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Antoniv A. A.

KIDNEYS FUNCTIONAL STATUS AND INFLAMMATION ACTIVITY IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND NONALCOHOLIC STEATOHEPATITIS ON THE BACKGROUND OF OBESITY, THEIR RELATIONSHIP WITH THE FUNCTIONAL STATE OF THE ENDOTHELIUM, ENDOGENOUS INTOXICATION SYNDROME AND OXIDATIVE STRESS

Higher State Educational Institution of Ukraine «Bukovinian State Medical University» (Chernivtsi)
antonivalona@ukr.net

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Introduction. Comorbidity of chronic kidney disease (CKD) with nonalcoholic steatohepatitis (NASH) in obese patients has a significant increase in the frequency of this type of comorbidity (15-30%) [1,2,3,4,5]. CKD affects up to 8% of the adult population of the world, and its prevalence increases significantly in the category of the elderly (up to 38%) that suffers from diseases such as obesity, metabolic syndrome, diabetes, arterial hypertension and smoking [6,7,8,9,10,11]. In our previous studies, it was found that the clinical course of NASH significantly impairs the comorbidity of CKD, which, in progress, is accompanied by an increasing degree of endogenous intoxication, oxidative and nitrosatitistic stress against the suppression of the antioxidant defense system and the natural system of detoxification, lipid distress syndrome, functional state of the endothelium, disorders of microcirculation, peripheral and organ blood circulation, growing fatty degeneration of hepatocytes (steatosis), cytolytic and cholestatic syndromes, activation of mesenchymal inflammation with the activation of biosynthesis of protein, carbohydrate-protein components of connective tissue extracellular matrix of the liver, kidneys and myocardium with development of their diffuse fibrosis [12,13]. At the same time, the degree of these disorders and features of the functional state of the kidneys for the comorbidity of the CKD with NASH have not been established yet.

The aim of the study – to establish the probable effect of the comorbid flow of nonalcoholic steatohepatitis on the functional state of the kidneys and the activity of kidney inflammation in patients with chronic kidney disease (pyelonephritis) of the I-III stage and to determine the pathogenetic role of endothelial dysfunction, lipid distress syndrome, endotoxicosis and oxidative stress in mechanisms of their mutual burden.

Object and methods of research. 240 patients with CKD (chronic bilateral peylonephritis) of the I-III stage were examined, 145 of which had comorbid NASH and obesity of the 1st degree (group 1), 95 patients were diagnosed with CKD I-III stages without comorbid pathology. Depending on the stage of the CKD, both groups were divided as follows: 1st group – into 3 subgroups: 51 patients with 1st stage CKD, 53 patients with 2nd stage CKD, 41 patients with 3rd stage CKD. The 2nd group was divided into 3 subgroups: 32 patients with 1st stage CKD, 35 patients with 2nd stage CKD, 28 patients with 3rd stage CKD. The control group consisted of 30 practically healthy persons (PHPs). The average age of patients was (49.8 ± 5.8) years. The diagnosis of NASH was established in accordance with the unified clinical protocol, approved by the order of the Ministry of Health of Ukraine No. 826 from 06.11.2014, in the presence of criteria for the exclusion of chronic diffuse liver disease of the viral, hereditary, autoimmune or medicinal genesis as causes of cholestatic or cytolytic syndromes, as well as the results of the USG survey. Diagnosis of obesity was established on the basis of calculating the body mass index (BMI) by the formula of Kettle: BMI = body weight (kg) / height2 (m). On the basis of an increase in BMI of 30-34.9 kg / m2, 1st degree it was established, with BMI 35-39.9 kg / m2 – 2nd degree, BMI above 40 kg / m2 – 3rd degree obesity. The diagnosis of CKD was carried out in accordance with the recommendations of the clinical guidelines of the State Institute "Institute of Nephrology, NAMS of Ukraine" (2012). The study included patients with CKD I-III stage without a nephrotic syndrome with chronic uncomplicated pyelonephritis in the phase of exacerbation. The glomerular filtration rate (GFR) was investigated by creatinine clearance, calculated using the Cockroft-Gaulta formula, as well as by the universal automatic calculator CKD-EPI. In addition to standard methods of research (blood creatinine, urea, proteinuria, ionograms, urinalysis, urine analysis by the methods of Nechyporenko, Zimnytsky, urine culture with the definition of the pathogen, its amount and sensitivity to antibiotics, etc.) we studied the intensity of oxidative stress – by malondialdehyde (MA) content in the blood, intensity of oxidative modification of proteins (OMP) – by the content of aldehyde- and ketone dinitrophenylhydrazones neutral (AKDNPH N) and basic (AKDNPH B). The degree of endogenous intoxication was studied based on the content of the mediumsmolecular peptides (MMP) in the blood and the activity of arginase. The lipid spectrum of blood was studied by the contents of common lipids in blood; total cholesterol (TC), low and high density cholesterol, lipoproteins and triacylglycerol (TG) using a set of reagents of the company Danish LTD (Lviv). The functional state of the endothelium and its regulation were studied in terms of the content of nitrogen monoxide (stable NO metabolites: nitrite/nitrate), hydrogen sulfide (H2S), endothelin-1,

