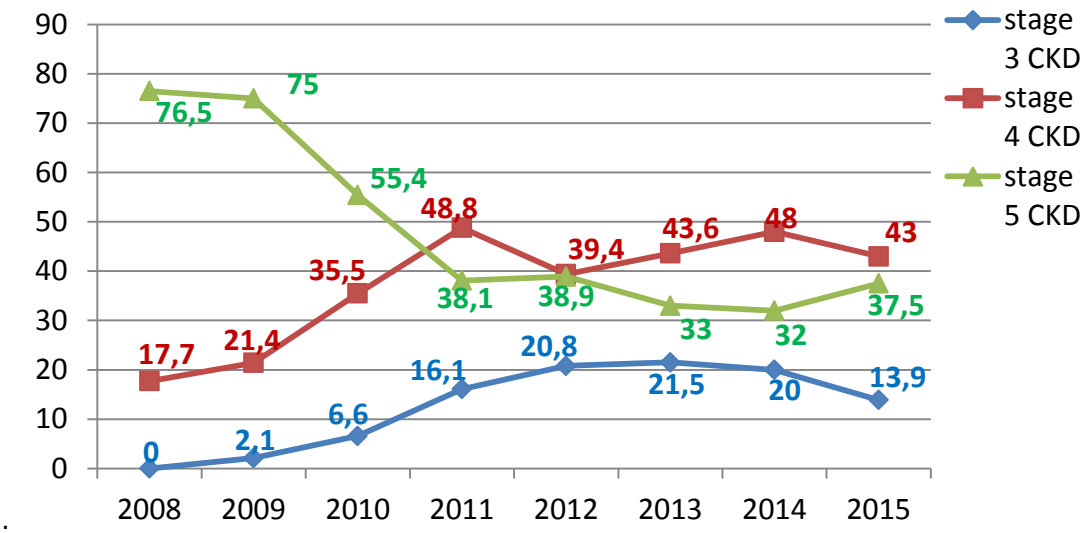


As it was mentioned earlier, UNR includes patients with stage 3-5 CKD: stage 5 - end stage renal failure (patients who had at the day of their registration serum creatinine level > 600 mcM/l, and glomerular filtration rate (GFR) ≤ 10 ml/min in patients without diabetes, and/or ≥ 500 mcM/l and GFR ≤ 15 mL/min for patients with type 1 or 2 diabetes mellitus), 4 stage – is a clinical stage, stage 3 – is a subclinical stage.

Analysis of the ratio of the number of registered patients in different stages of the disease to the total number of the registered cases for the same time period indicated that patients at irreversible stages of CKD tend to apply for registration in UNR more often than others (stage 4 – is a clinical and 5 – is the terminal stage of chronic renal failure). Thus, 17.7% of all patients fall on patients with **stage 3 CKD**, 42.3% - on **stage 4 CKD** - CKD and 40% - fall on **stage 5 CKD**.

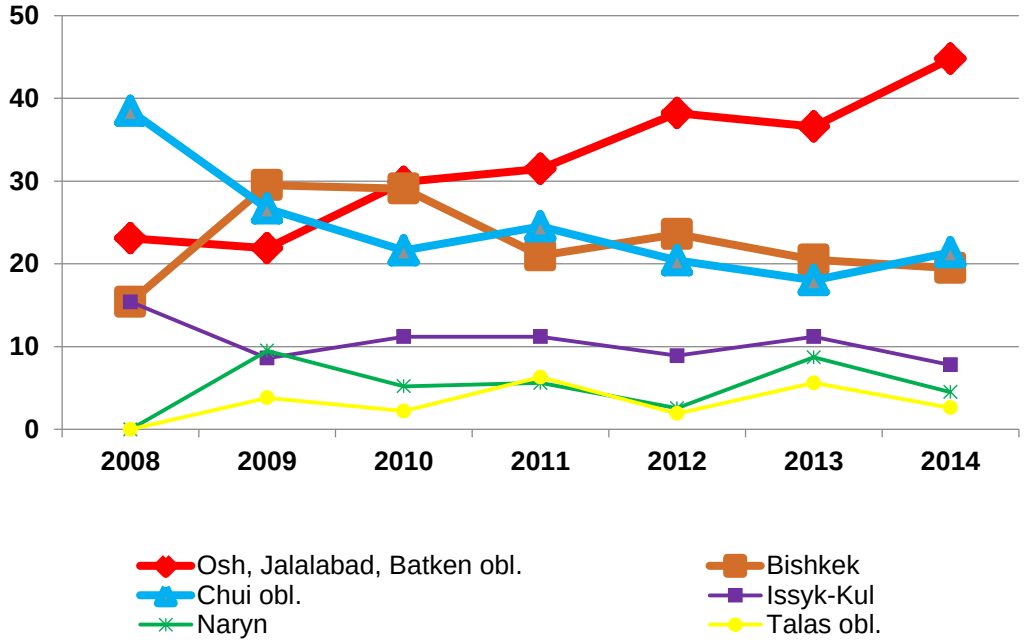
Data breakdown by years suggests that the share of end-stage renal disease (stage 5) was predominant in the early years of registration since July 2008 to 2010 (76.5% - in 2008, 75% - in 2009, 55, 4% - in 2010). And the share of patients with stage 4 CKD became predominant from 2011 to October 2015 (2011 - 48.8%, 2012 - 39.4%, 2013 - 43.6% 2014 - 48% , 2015 - 43%). More and more patients in the stage 3 CKD began to get registered in recent years. The trend towards an increase in a number of stages 3 and 4 CKD patients' requests to be registered in UNR may indicate that the attitude of primary and secondary level health professionals towards diagnosis and management of patients with risk factors for CKD is changed; physicians of different levels and specialties have increased attention to detection of CKD patients on predialysis stage and to management of this disease at its early stage.

