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ACUTE AND CHRONIC ENCEPHALOPATHIES AND OTHER VASCULAR CATASTROPHES IN PATIENTS WITH CKD AND THEIR RELATIONSHIP WITH CYSTATIN C

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Abstract:

Vascular diseases of the brain are one of the topical issues of modern medicine. In most developed countries, vascular diseases of the brain account for up to 15% of the total mortality. At the same time, the number of not only strokes, but also encephalopathies is steadily increasing.. In recent years, special attention has been paid to encephalopathies developing as a result of renal pathology, since kidney diseases, namely Chronic kidney disease (CKD) is a huge socio-economic problem that leads to cerebral complications, with a significant deterioration in the quality of life, a sharp loss of working capacity, and a high percentage of mortality.

Keywords: CKD, vascular diseases, encephalopathy, PRESS syndrome

INTRODUCTION: The problem of cerebrovascular diseases (CVD) and their most threatening manifestation of stroke has extremely high medical and social significance in Uzbekistan, where the incidence of cerebral stroke ranges from 0.9 to 1.5 per 1000 population and the frequency of acute cerebral circulatory disorders tends to increase (Majidov N.M., 1990, 2001; Rakhimdzhanov A.R., 1997, 2000; Gafurov B.G., 2000, 2002, 2004; Asadullaev M.M. et al., 2002, 2003; Kilichev I.A., 1999; Mirjuraev E.M., 1999, 2000; Akhmedov O.T. Kholmirzaev P.H. et al., 2002; Khodjaev A.I. et al., 2001; Majidova E.N.. et al., 2011). At the same time, the number of not only strokes, but also encephalopathies is steadily increasing. Encephalopathy is a nonspecific brain lesion that occurs under the influence of various pathological factors: toxic, traumatic, metabolic, vascular, infectious. Consequently, regardless of the cause, encephalopathy is accompanied by progressive focal and cerebral neurological disorders, neuropsychological and mental symptoms and cognitive impairments. In recent years, special attention has been paid to encephalopathies developing as a result of chronic kidney disease (CKD). In numerous large-scale studies (ACCOMPLISH, ADVANCE, ALTITUDE, CARRESS-HF, ONTARGET, ROADMAP 2010) it was confirmed that CKD has a fairly high prevalence (10-15% of the population) and occupies one of the leading places in the overall structure of mortality and morbidity of the population, along with diseases such as coronary heart disease (CHD), hypertension, diabetes mellitus [Ronco et al., 2008.; Ronco et al., 2010]. GFR (glomerular filtration rate) is an indicator of renal function and its decrease is an independent predictor of an unfavorable outcome in AI (ischemic stroke) and GI (hemorrhagic stroke), associated with higher mortality (Yahalom G. Et al., 2009). In addition, there is another important predictor of the development of CVD - Cystatin C. Cystatin C is an inhibitor of cysteine protease, it is a highly sensitive biomarker of kidney damage.

A prospective cohort study in 2009 showed that elevated biomarkers, including serum creatinine (SCR) and cystatin C (CYS C), were independent predictors of mortality and poor prognosis in cerebrovascular disorders in patients with CKD.[1]

According to literature data, an increase in the concentration of cystatin C serves as an independent risk factor for the development of severe atherosclerotic lesions of the main arteries feeding the brain. The content of cystatin C in patients with end-stage renal insufficiency, who were first admitted to program hemodialysis, on average exceeded the norm by 2-2.5 times [2]. The role of cystatin C as a risk factor for cerebral complications was shown in the work of N. Hashimoto et al. [3], in which researchers, having studied echocardiogram data in patients with stable and unstable atrial fibrillation, found that a calculated analysis using cystatin C in blood plasma may allow predicting cerebral disorders at the predialysis stage of CKD.

