



**BRITISH**

**MEDICAL JOURNAL**



**British Medical Journal**

**Volume 2, No 1., 2022**

**Internet address:** <http://ejournals.id/index.php/bmj>

**E-mail:** [info@ejournals.id](mailto:info@ejournals.id)

Published by British Medical Journal

Issued Bimonthly

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**British Medical Journal** Volume-2, No 1

## **THE SIGNIFICANCE OF CKD RISK FACTORS IN ITS PROGRESSION AT THE LEVEL OF PRIMARY HEALTH CARE**

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**Relevance of the study.** In today's world, many studies are focusing on the development and progression of chronic kidney disease (CKD). According to the World Health Organization, kidney disease is classified as one of the socially significant non-communicable diseases. In the history of medical science at the beginning of the 21st century, the US National Kidney Foundation (NKF) was the first official organization that paid attention to the problem of chronic kidney failure. Numerous studies on the development and determination of the risk of progression, as well as various types of therapy for chronic kidney failure showed that terminological concepts stood as the basis for the development of the concept of chronic kidney disease. The prevalence of CKD is high and is not inferior to the prevalence of such socially significant diseases as chronic heart failure, diabetes mellitus, and hypertension.

One of the problems of timely recognition of chronic kidney disease throughout the world and in our country is the low alertness of primary care physicians in relation to this disease. One of the methods of nephroprotection is not only therapeutic, but also preventive measures, as well as early diagnosis of kidney disease. At the same time, early detection of impaired renal function will help reduce the progression of the disease, disability and mortality of patients. The concept of "CKD progression" is a highly variable value and depends on the underlying, primary disease, its severity, the nature of the course and the presence of additional risk factors. In accordance with the analysis of the literature, it can be concluded that there is a need for research at the level of primary health care for early diagnosis, as well as the prevention of progression and lengthening of the pre-dialysis period of CKD.

The aim of the study was to study and establish the relationship between renal and extrarenal manifestations of CKD and their predictive significance in the progression of the disease in the primary health care setting.

**Material and research methods.** Based on the analysis of literature data, during admission to primary health care out of 500 people from outpatient reception 217 patients with CKD stages 2-4 were selected for the study, the average age of which was  $46.17 \pm 0.63$  years, among them there were 110 men (50.69%) and women 107 (49.31%) and 20 healthy people.

In this study, three stages can be distinguished: stage 1 - during the initial examination, the inclusion of patients in the study, the second stage - the study of changes in the patients' conditions in the studied parameters after 180 days (6 months) months from inclusion in the study, the third stage consisted of studying changes in the studied parameters after 12 months from inclusion in the study.

At the first stage of the study, a comparative analysis of the data from the questionnaire and examination of the patient was carried out. At the same time, patients were divided into 4 comparison groups according to the GFR category of chronic kidney disease according to KDIGO 2012: Group 1 GFR 60-89 ml/min/1.73 m<sup>2</sup> (n=54); group 2 GFR 45-59 ml/min/1.73m<sup>2</sup> (n=53); group 3 GFR 30-44 ml/min/1.73m<sup>2</sup> (n=58) and group 4 GFR 15-29 ml/min/1.73m<sup>2</sup> (n=52), 20 healthy people made up the control group. At the second (n = 217) and third (n = 204) stages, the dynamics of changes in clinical and laboratory data of patients, changes in the cohort of patients, progression and regression of the disease, and analysis of developed complications were studied.

Clinical examination of all patients included: analysis of outpatients using the collection of clinical anamnesis according to the developed questionnaires for the study of patients. The laboratory examination was carried out in the clinical diagnostic laboratory of the primary link-polyclinic and included: complete blood count, biochemical blood test, general urinalysis, which were carried out according to standard methods.

To assess the filtration function of the kidneys, serum concentrations of creatinine and cystatin C, levels of proteinuria (albuminuria), ultrasound examination of the kidneys were studied. The filtration function of the kidneys was assessed by endogenous creatinine clearance with the calculation of glomerular filtration rate (GFR) using the CKD-EPI formulas (2011) for serum creatinine:  $GFR (ml / min / 1.73 m^2) = 175 \times (\text{serum creatinine, } \mu\text{mol} / l / 88.4)^{-1.154} \times (\text{age, years})^{-0.203}$ , for women the result was multiplied by 0.742. The second method for determining the filtration function of the kidneys is the calculation of GFR from the serum concentration of cystatin. The marker was determined in the same blood sample as creatinine. Calculation of GFR by cystatin C using the Stevens L.A. et al. (2008):  $GFR (ml/min/1.73m^2) = 76.7 \times \text{cystatin C} - 1.19$  (using the on-line calculator at <http://nefrosovet.ru/>).

In the course of the study, depending on the initial kidney function, the following were carried out: a comparative analysis of patient examination data to establish a relationship between renal and extrarenal markers in the progression of CKD.