Figure 7. Changes in the ratio of patients with 3-5 stage CKD registered in UNR



Registration trends of patients with stage 5 CKD suggests that the number of requests submitted by residents of the southern regions (Osh, Jalalabad and Batken oblasts) increased sharply in recent years, and at the same time it has been gradually decreasing in other regions. This indicates that patients from these regions seek care, get registered, and diagnosed respectively at earlier CKD stages, when it is yet possible to prevent irreversible consequences.

Figure 8. Dynamics in a number of registrations of patients with stage 5 CKD by regions and years

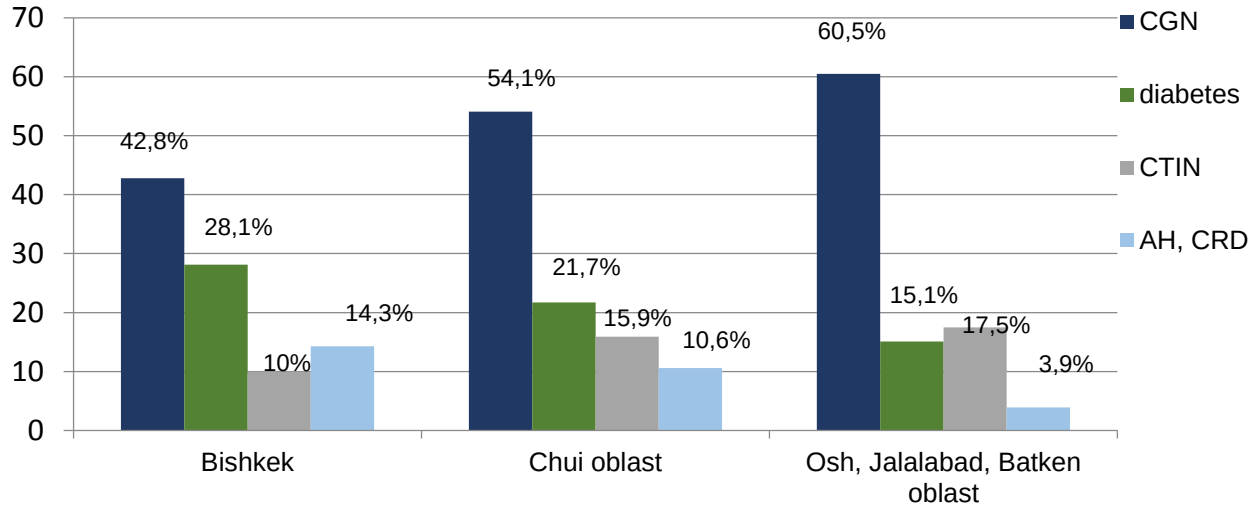


Data analysis of stage 5 CKD patients, registered in UNR based on nosological causes, by regions, suggest that development of the stage 5 CKD was mainly caused by CGN, and average age of this group of patients was 38,6 years.