OBJECTIVE:

To study the frequency of development and clinical manifestations of acute and chronic encephalopathies and other acute vascular catastrophes in CKD and the relationship of their development with cystatin C

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MATERIALS AND METHODS OF RESEARCH:
Under our supervision there were 101 patients diagnosed with CKD who received inpatient treatment and program hemodialysis in the multidisciplinary clinic of the center for the development of professional qualifications of medical workers. CKD was diagnosed based on the KDIGO (Kidney Disease: Improving Global Outcomes) criteria developed in 2002 [4]. KDIGO, 2012. Clinical Practice Guidelines for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl. 2013;3:1-136.

According to the Classification of the International Classification of Diseases 10 (N18), all patients are divided into 3 groups:
1. Predialysis patients (N 18.1 18.2 18.3 18.4) SLE: From 1>90; From 2 60-89; 3a 45-59; From 3 b 30-44; From 4 15-29. The total number of patients is 28 (27.7%).
2. Patients on programmed hemodialysis (N 18.5) GFR <15.The total number of patients is 30 (29.7%).
3. Patients after kidney transplantation (Z94.0) – 43 patients (42.5%).

The distribution of patients by gender and age gradation is shown in Table №. 1

Table №. 1

Researchgroups	**Total (n)**	**gender**				**Averageage (M±m)**
		Men		Women		
		Number	%	Number	%	
Controlgroup	30	15	50	15	50	41,8±0,9
Predialysispatients	28	15	53,5	13	46,6	56,1±12,1
Patients on programmed hemodialysis	30	18	60	12	40	53,1±13,3
Patients after kidney transplantation	43	33	76,7	10	23,2	34,8±9,3

Of these, 66 (65.3%) are men, and 35 (34.3%) are women. The average age of all patients was 46.2±15.01 years, while the average age of men was 42.2±12 years, the average age of women was 39.3±11.5 years. The control group included 30 practically healthy people (average age – 41.3 years (20-66 years)), of which 15 were men (50%), 15 women (50%). From this table it can be seen that male patients predominate in each of the groups

RESULTS OF THE STUDY: The frequency of encephalopathy and other acute vascular catastrophes in patients with CKD

Complications	**Predialysispatients N=28**		**Patients on programmed hemodialysis N=30**		**Patients after kidney transplantation N=43**	
	absoluteval ue	**%**	**absoluteval ue**	**%**	**absoluteval ue**	**%**
Hypertensiveencephalopathy	**15**	**53,5**	**6**	**20**	**8**	**18,6**
Uremicencephalopathy	**6**	**21,4**	**10**	**33,3**	**10**	**23**
Mixedencephalopathy	**0**	**0**	**6**	**20**	**6**	**14**
Transientischemicattack	**4**	**14,2**	**2**	**6,6**	**4**	**9,3**
Ischemicstroke	**3**	**10,7**	**2**	**6,6**	**0**	**0**

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Hemorrhagicstroke	**0**	**0**	**1**	**3,3**	**0**	**0**
PRESS syndrome	**0**	**0**	**4**	**13, 3**	**2**	**4,6**