Table 1.

Characteristics of the intensity of the inflammatory process in patients with CKD and NASH, obesity and CKD without comorbidity depending on the stage of the CKD

Indicators, units measurement	PHPs (n=30)	Groups of patients surveyed					
		Group 1 (NASH, CKD) (n=145)			Group 2 (CKD) (n=95)		
		CKD I st. (n=51)	CKD II st., (n=53)	CKD III st. (n=41)	CKD I st., (n=32)	CKD II st., (n=35)	CKD III st. (n=28)
Number of leukocytes / 1 ml	753,0± 23,5	5239,0± 101,4 *	6023,4± 138,5 *	8342,4± 246,3 *	4316,5± 122,1 */**	5194,2± 217,9 */**	6149,3± 269,4 */**
Number of erythrocytes / 1 ml	214,3± 12,1	1223,1± 25,1 *	1497,3± 31,7 *	1588,1± 42,0 *	989,1± 22,8 */**	1195,0± 33,2 */**	1283,5± 38,2 */**
Amount of protein (g/day)	0,02± 0,001	1,5± 0,02*	1,7± 0,01*	1,9± 0,03 *	1,4± 0,01 */**	1,6± 0,03 */**	1,7± 0,02 */**
Number of cylinders	2,5± 0,2	12,2± 0,4 *	15,7± 0,5 *	19,6± 0,6 *	9,1± 0,5 */**	11,0± 0,4 */**	17,3± 0,7 */**
Number of bacteria / ml	0,56x 10^2±0,1	4,8x 10^5±0,2*	6,9x 10^6±0,3*	4,2x 10^7±0,2*	2,2x 10^4±0,3*/**	4,8x 10^5±1,2*/**	5,7x 10^6±0,6*/**

Notes: 1. * – changes are probable compared to the index in the PHPs (p <0,05); ** ** – changes are probable in comparison with the indicator in the group of patients of the corresponding stage of CKD with a comorbid flow of NASH and obesity (p <0,05).

homocysteine, cytokeratin-18, induction and endothelial NO synthase activity (iNOS, eNOS) using enzyme-linked immunosorbent assay (ELISA).

The statistical analysis of the results was carried out in accordance with the type of research carried out and the types of numerical data that were obtained. Distribution normality was verified using Liliefors, Shapiro-Uilka tests and the direct visual evaluation of eigenvalues distribution histograms. Quantitative indices having a normal distribution are represented as mean (M) ± standard deviation (S). Discrete values are presented in the form of absolute and relative frequencies (percentage of observations to the total number of surveyed). For comparisons of data that had a normal distribution pattern, parametric tests were used to estimate the Student's t-criterion, Fisher's F-criterion. In the case of abnormal distribution, the median test, Mann-Whitney Rank U-Score, and Wilcox's T-criterion (in the case of dependent groups) were used for multiple comparison. Statistica for Windows version 8.0 (Stat Soft inc., USA), Microsoft Excel 2007 (Microsoft, USA) software packages were used for statistical and graphical analysis of the obtained results.

