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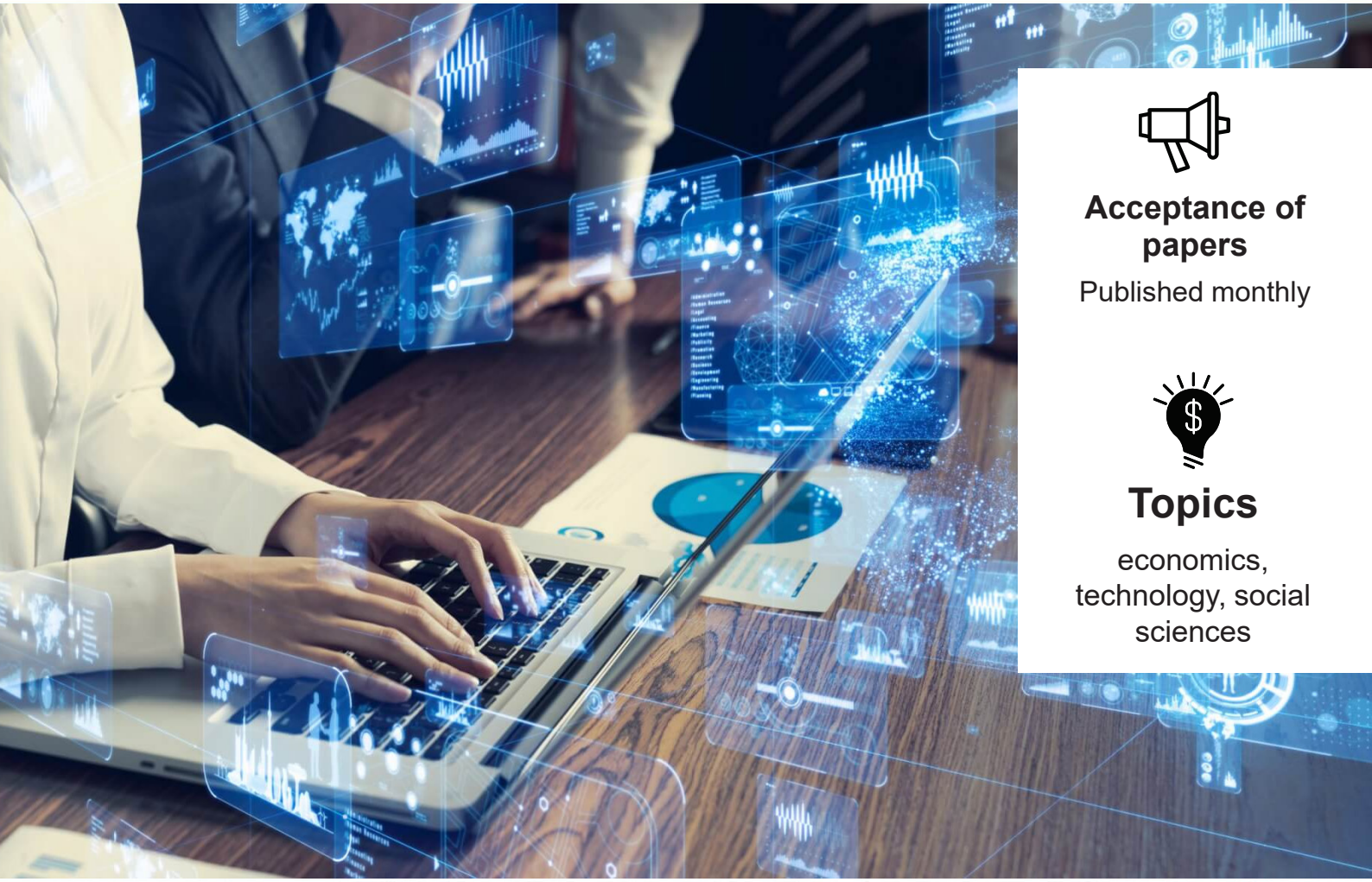

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NEPHROGENIC ANEMIA AS A RISK FACTOR FOR THE DEVELOPMENT OF CARDIOVASCULAR DISORDERS IN CHILDREN WITH CHRONIC KIDNEY DISEASE