60.5% of all patients with stage 5 CKD caused by CGN (applied for registration) – are from 3 oblasts: Osh, Jalalabad and Batken, 54,1% - are from Chui oblast, and 42.8% - from Bishkek. There is a fairly high prevalence of diabetic nephropathy (DN), which leads to development of end-stage CKD. 25.8% of all CKD stages were caused by type 1-2 diabetes, including more than 80% of patients with stage 5 CKD. A high proportion of patients with stage 5 CKD caused by diabetes may indicate that patients with diabetes are poorly managed or not properly diagnosed, which leads to an increased share of diabetic nephropathy among causes of end-stage CKD.

As far as cardiovascular diseases as a cause for CKD development are concern, based on UNR data, one may conclude that stage 5 CKD tend to develop more often in patients of the older age group, the average age was 59 years (± 5 years). The share of registered patients with stage 5 CKD caused by cardiovascular diseases in Bishkek was 14.3%. This could be related to better diagnosis of secondary nephropathy and patients' awareness.

Figure 9. Nosological causes for stage 5 CKD development, by regions



5.6. Detection of the main factors of chronic glomerulonephritis (CRF) contributing to development and progression of CKD.

5.6.1. The main causes of chronic glomerulonephritis

Glomerulonephritis – is a kidney disease of immunoinflammatory origin, characterized by a primary lesion of the glomeruli, formed by small capillary vessels in the kidney parenchyma, where the main function of kidneys occur (exchange, filtration, depuration, etc.), followed by the damage of the remaining kidney tissues.

UNR data analysis of patients with 3-5 stages CKD showed a high prevalence of patients with glomerulonephritis, and average age of this group is 38.6 years.

There are only few studies on glomerulonephritis epidemiology were done in the Kyrgyz Republic[6]. These studies reviewed the causes of the spread of glomerulonephritis in the

[6] Калиев Р.Р., Будайчиева А.Б., Туменбаева Д.А., «Эпидемиология гломерулонефритов в Кыргызской Республике», ЦАМЖ, 2005;

country, the clinical features of acute and chronic glomerulonephritis in the Kyrgyz Republic, analyzed main reasons for the disease progression and highlighted the problems of diagnosis, treatment and prevention of glomerulonephritis in Kyrgyzstan.

Findings of these studies suggest that well-known causes of glomerulonephritis development include:

- acute and chronic communicable diseases: quinsy, pneumonia, pharyngitis, flu, viral hepatitis, ear infections, scarlet fever, typhoid;
- systemic rheumatic diseases: vasculitis, polyarteritisnodosa, systemic lupus erythematosus, rheumatoid arthritis, scleroderma, CRHD;
- medications intake: medications containing gold, some antibiotics, drugs used to lower blood sugar (maninil), cytostatics, etc .;
- alcohol abuse;
- parasitic infestation;
- malignant tumors of various organs (paraneoplastic nephropathy);
- allergies: food allergies, seasonal fever, drug disease;
- administration of vaccines and serums;
- pregnancy complications (as the transition of late toxicosis);
- hypothermia;
- stress; genetic predisposition.

5.6.2. Analysis of treated cases with CKD in Nephrology Unit of the National Hospital

In order to identify the specific causes for the development and progression of chronic glomerulonephritis, an analysis of treated cases in the Department of Nephrology was carried out at the National Hospital of the MoH (NH) for 2014 and 10 months of 2015.

In 2014, totally 610 patients were treated with various forms of nephropathy, including 267 patients with chronic glomerulonephritis (43.8%), and 114 patients with diabetic nephropathy (18.7% - and their share increased up to 23.4% in 2015), 62 patients with hypertensive nephropathy (10.2%), 42 – with urinary tract infections (6.9%), 38 - with abnormal kidney development (6.2%). Furthermore, about 40% among these patients were admitted with the stage 5 CKD, and more than half of them were diagnosed for the first time.

Table 11. Treated cases in NH's nephrology unit by nosologies

Time period	No of treated cases	CGN	CTIN	Diabetes	Hypertension	Abnormal kidney development	ESRD
2014	610	267	42	114	62	38	243
		43,8%	6,9%	18,7%	10,2%	6,2%	39,8%
10 months of 2015	370	150	20	86	59	16	131
		40,5%.	5,5%	23,4%	15,8%	4,3%	35,4%

Калиев Р.Р., Будайчиева А.Б., Туменбаева Д.А., «Острый постстрептококковый гломерулонефрит: современные взгляды на проблему», «Здравоохранение Кыргызстана» 1/2010, с 11-18.

Qualitative interviews with a group of neurologists aimed at identifying the challenges faced by practitioners during the examination and treatment of their patients have revealed that diagnosis of glomerulonephritis is the first problem. Early diagnosis of patients with CKD at primary and secondary health care levels is lacking, available preventive methods are used inefficiently.