Results of the research and their discussion. In the study of indicators of inflammatory process activity in patients with CKD and comorbidity with NASH in comparison with the isolated course of CKD, the following data were obtained **(table 1).** When comparing the number of leukocytes in urine analysis by Nechyporenko method, a significant difference in the indicators was established. So, in patients with CKD I st. in group 1 indicators exceeded the data in the PHPs by 6.9 times (p <0,05), and in 2 groups – by 5,7 times (p <0,05) **(table 1).** In patients with CKD II st. in group 1, the number of leukocytes in 1 ml of urine exceeded the normative by 7.9 times against the increase in 6.8 times in group 2 (p <0,05). In patients with CKD III st. the content of leukocytes in the urine in patients of group 1 exceeded the normal values by 11.1 times (p <0,05), in group 2 – by 8,2 times (p <0,05), in all cases with the probable difference between the groups (p <0.05). When comparing the number of erythrocytes in the analysis of urine by Nechyporenko method we found that in patients with CKD 1 st. in group 1 exceeded the data in the PHPs by 5.7 times (p <0,05), and in group 2 – by 4,6 times (p <0,05) **(table 1).** In patients with CKD of the II st. in group 1 the content of red blood cells exceeded the normal values by 6.5 times (p <0,05). In patients with CKD of the III st. the content of red blood cells in patients in group 1 exceeded the normal values by 7.4 times (p <0,05), in group 2 – by 6,0 times (p <0,05), in all cases with a probable difference between the groups (p <0.05).

Analysis of the daily proteinuria showed a significant difference between the comparison groups **(table 1).** At patients with CKD I st. in group 1 exceeded the data in PHPs by 7.5 times (p <0,05), and in group 2 – by 7,0 times (p <0,05). In patients with CKD II st. in group 1 of proteinuria exceeded the index in the PHPs by 8.5 times against the increase in 8.0 times in group 2 (p <0.05). In patients with CKD of the III st. urine protein loss in group 1 exceeded the norm by 9.5 times (p <0,05), in group 2 – by 8,5 times (p <0,05), in all cases with a probable difference between the groups (p <0.05).

Analysis of indicators of the functional state of the kidneys showed that the creatinine content in the blood of 1st and 2nd group patients of CKD I st. statistically significantly different. Thus, in patients of group 1, the indicator exceeded the data in the PHPs by 1.5 times (p <0,05), in group 2 – in 1,3 times (p <0,05) **(table 2).** In patients with CKD II st. In group 1, the creatinine content exceeded the index in PHPs by 1.7 times against 1.5 times in group 2 (p <0.05). Accordingly, in patients with CKD of the III st. the content of creatinine in patients with group 1 exceeded the data in PHPs by 2.3 times (p <0.05), in group 2 – by 1.9 times (p <0.05), in all cases with the probable difference between groups (p <0.05) **(table 2).** Thus, comorbidity with NASH significantly affects the functional parameters of the state of the kidneys, in particular, their nitrogen-containing function. This position is confirmed by the obtained data on the content of urea in the comparative aspect between the groups **(table 2).** Thus, the urea content in blood in pa-

Table 2.