After the end of the observation period and data collection, the results were recorded in the summary tables of the Excel editor for statistical processing. The arithmetic mean, standard error, median were calculated, the significance of the intergroup difference was determined using the Student's t-test for paired and unpaired differences, and in the case of multiple comparisons, using the Bonferroni correction. When assessing qualitative traits by frequency of occurrence in groups with the calculation of intergroup differences, the Chi-squared test was used.

**Results and its discussion.** During the study, during repeated examinations, some changes were noted in the cohort of observed patients. When examining patients after 6 months, it was noted: in the study were under observation: men 110 (50.69%), women 107 (49.31%), cardiovascular complications were detected in 7 (3.26%) patients, terminal renal failure (ESRD) in 4 (1.84%) patients. Lethal

outcomes were detected in 8 (3.69%) patients, of which 6 (2.76%) were men, 2 (0.92%) were women. A lethal outcome from cardiovascular complications was observed in 6 (2.76%) patients, and from ESRD in 2 (0.92%). At stage 3, the number of observed patients was 208 (in 12 months) people, of which 103 (49.52%) men, 105 (50.48%) women, while cardiovascular complications were detected in 9 (4.33%) patients, ESRD in 1 (0.48%) patient. 1 (0.48%) patient withdrew from the study due to moving to another city (Table 1).

A clinical and laboratory examination was carried out, correction of antihypertensive therapy was carried out, extrarenal manifestations were studied. Lethal outcomes were detected in 5 (2.40%) patients, including 4 (1.92%) men and 1 (0.48%) women. Lethal outcome from cardiovascular complications (CVS) 4 (1.92%) and ESRD 1 (0.48%).

Table 1. Overall results of a year-long study in three stages.

Outcomes	initial n=217 (%)	After 6 months, n=217 (%)	After 12 months n=208(%)
Under observation	217 (100%)	217 (100%)	208 (100%)
Men	110 (50,7%)	110 (50,69%)	103 (49,52%)
Women	107 (49,3%)	107 (49,31%)	105 (50,48%)
Died:	-	9(4,15%)	5(2,40%)
Men		7(3,2%) /	4(1,92%) /
Women		2(0,92%)	1(0,48%)
MTR	-	7(3,2%)	9(4,33%)
Died from MTR	-	6(2,8%)	4(1,92%)
ESRD	-	4(1,84%)	1(0,48%)
Death from ESRD	-	3(1,38%)	1(0,48%)
Dropped out of the study	-	-	1(0,48%)

During the study of patients after 6 and 12 months, a redistribution of patients according to the stages of CKD was found in the direction of progression. After 6 months, there is a redistribution of 17 patients of the first group (CKD stage 2) to the second (3Ast - 10 patients), the third group (3Bst - 3 patients) and the 4th group (4st - 4 patients). It is also noted that 3 patients switched from 3Ast to 3Bst. And 8 patients from 3B to stage 4. At the same time, 9 patients died from complications of CVS and ESRD (Table 2).

Table 2. Distribution of patients by groups after 6 and 12 months

Stages	1 stage	6 months		12months	
		Number of patients n=208	Died n=9	Number of patients	Died n=5
1gr -2st CKD	n=54	n=37(54-17)	-	n=24(37-13)	-
2g - 3Ast CKD	n=53	n=58 (53+10-3-2)	2	n=54 (58+5-8-1)	1
3gr – 3Vst CKD	n=58	n=54(58+3+3-8-2)	2	n=52 (54+6+3-10-1)	1
4gr - 4st CKD	n=52	n=59(52+4+8-5)	5	n=73 (55+2+5+10-	3

After 12 months, there is a redistribution of 13 patients of the first group (stage 2 of CKD) to the second (3Ast - 5 patients), the third group (3Bst - 6 patients) and the 4th group (4th stage - 2 patients). At the same time, it was also noted that 3 and 5 patients moved from 3A to 3B and 4st, respectively, and 10 patients moved from 3B to 4st (Fig. 1). Thus, in 59 patients progression of the stage of the disease was noted, which amounted to 27.19% of the entire sample of patients.