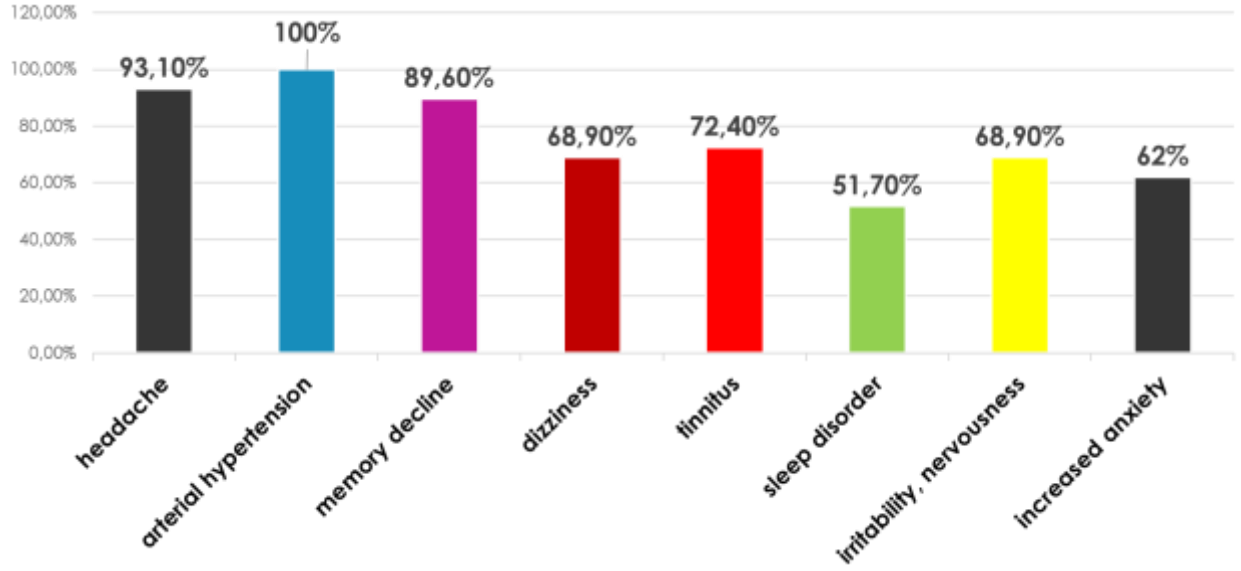
At the predialysis stage of CKD (C1-C4), when the predominant complaint of patients was hypertension (arterial hypertension) in a significantly larger number of 15 (53.5%) (p=0.001), developed a hypertensive encephalopathy. Uremic encephalopathy was diagnosed in 6 (21.4%) patients who were at stage C4 of CKD and had high urea and creatinine levels. There were also cases of acute conditions, 4 (14.2%) patients developed TIA, which resolved within a few hours. 3 (10.7%) were diagnosed with ischemic stroke. All patients with acute conditions were transferred to the intensive care unit.

In the group of patients who are on programmed hemodialysis, where patients are more concerned about the symptoms of uremic intoxication, there were significantly more patients with uremic encephalopathy 10(33.3%) (p=0.001), Hypertensive encephalopathy and mixed encephalopathy were found in almost the same number 6 (20%) and 6 (20%) accordingly. PRESS syndrome 4 (13.3%) was relatively more common compared to ischemic stroke 2 (6.6%); as well as with TIA 2(6.6%). There was also 1 case ofhemorrhagic stroke in a patient who was on routine hemodialysis for a long period of time and had a history of atrial fibrillation. The number of patients with chronic encephalopathy (hypertensive 8 (18.6%); uremic 10 (23.3%); mixed 6 (14%) acute encephalopathy 2 (4.7%) and acute cerebrovascular (TIA 4 (9.3%) significantly (p=0.001) decreased in the group after kidney transplantation. The clinical course of such conditions proceeds more favorably.

The main parameters of subjective symptoms of certain types of encephalopathy

All patients with hypertensive encephalopathy (see diagram No. 1)29 (100%) complained of an increase in blood pressure, and hypertension was difficult to correct with antihypertensive drugs. Headaches were also one of the main complaints (93.1%), and half of the patients associated headache with an increase in blood pressure and nervous overstrain and noted a decrease in pain intensity with a decrease in blood pressure. The pains were of a compressive, pulsating nature, mainly localized in the occipital and parietal-occipital regions. 89.6% of patients complained of memory loss. 72.4% of patients were concerned about dizziness. Dizziness was often systemic in nature, and more often disturbed when changing the patient's posture, for example, when the patient abruptly got up from the pastel. Also, 68.9% of patients were concerned about irritability and nervousness; 62% increased anxiety; 51.7% sleep disorder