Indicators of the functional state of the kidneys in patients with CKD and NASH, obesity, patients with CKD depending on the stage of CKD (M ± m)

Indicators, units measurement	PHPs (n=30)	Groups of patients surveyed					
		Group 1 (NASH, CKD) (n=145)			Group 1 (NASH, CKD) (n=145)		
		XXH I ст., (n=51)	XXH II ст., (n=53)	XXH III ст., (n=41)	XXH I ст., (n=32)	XXH II ст., (n=35)	XXH III ст., (n=28)
Creatinine, µmol / l	75,0± 2,0	113,2± 2,2 *	125,2± 1,4 *	169,2± 2,5 *	101,2± 2,3 */**	114,2± 1,9 */**	143,2± 2,4 */**
Urea, mmol / l	3,8± 0,1	9,0± 0,3 *	9,5± 0,1 *	10,9± 0,2 *	8,5± 0,4 *	9,0± 0,1 */**	9,5± 0,2 */**
Albumin, g/l	40,2± 1,3	32,2± 0,8 *	27,2± 0,5 *	26,3± 0,4 *	33,9± 1,0 *	29,5± 0,3 */**	28,0± 0,4 */**
Creatinine Clearance ml/ min	102,2± 2,6	90,0± 1,2 *	62,0± 1,1 *	45,0± 0,7 *	95,0± 1,5 *	76,0± 1,0 */**	57,0± 0,9 */**
GFR CKD-EPI, ml/ min/1,72m^2	101,2± 1,6	68,0± 1,3 *	54,0± 1,0 *	37,0± 0,6 *	77,0± 1,2 */**	64,0± 1,2 */**	46,0± 0,7 */**

Notes: 1. * – changes are probable compared to the index in the PHPs (p <0,05); ** ** – changes are probable in comparison with the indicator in the group of patients of the corresponding stage of CKD with a comorbid flow of NASH and obesity (p <0,05).

tients with CKD I st. exceeded the indicators in PHPs, respectively, in 1st and 2nd group – in 2,4 and 2,2 times (p <0,05). In patients with CKD II st. in group 1 the urea content exceeded the index in PHPs by 2.5 times compared with 2.4 times in group 2 (p <0.05). Accordingly, in patients with CKD of the III st. the content of urea in patients with group 1 exceeded the data in the PHPs by 2.9 times (p <0.05), in group 2 – by 2.5 times (p <0.05), with the presence of a probable difference between the groups (p <0.05).

As a result of the established changes, there was a significant decrease in the GFR for creatinine clearance by the Cockroft-Gault formula and calculated by the CKD-EPI **(table 2).** Thus, the indicator of clearance of creatinine by the Cockroft-Gaulta formula in patients with CKD I st. was lower than that in PHPs only in group 1 patients (11.8%) (p <0.05); in patients of the group 2, changes were unlikely and no significant difference was found between the groups (p> 0.05). In patients with CKD II st. In group 1, the creatinine clearance score was lower than the PHPs by 39.2% versus a decrease of 25.5% in group 2 (p <0.05) with a confirmation of statistically significant difference between the groups (p <0.05). At the same time, in patients with CKD III st. the rate of creatinine clearance in patients in group 1 was lower than the normative at 55.9% (p <0.05), in group 2 – by 44.1% (p <0.05), with the presence of a probable difference between patients with a combined course NASH and CKD in comparison with patients with CKD without comorbid diseases (p <0,05). Calculation of GFR using CKD-EPI points to a higher accuracy of GFR evaluation, since the index significantly differed between the comparison groups, indicating the probability of our working hypothesis. So, the index of GFR in patients with CKD I st. was lower than that in PHPs in patients of group 1 in 1,5 times (p <0,05), in patients of group 2 – in 1,3 times (p <0,05) with confirmation of statistically significant difference between groups (p < 0.05). In patients with CKD II st. in group 1 GFR was 1.9 times lower than the PHPs, compared with a decrease of 1.6 times in group 2 (p <0.05), with a statistically significant difference between the groups (p <0.05). At the same time, patients with CKH III st. the rate of GFR in patients in group 1 was lower than the standard in 2.7 times (p <0,05), in group 2 – in 2,2 times (p <0,05), with the presence of a probable difference between patients with a comorbid flow of NASH and CKD II st. and CKD III st. in comparison with patients with isolated CKD of the corresponding stage (p <0,05). Thus, the functional state of the kidneys in patients with CKD and comorbidity with NASH regarding the rates of excretion of nitrogenous slags, albumin loss and integral index – GFR is significantly lowered compared to those in patients with CKD without comorbidity.