Treatment of patients with CKD, particularly with CGN is done on a pattern less manner, since there are no developed and approved clinical practice guidelines for glomerulonephritis.

Based on a review of patients' medical records of NH's nephrology department, the main causes that lead to CGN development were identified:

- Lack of timely sanation of foci of chronic infection: carious teeth in almost 100% of cases are causing CGN, frequent relapses of tonsillitis, frequent quinzies, maxillitis, otitis, sinusitis, viral infections, influenza, pustular infections (pyoderma);
- Seeking care of qualified health professionals at late stages;
- Unfavorable working and living conditions, frequent cases of alcohol intoxication;
- Non-observance of physicians' recommendations: no motivation of patients to adhere to a healthy lifestyle, healthy nutrition, regular monitoring of test results. No adherence to the prescribed treatment and prescribed diets. Patients often tend to cancel uncontrollably their treatment due to the high cost of medications;
- Great popularity of indigenous medicine among people, living in provinces, which result in a loss of time and admission of patients to a hospital with severe irreversible complications of the kidneys' function;
- Low involvement of family doctors into infections control of the genitourinary system. Specialty physicians (urologists, nephrologists) are not always available locally to see patients from rural and remote areas for ongoing monitoring.

5.6.3. Main factors leading to CKD development in patients with diabetes based on the data of the Registry of patients with diabetes in Bishkek CEC.

Currently, insufficient disease compensation (failure to achieve target levels of blood glucose, cholesterol, blood pressure, body mass index) and high protein intake with food are the main risk factors of diabetic nephropathy (DN) and the progression of stage 5 CKD in DM. Progression of the DN often leads to the development of end-stage renal disease (ESRD).

According to A.J. Collins et al. the prevalence of CKD in absence of cardiovascular pathology and diabetes in the covered population is 6.8%. In the presence of arterial hypertension (AH), it increases to 15.2%, and the combination of diabetes and hypertension reaches 43.0%[7].

The term "diabetic nephropathy" often includes microalbuminuria (MAU), arterial hypertension (blood pressure> 130/85 mm Hg.), anemia (Hb<120 g / L), the latent decline in renal function (ie, which is not detected by creatinine, but by measuring glomerular filtration rate (GFR). However, these criteria are manifested in the stage 2 DN, while stage 1 DN is characterized by the absence of the MAU, the absence of anemia and normal blood pressure, but the presence of glomerular hyperfiltration, that is, when a patient has GFR> 120 ml/min and a normal level of serum creatinine.

[7] Collins A.J., Foley R.N., Herzog C. et al. United States Renal Data System 2008 Annual Data Report. Am. J. KidneyDis. 2009; 53: S1-S374.

Interviews with endocrinologists identified several key problems: the first two DN stages out of five remain in the zone of undiagnosed CKD symptoms. Family doctors at the local level do not pay attention to such problems that don't have a laboratory manifestations as diabetic nephropathy, since they believe that its diagnosis and treatment of nephrologists' prerogative. The nephrologists believe, at the same time, that timely diagnosis and a clear understanding of the tasks of kidney damage urinary tract infections treatment and prevention in diabetic patients should be mandatory for family physicians.

Analysis of the registry data related to patients with diabetes suggest that patients that have already developed diabetes and such complications as stages 3-5 CKD tend to get registered on dispensary registration books. An analysis of the register of patients with diabetes in Bishkek 2011-2014 indicated that there was a dynamic growth of the total number of patients with diabetes (type 1 and 2).

Table 12. Patients with type 1-2 diabetes based on Registry of Patients with Diabetes, Bishkek, City Endocrinology Center

DIABETES	**2011**	**2012**	**2013**	**2014**
Type 1 diabetes	487	513	583	592
Type 2 diabetes	5267	7444	8692	9273
TOTAL	**5754**	**7957**	**9275**	**9865**

Review of outpatient medical records of patients with type 1 and type 2 diabetes registered in the Bishkek City Endocrinology Center (CEC), who developed a DN as a complication showed that the progression to diabetes complications was caused by decompensated state of carbohydrate metabolism, uncompensated cholesterol, not reaching the targeted level of blood pressure.

Target values in treatment of diabetic nephropathy include a normal glycated hemoglobin (as recommended by the American Diabetes Association - less than 7%, 6.2% - if possible), blood pressure - less than 130/80 mm, inhibition (decrease) in the MAU/proteinuria, reduced atherogenic ratio <3.5 in men and <2.2 in women, lack of urinary symptoms and anemia.