Diagram № 1



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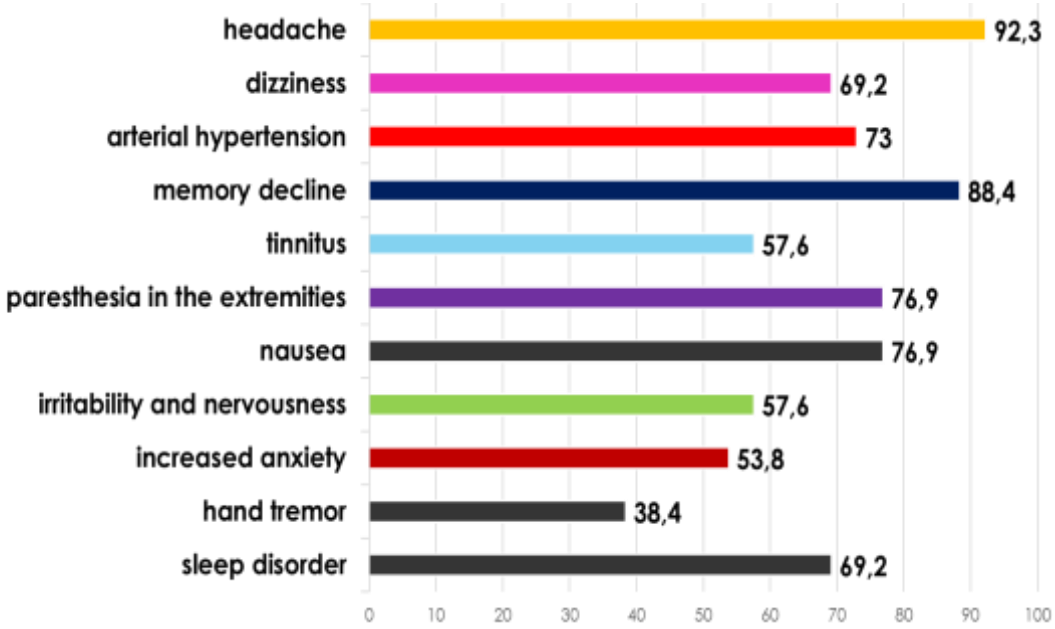
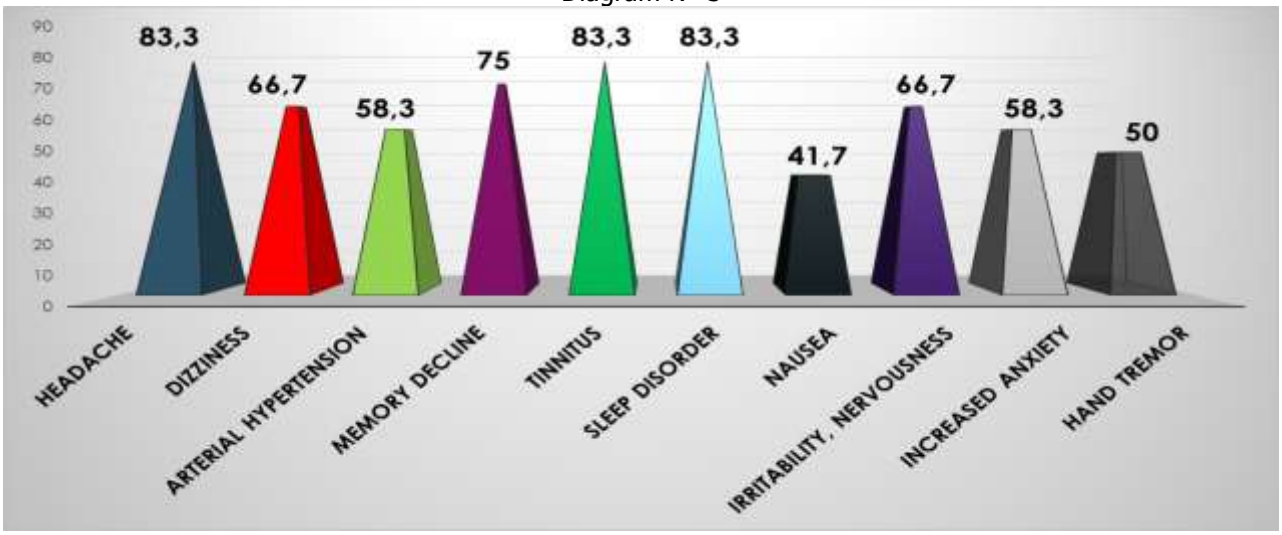
In uremic encephalopathy (see diagram No. 2)the main symptoms were signs of intoxication syndrome in the form of: aching headaches of a chronic character, which bothered patients in 92.3% of cases. Memory loss was complained of in 88.4% of cases. Also, patients were concerned about unpleasant sensations in the legs in the form of burning sensation and the feeling of moving their legs all the time (restless legs syndrome) in 76.9%, which largely led to sleep disorder in 69.2%. Hypertension was observed in 73% of cases, 69.2% dizziness, 53.8% increased anxiety, 57.6% irritability and nervousness, 57.6% tinnitus, 38.4% nausea.