The correlation analysis shows that there is an average strength and a strong correlation between the GFR indices and the intensity of lipoperoxidation (increase MA content in blood) and the oxidative modification of the proteins (increase in the AKDNPH B content in blood) **(table 3),** the degree of endotoxicosis (increase of MMP in the blood, decrease in the activity of arginase), growth of fractions of proatherogenic fractions: LDL, cholesterol, TG and lowering of blood HDL – antiatherogenic LP in blood, due to their dysregulation

Table 3.

Matrix of correlation relations between CKD-EPI and indicators of lipid homeostasis, endotoxicosis, oxidative stress, functional state of endothelium in obesity and non-alcoholic steatohepatitis patients (r, p)

Indicator	MA	AKDNPH B	Arginase	MMP	H_2S	NO	Endothelin-1	Homocysteine
GFR	-0,68*	-0,63*	0,72*	-0,69*	0,75*	-0,63*	-0,45*	-0,64*
Indicator	TC	TG	LDL	HDL	Leptin	Adiponectin	iNOS	Cytokeratin-18
GFR	-0,44*	-0,49*	-0,61*	0,67*	-0,51*	0,43*	-0,62*	-0,57*

Note: * – statistically significant correlation coefficient (p <0,05).

by adipocytokines: hyperleptinemia, hypoadiponectinemia, hypercytocreatinemia (p <0.05), indicating the participation of these factors in the reduction of GFR for comorbidity with NASH and the progression of CKD.

It should be noted significant impact on GFR indicators that contribute to endothelium dysfunction, and its direct biochemical markers. In particular, the significant influence of hydrogen sulfide deficiency, hyperhomocysteinemia, hyperproduction of endothelin-1 and overexpression of iNOS on GFR was established, resulting in hyperproduction and violation of the excretion of metabolites of nitrogen monoxide with activation of nitrosatitistic stress and redistributive impaired renal vascular tone [12], which also affected the decrease in GFR in patients with CKD and NASH (p <0,05). The obtained data substantially complement the concept of the pathogenesis of the mutual burden of CKD and NASH with obesity, contribute to the search for new, previously unknown mechanisms for their progression.

Conclusions

1. Non-alcoholic steatohepatitis affects the functional state of the kidneys in patients with CKD I-III stages with a possible reduction of nitrogen function, glomerular filtration rate, increase in the intensity of hypopalbuminemia, proteinuria, leukocyturia, erythrocyturia, cylinduria, bacteriuria than in the isolated course of CKD.

2. For the comorbidity of the CKD with NASH with a decrease in GFR characterized by an increase in the intensity of oxidative stress, endotoxicosis, the depth of the lipid distress syndrome, the degree of violation of the functional state of the endothelium: an increase in the activity of iNOS, the content of nitrites/nitrates in blood, endothelin-1, homocysteine, cytokeratin-18, decrease in the activity of arginase, H2S content (p <0,05), which correlate with the intermediate and high power interactions with the index of GFR (p <0,05).

The prospect of further scientific research in this direction direction is to study the factors of regulation of renal functions, the functional state of the endothelium and the development of methods for their correction in patients with a comorbid flow of nonalcoholic steatohepatitis and CKD: chronic pyelonephritis.

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ФУНКЦІОНАЛЬНИЙ СТАН ТА АКТИВНІСТЬ ЗАПАЛЕННЯ НИРОК У ХВОРИХ НА ХРОНІЧНУ ХВОРОБУ НИРОК ТА НЕАЛКОГОЛЬНИЙ СТЕАТОГЕПАТИТ НА ТЛІ ОЖИРІННЯ, ЇХ ВЗАЄМОЗВ'ЯЗОК З ФУНКЦІОНАЛЬНИМ СТАНОМ ЕНДОТЕЛІЮ, СИНДРОМАМИ ЕНДОГЕННОЇ ІНТОКСИКАЦІЇ ТА ОКСИДАТИВНОГО СТРЕСУ

Антонів А. А.