Review of the Registry of patients with diabetes shows an annual increase in patients with stages 3-5 CKD. So, in 2014 more than 8% of patients with diabetes that are registered in CEC have 3-5 stages CKD.

Table 13. Patients with stage 3-5 DN, 2011-2014

		2011	**2012**	**2013**	**2014**
Type 1 and 2 diabetes	Total no. of patients	5754	7957	9275	9865
DN (stage 3-5 CKD)	Absolute numbers	67	115	333	686
	%	1,16%	1,45%	3,59%	6,95%
DN (stage 5 CKD, end-stage)	Absolute numbers	20	37	70	161
	%	0,35%	0,46%	0,75%	1,63%

Screening for MAU in patients with diabetes is recommended to be done at least once a year, however, it is not done on a regular basis due to lack of appropriate diagnostic supplies locally in FMCs. Even Bishkek CEC does not perform this type of diagnostics regularly.

Insufficient compensation of carbohydrate metabolism, or, the excess of glucose in the blood has a toxic effect on the kidneys and blood vessels leading to the development of diabetic nephropathy.

Data analysis of CEC lab tests indicates that in most cases patients have decompensated carbohydrate metabolism. This means that it is not possible to maintain by any means a normal level of blood glucose. For example, data for 11 months of 2015 CEC of lab tests show that 60% of patients who have this kind of test have decompencation of glycated hemoglobin level (more than 9%), more than 80% of patients have decompensated level in the fasting blood sugar (Figure 10).

Also, many patients have high levels of cholesterol and triglycerides. Decompencation is developed mainly due to poor dietary habits and irregular use of antidiabetic drugs.

Figure 10. CEC lab test results from January to November 2015

Лабораторные исследоывания

Период с 01.01.2015 по 11.11.2015

№	Показатели	Всего пациентов	Компенсация	Декомпенсация
1 тип СД				
1	HbA%	422	119	259
2	Сахар крови на тощак	744	124	606
3	Сахар крови через 2-часа	169	39	106
4	Общий холестерин	456	218	35
5	Триглицериды	175	135	12
6	Микроальбуминурия	621	578	15
7	Креатинин	441	408	29
2 тип СД				
8	HbA%	5438	1362	3086
9	Сахар крови на тощак	14695	3085	11313
10	Сахар крови через 2-часа	5031	731	3213
11	Общий холестерин	10906	2904	1942
12	Триглицериды	3318	1496	837
13	Микроальбуминурия	6703	6357	111
14	Креатинин	9092	8658	419
другие типы диабета в т.ч. гестационный диабет				
15	HbA%	0	0	0
16	Сахар крови на тощак	0	0	0

Based on the review of DM Registry data and interview with nephrologists, **the main causes of DN incidence growth and its progression to ESRD in diabetes were identified**:

- Low detection rate of diabetes at PHC level, which result in late diagnosis of diabetes, poor control of factors leading to diabetic nephropathy at PHC level. Family doctors believe that the control and prevention of renal complications is only nephrologists' business, rather than a family doctor.

- Family doctors do not use the developed and approved clinical practice guidelines and clinical protocols for diagnosis, treatment and prevention of type 2 diabetes, and don't have developed clinical practice guidelines and protocols for type 1diabetes, which is the main reason why family doctors do not manage the diabetes at PHC level properly.
- Lack of public awareness about the diabetes symptoms, risk factors for diabetes, its possible consequences, insufficient compensation of carbohydrate metabolism, which leads to the toxic effects on the kidney blood vessels as a result of dietary violations and withdrawal of glucose-lowering medication by a patient without permission of a doctor, and lack of control over the blood pressure, increased rates of blood cholesterol and triglycerides.
- Facilities at FMC level, especially in the regions, do not perform diagnostics for MAU, glycosylated hemoglobin due to unavailability of these types of tests (they must to be done once a year for patients with diabetes).