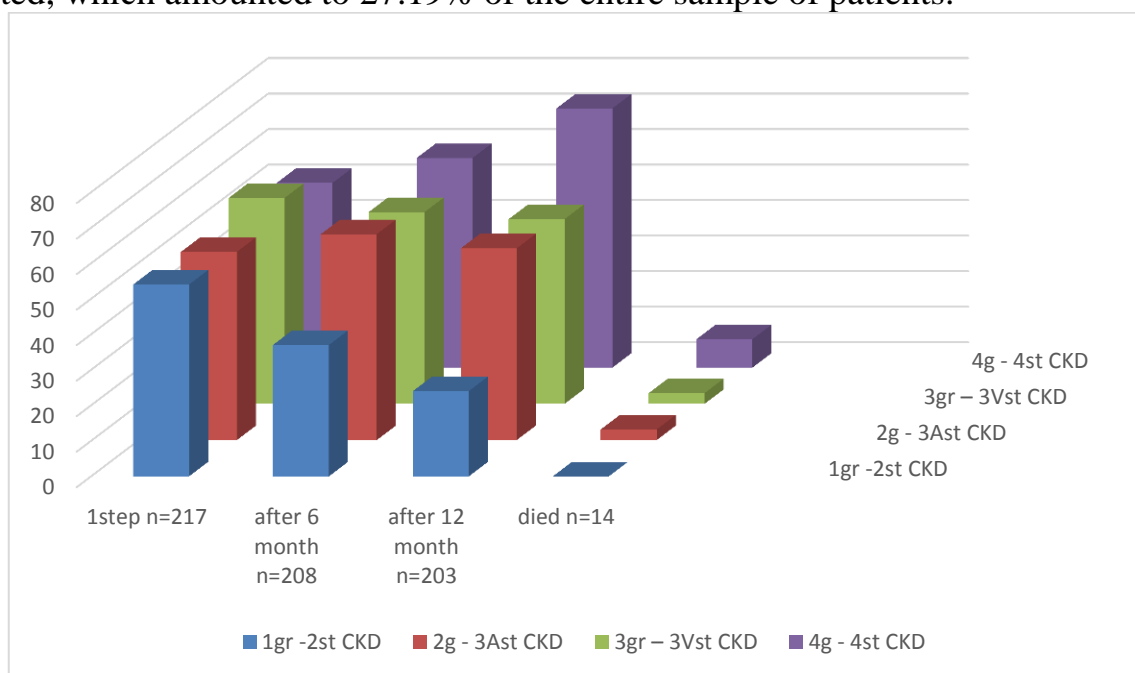


Fig.1. Redistribution of patients by groups and stage of CKD during the study.

This observation indicates a steady progression of the disease, therefore, early diagnosis is necessary, which will help in reducing the rate of progression of patients with CKD and delay end-stage renal failure.

As a result of the study, progression of the CKD stage was noted in 59 patients. When analyzing the prevalence of extrarenal manifestations and their predictive significance in this category of patients, a high relative risk of progression was noted in those over 48 years of age (6.27 times), anemia with a hemoglobin level of less than 102 g/l (6.4 times), arterial hypertension over 150/80 mm Hg st (6.09 times), smoking - 5.20 times, urea with an indicator of more than 8 mmol / l - 11.32 times and male sex - 4.24 times.

Table 3. Extrarenal manifestations of CKD progression and their predictive significance

Prognostic indicator of progression (median used)	Progression in the presence of a factor (%)	Progression with missing factor (%)	Chi squared (validity)	Relative risk of progression in the presence of a factor
Age, over 48	50/102 (49,02%)	9/115 (7,82%)	46.335 (p<0,001)	6,27
Gender, male	48/110(43,63 %)	11/107 (10,28%)	30.484(p<0,001)	4,24
hereditary predisposition	21/32 (65,62%)	38/185 (20,54%)	28.011(p<0,001)	3,19
Gr of blood, 3-4	44/113 (38,94%)	15/104 (14,42%)	16.441 (p<0,001)	2,70
Smoking	30/36 (83,33%)	29/181 (16,02%)	68.724 (p<0,001)	5,20
	16/31 (51,61%)	15/186 (8,06%)	10.898 (p<0,01)	6,40
Hemoglobin less than 102g/l	51/111 (45,95%)	8/106 (7,55%)	40.384 (p<0,001)	6,09
AH, more than 150/80 mm Hg	52/86 (60,46%)	7/131 (5,34 %)	79,683 (p<0,001)	11,32
Urea more than 8 mmol/l	43/98 (43,88%)	16/119 (13,45%)	25.141 (p<0,001)	3,26

Other factors also had a high risk of progression. At the same time, practically all of them have a significant Chi-squared test (using the median): one of the most significant was urea over 8 mmol/l Chi<sup>2</sup>=79.683 (p<0.001), smoking Chi<sup>2</sup>=68.724 (p<0.001), age over 48 years Chi<sup>2</sup>= 46.335 (p<0.001), as well as blood pressure over 150/80 mm Hg. Art. Chi<sup>2</sup>=40.384 (p<0.001).

Thus, the identification of the main risk factors and their predictive significance in the progression of CKD at the level of primary health care physicians will make it possible to identify a group of patients at increased risk for CKD prediction.

**Conclusions.** Risk factors in the progression of CKD with high predictive significance are age over 48 years (relative risk increases by 6.27 times by stage 4), anemia with a hemoglobin level below 100 g/l (relative risk increases by 6.40 times

by stage 4), AH more than 150/80 mm Hg (relative risk increases by 6.09 times by stage 4), smoking (relative risk increases by 5.20 times by stage 4), urea (by 11.32 times), and also these indicators had high criterion  $\chi^2$

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