Резюме. У статті наведено теоретичне узагальнення дослідження особливостей функціонального стану нирок за коморбідності хронічної хвороби нирок (ХХН): хронічного пієлонефриту з ожирінням та неалкогольним стеатогепатитом (НАСГ) залежно від стадії ХХН, який характеризується вищим ступенем зниження швидкості клубочкової фільтрації (ШКФ), ступенем гіпоальбумінемії, протеїнурії, лейкоцитурії, еритроцитурії, бактеріурії, ніж за ізольованого перебігу. Для коморбідного перебігу ХХН із НАСГ із зниженням ШКФ характерне зростання інтенсивності оксидативного стресу, ендотоксикозу, глибини ліпідного дистрес-синдрому, ступеня порушення функціонального стану ендотелію: зростання активності iNOS, вмісту в крові нітритів/нітратів, ендотеліну-1, гомоцистеїну, цитокератину-18, зниження активності аргінази, вмісту в крові H_2S (p<0,05), які у взаємозалежності середньої та високої сили корелюють із ШКФ (p<0,05).

Ключові слова: хронічна хвороба нирок, неалкогольний стеатогепатит, швидкість клубочкової фільтрації, оксидативний стрес, ендотоксикоз, ліпідний дистрес-синдром, функціональний стан ендотелію.

ФУНКЦИОНАЛЬНОЕ СОСТОЯНИЕ И АКТИВНОСТЬ ВОСПАЛЕНИЯ ПОЧЕК У БОЛЬНЫХ ХРОНИЧЕСКОЙ БОЛЕЗНЬЮ ПОЧЕК И НЕАЛКОГОЛЬНЫМ СТЕАТОГЕПАТИТОМ НА ФОНЕ ОЖИРЕНИЯ, ИХ ВЗАИМОСВЯЗЬ С ФУНКЦИОНАЛЬНЫМ СОСТОЯНИЕМ ЭНДОТЕЛИЯ, СИНДРОМАМИ ЭНДОГЕННОЙ ИНТОКСИКАЦИИ И ОКСИДАТИВНОГО СТРЕССА

Антонив А. А.

Резюме. В статье приведено теоретическое обобщение результатов исследования особенностей функционального состояния почек при коморбидности хронической болезни почек (ХБП): хронического пиелонефрита с ожирением и неалкогольного стеатогепатита (НАСГ) в зависимости от стадии ХБП, который характеризуется высокой степенью снижения скорости клубочковой фильтрации (СКФ), степенью гипоальбуминемии, протеинурии, лейкоцитурии, эритроцитурии, бактериурии, чем при изолированном течении. При коморбидном течении ХБП с НАСГ со снижением СКФ характерен рост интенсивности оксидативного стресса, эндотоксикоза, глубины липидного дистресс-синдрома, степени нарушения функционального состояния эндотелия: рост активности iNOS, содержания в крови нитритов / нитратов, эндотелина-1, гомоцистеина, цитокератина-18 снижение активности аргиназы, содержания в крови H2S ($p < 0,05$), которые во взаимозависимости средней и высокой силы коррелируют с СКФ ($p < 0,05$).

Ключевые слова: хроническая болезнь почек, неалкогольный стеатогепатит, скорость клубочковой фильтрации, оксидативный стресс, эндотоксикоз, липидный дистресс-синдром, функциональное состояние эндотелия.

KIDNEYS FUNCTIONAL STATUS AND INFLAMMATION ACTIVITY IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND NONALCOHOLIC STEATOHEPATITIS ON THE BACKGROUND OF OBESITY, THEIR RELATIONSHIP WITH THE FUNCTIONAL STATE OF THE ENDOTHELIUM, ENDOGENOUS INTOXICATION SYNDROME AND OXIDATIVE STRESS

Antoniv A. A.