6. KEY FINDINGS AND DISCUSSIONS

- A dominant share of patients with CKD (45.2%) with developed chronic glomerulonephritis as CKD complications based on the data of registered patients with CKD in the UNR, is a distinctive feature of CKD prevalence in the Kyrgyz Republic. In 25.8% of cases type 1 and 2 diabetes mellitus became the consequence of CKD and cardiovascular diseases (hypertension, heart failure, atherosclerosis, etc.) in 7.3% of cases have led to CKD development. International researches of nosology causes of CKD development that lead to ESRD suggest that diabetic nephropathy (DN) is one of the most common CKD causes in the world, cardiovascular diseases are the second most common cause of CKD. At the third position - the secondary tubulointerstitial renal disease and at the fourth position is chronic glomerulonephritis, leading to the development of CKD[8]. Given that the glomerulonephritis is diagnosed empirically in the KR, without confirmation by the relevant diagnostic tests due to the lack of their availability (renal biopsy), it is possible that the true picture of the chronic glomerulonephritis incidence may be different. In this connection it is necessary to conduct a thorough analysis of diagnostic methods that confirm this condition.

- The increasing number of new registered CKD cases in UNR leads to increase in a number of dialysis patients, despite the fact that the number of patients after transplantation increases. Currently (as of December 1, 2015), only 349 people receive program hemodialysis, financed by the state, and about 70 patients pay out-of pocket for their dialysis in private centers and more than 1,500 patients registered in the UNR are at the pre-dialysis stage of CKD.

- Usually, patients with irreversible CKD stages (stage 4 – is a clinical stage and the stage 5 – is the end-stage of chronic renal failure) most frequently apply to registration in UNR and the number of patients with CKD among active working age population (30 - 65 years) tends to be growing. This fact indicate on a late CKD diagnosis, which is related both to associated with lack of awareness among both patients and the lack of interventions at the PHC level.

[8]Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012.Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney international, Suppl.2013; 3: 1–150

- High chronic glomerulonephritis prevalence among CKD causes is related to the fact that foci of infection (carious teeth, chronic tonsillitis, otitis, sinusitis, viral infections) are not treated in a timely manner at PHC level. Family doctors are not involved in the process of detection and management of patients with urinary tract infections. This fact is aggravated by the lack of clinical practice guidelines and clinical protocols for diagnosis, treatment and prevention of glomerulonephritis at PHC level.

- CVDs in Kyrgyzstan are included into priority programs as part of the health reform program, and many interventions aimed at the control of these diseases were made in this relation, especially at the primary health care level. Health professionals from the NHC&T noted that the number of patients with hypertension who develop CKD has become smaller currently.

- Providers better control blood pressure at the primary level now, which could be a result of development and implementation of CPG/CP for diagnostic and treatment of hypertension at the primary level in 2010. Perhaps not very high prevalence of CVD causes that lead to CKD is related to that. However, these documents need to be updated, and data on preventive interventions to reduce the risk of CKD development need to be revised.

- Family doctors are not committed to manage diabetes at the primary level properly. Identified key factors in diabetes that lead to CKD indicate late diagnosis of diabetes at the primary level and poor control of the factors that lead to diabetic nephropathy. Family doctors do not follow up patients with diabetes, these functions are fully assigned to endocrinologists. Accessibility to endocrinologists is limited in the provinces, and remote FGP. Only nephrologists deal with diagnostics and management of diabetic nephropathy, and their availability at province level is also limited. Family doctors do not have developed and approved clinical protocols for type 1 diabetes, have not been trained on use of the approved clinical practice guidelines for type 2 diabetes and the clinical protocol for diabetic nephropathy. Approved CPG/CP for type 2 diabetes have not been implemented into the health sector.

- Diagnostics for detection of MAU, glycosylated hemoglobin, which can detect diabetic nephropathy in the earliest stages for the timely prevention of CKD is not done at the primary level – in FMC/FGP, especially in the provinces, due to unavailability of these tests (it should be carried out once a year for diabetic patients).

7. RECOMMENDATIONS

- To carry out interventions at the PHC level to raise patients' awareness about the risk factors associated with CKD (through mass media, patient education schools, engaging patients' associations, HPUs, distributing leaflets for patients, etc.)

- In order to prevent or slow down CKD progression through early and effective treatment of patients with diabetes, hypertension, cardiovascular diseases (coronary heart disease, chronic heart failure, peripheral vascular and cerebrolvascular diseases) it is necessary to carry out a number of preventive interventions at PHC level, including assessment of cardiovascular risk and associated diseases, monitoring of laboratory tests, and perform regular measurement of GFR and ACR for CKD.

- CPG/CP for management of type 1 diabetes have to be developed and introduced at PHC level, CPG for type 2 diabetes has to be revised focusing on early diagnosis and treatment of diabetic nephropathy and risk factors for development and progression of CKD.

- To develop the CPG/CP for diagnosis of bladder infections, chronic glomerulonephritis for PHC level with emphasis on increasing the recognition, early detection, treatment and self-control of CKD.

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