DiagramN№2



With mixed encephalopathy (see diagram no.3) the brain is under the influence of several damaging factors. Also, one of the main complaints with this type of encephalopathy was headache, which was observed in 83.3%. In the same percentage, 83.3% of patients were disturbed by tinnitus and sleep disorder. More than a quarter of 75.6% of patients complained of memory loss. Irritability, nervousness and dizziness were present in the same number of patients 66.7%. An increase in blood pressure was observed at 58.3; increased anxiety at 58.3%; tremor of the hands at 50%; 41.7% nausea.

Diagram № 3



With PRESS syndrome (see diagram No. 4), as with other encephalopathies, the prevailing symptoms were headache (100%) (p=0.001), hypertension (100%) (p=0.001), while the headache was acute, thunderous.

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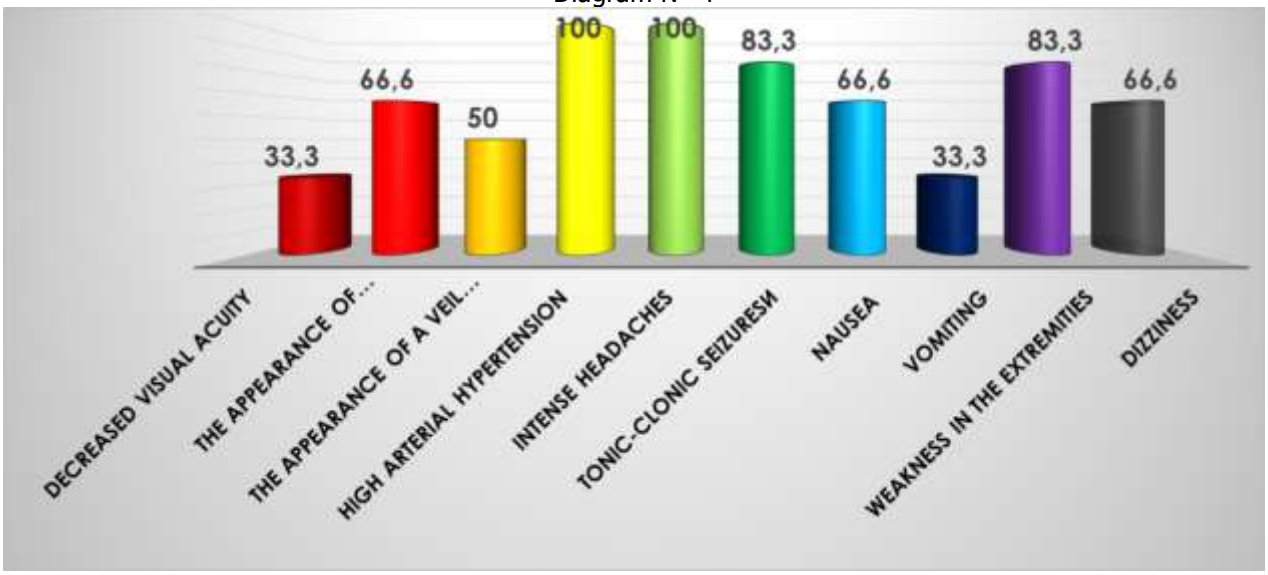
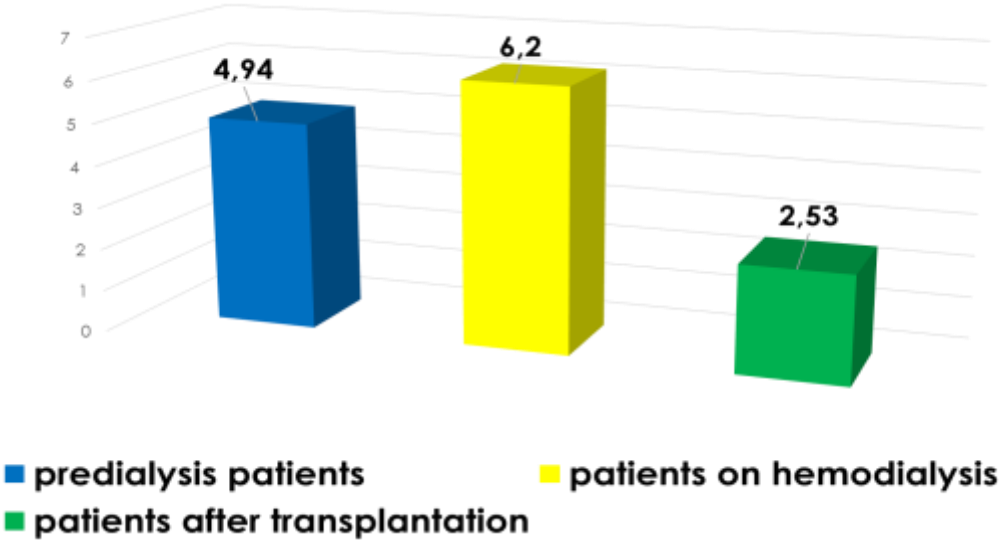
Symptoms such as tonic-clonic convulsions (83.3%), paresis of the extremities (83.3%); visual disturbances in the form of decreased visual acuity (50%); the appearance of flickering cattle in front of the eyes (66.6%) and veils in front of the eyes (50%) of cases were also added. 66% of patients were concerned about nausea; 33.3 vomiting; 66.6 dizziness.

Diagram № 4



All patients under our supervision were determined in the blood serum of the level of cystatin Using the method of enzyme immunoassay. Cystatin C levels depending on the stage of the disease: The average value of cystatin C in the group of patients at the predialysis stage of CKD was 4.94±0.97, in the group of patients receiving programmed hemodialysis, this value was higher, indicating a progression of renal function decline-6.2±1.97, in the group of patients who underwent kidney transplantation, the average value of Cystatin C was equal to 2.53±1.45.



In addition, the level of cystatin C was studied depending on the complications that developed. Thus, in patients with enceph5alopathies, the average level of cystatin C was m=4.4±0.75 (p=0.001); in patients with TIA ischemic stroke and PRESS syndrome m=6.1±1.2 (p=0.001); in patients with hemorrhagic strokem=6.9±1.7 (p=0.001)..

It was found that all patients had an increase in the level of cystatin C.