Abstract. *The aim of the study* was to find out the probable effect of the comorbid flow of nonalcoholic steatohepatitis (NASH) on the functional state of the kidneys and the activity of inflammation of the kidneys in patients with chronic kidney disease (pyelonephritis) (CKD) of the I-III stage, to determine the pathogenetic role of endothelial dysfunction, lipid distress syndrome, endotoxicosis and oxidative stress in the mechanisms of their mutual burden.

Object and methods of research. 240 patients with CKD (chronic bilateral peylonephritis) of the I-III stage were examined, 145 of which had comorbid NASH and obesity of the 1st degree (group 1), 95 patients were diagnosed with CKD I-III stages without comorbid pathology. Depending on the stage of the CKD, both groups were divided as follows: 1st group - into 3 subgroups: 51 patients with 1st stage CKD, 53 patients with 2nd stage CKD, 41 patients with 3rd stage CKD. The 2nd group was divided into 3 subgroups: 32 patients with 1st stage CKD, 35 patients with 2nd stage CKD, 28 patients with 3rd stage CKD. The control group consisted of 30 practically healthy persons.

Results of research and their discussion. It was established that non-alcoholic steatohepatitis affects the functional state of the kidneys in patients with CKD I-III stages with a possible reduction of nitrogen function, velocity of glomerular filtration, increase in the intensity of hypoalbuminemia, proteinuria, leukocyturia, erythrocyturia, cylinduria, bacteriuria than in isolated course CKD.

Conclusion. For the comorbidity of the CKD with NASH and a decrease in GFR, an increase in the intensity of oxidative stress, endotoxicosis, lipid distress syndrome, degree of violation of the functional state of the endothelium: increased activity of iNOS, nitrite/nitrate content, endothelin-1, homocysteine, cytokeratin-18, decrease in the activity of arginase, H2S content ($p < 0,05$), which correlate with the intermediate and high power interactions with the index of GFR ($p < 0,05$).

Key words: chronic kidney disease, nonalcoholic steatohepatitis, glomerular filtration rate, oxidative stress, endotoxicosis, lipid distress syndrome, functional state of the endothelium.

Рецензент – проф. Костенко В. О.
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Багацька Н. В.

ОЦІНКА РІВНЯ ХРОМОСОМНИХ АБЕРАЦІЙ У ЛІМФОЦИТАХ КРОВІ ХВОРИХ З РІЗНИМИ ФОРМАМИ ТРИВОЖНИХ РОЗЛАДІВ IN VITRO

ДУ «Інститут охорони здоров'я дітей і підлітків НАМН України» (м. Харків)
nv_bagatska@ukr.net

Зв'язок публікації з плановими науково-дослідними роботами. Робота виконана у рамках комплексної науково-дослідної теми ДУ «ІОЗДП НАМН» «Вивчити вікові особливості механізмів формування тривожно-фобічних розладів у дітей» (2016-2018 рр.), № державної реєстрації 01164003036, шифр НАМН 89/16.

Вступ. Основною концепцією ВООЗ, викладеної в Глобальній стратегії охорони здоров'я жінок, дітей і підлітків (2016-2030 рр.), є забезпечення до 2030 року кожній жінці, кожному підлітку, кожній дитині в будь-якому місті світу можливості для здійснення права на фізичне і психічне здоров'я, соціальні і економічні можливості… [1]. Саме тому, в останні роки особливу стурбованість викликає проблема виникнення психічних розладів у дитячому та підлітковому віці. Тривожні розлади є найбільш частими серед усіх категорій психічних порушень і реєструються в 3,7-5,1 % випадків; вони відрізняються значним поліморфізмом клінічних проявів, динамічністю і нерідко є причиною труднощів у терапії. Факторами ризику виникнення тривожних розладів є спадкова обтяженість до психосоматичних та психічних хвороб, особистісні характеристики матері та акцентуйовані риси харак-