In patients with encephalopathies, the level of cystatin C in serum was lower compared to TIA PRESS and

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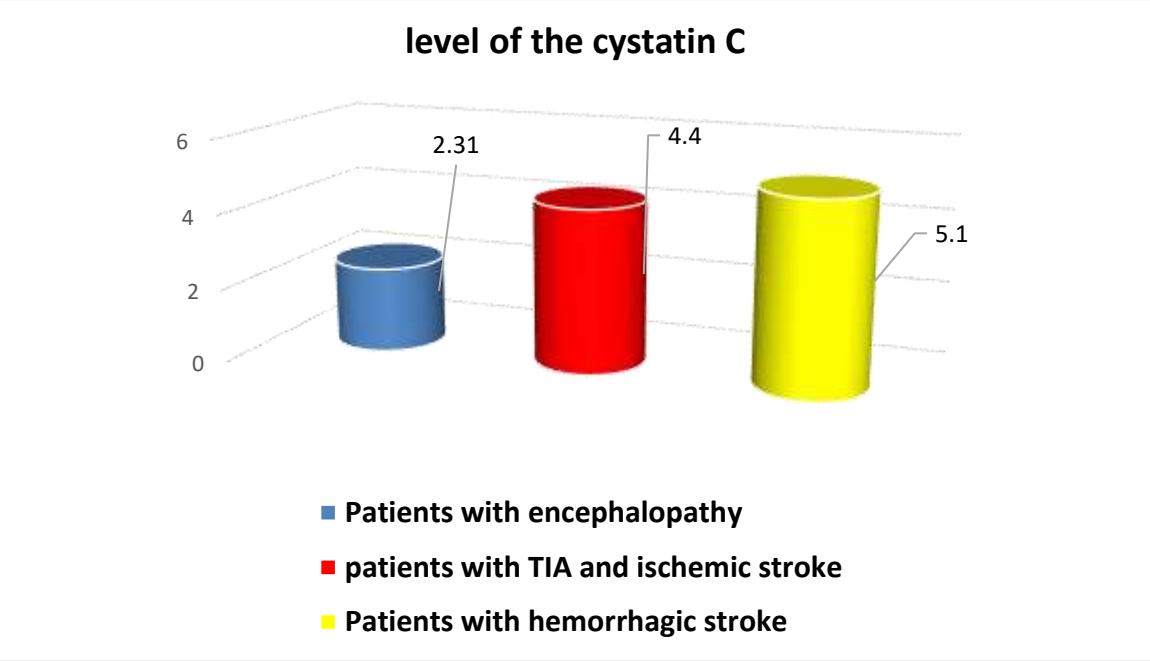
ischemic stroke , the highest indicator was in patients with hemorrhagic stroke



CONCLUSIONS:

According to our data, complications from the central nervous system (CNS) accompany almost all patients with CKD, regardless of the stage of the disease. Studies show that for each stage of CKD, complications for this period are specific, depending on the predominant effect of the damaging factor. Patients with CKD had chronic complications in the form of hypertensive encephalopathy, uremic encephalopathy and mixed encephalopathy; and also at the dialysis stage of CKD when mechanisms such as oxidative stress, arterial hypertension, impaired mineral metabolism and subsequent vascular calcification, the formation of vascular access and the use of anticoagulant therapy during a hemodialysis session increase the risk of acute vascular catastrophes: TIA, ischemic stroke , hemorrhagic stroke, PRESS syndrome. Kidney transplantation partially restores renal function, improves the condition of patients and reduces the risk of vascular complications. However, due to the possible development of recurrent nephropathy, lifelong use of GCS and immunosuppressants, untimely treatment, leave patients after transplantation at an increased risk of encephalopathy compared to the general population
According to the results of our study, an increase in the level of cystatin C in the serum of patients with CKD has an adverse effect and prognosis on the development and course of chronic and acute forms of encephalopathy. It was revealed that all patients had significantly high levels of cystatin C, compared with reference values (ref.values. 0.40-1.20 mg/l). Based on this, it can be assumed that cystatin C is not only a biomarker of the progression of kidney damage, but also a predictor of the development of acute and chronic forms of encephalopathy and other acute vascular catastrophes.

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