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Abstract: A total of 260 children with chronic kidney disease (CKD) were examined. Anemia was present in 217 patients, accounting for 83.5%, and among children with cardiovascular disorders, it was observed in 90.2% of cases (110 out of 122 patients). The interrelation between cardiovascular disorders, CKD, and anemia lies in the fact that anemia affects the course of CKD and the development of cardiovascular pathology. Anemia in children with CKD plays a key role in the pathogenesis of cardiovascular damage through hypoxic injury to the myocardium. Restoration of hemoglobin levels is essential even at the early stages of CKD, as it is crucial for preventing cardiovascular complications, which are the leading cause of death among children and adolescents with CKD.

Key words: Nephrogenic Anemia, Chronic Kidney Disease (CKD), Cardiovascular Disorders, Children, Risk Factor, Erythropoietin (EPO), Iron Deficiency, Hypertension, Left Ventricular Hypertrophy, Cardiovascular Morbidity.

INTRODUCTION

Recent studies on the course of chronic kidney disease (CKD) have revealed a close relationship between the progression of renal pathology and the condition of the cardiovascular system [2, 3, 5, 6, 11]. The development of cardiovascular disorders (CVD) is associated with the emergence of risk factors arising from the progression of CKD, one of which is anemia [3, 7, 11]. The chronic inflammatory process in kidney tissue leads to renal shrinkage and a decrease in the number of peritubular cells in the proximal nephron, thereby impairing the production of erythropoietin — a key component of hematopoiesis [10]. Nephrogenic anemia predictably complicates the course of CKD and is more commonly diagnosed when the glomerular filtration rate (GFR) declines to 40–60 ml/min/1.73 m², although it can be detected at earlier stages of the disease [1, 12]. Anemia is associated with complications such as increased rates of hospitalization and mortality, as well as the progression of cardiovascular risk factors, including left ventricular hypertrophy (LVH) [4, 9, 12]. The increased oxygen demand of the myocardium contributes to subendocardial ischemia, increased ventricular stiffness, reduced aortic compliance, and greater arterial stiffness — all of which underlie the development of diastolic heart failure [3, 5].

LITERATURE REVIEW ON THE TOPIC

To determine the significance of nephrogenic anemia as a factor in the development of cardiovascular disorders in children with chronic kidney disease.

After the task force publication, Parekh et al.4 used the USRDS database to evaluate the risk of cardiac death in children and young adults (aged 0–30 years) in 2002. Of 1380 deaths recorded between 1990 and 1996, 311 (23%) were due to cardiac causes. These data are in sharp contrast to the general pediatric population, in which CVD mortality is very low and accounts for <3% of all deaths.

Subsequent reports from international registries confirm that CVD is the leading cause of death in both children with ESRD and in adults with childhood onset of CKD. The Australia and New Zealand Dialysis and Transplant,5 Dutch national cohort study,6 and a large German study7 reported that 40%–50% of all deaths are from cardiovascular or cerebrovascular causes.

RESEARCH METHODOLOGY

We examined 260 children with CKD in pre-dialysis stages (stages I–IV), aged 5 to 17 years. The underlying causes of CKD were chronic glomerular pathology in 56.8% of cases and congenital anomalies of the urinary system in 43.2%. Based on clinical, laboratory, and instrumental assessments, the children were divided into two groups. The first group included 122 children with diagnosed cardiovascular abnormalities — such as conduction system blocks on ECG, left ventricular myocardial hypertrophy, repolarization disorders, metabolic changes in the myocardium, and signs of cardiac remodeling on echocardiography (EchoCG). The second group included 138 patients without such changes.

ANALYSIS AND RESULTS

We analyzed the clinical course of CKD in children depending on the presence of cardiovascular disorders. Our findings revealed that CVD in children most frequently develops during stages 3 and 4 of CKD. The data are presented in Table 1.

Table 1. Distribution of Examined Children With and Without Cardiovascular Disorders Depending on the Stage of Chronic Kidney Disease (CKD)

Number of patients 1 st. CKD		**Stages of CKD**			
		2 st. CKD	**3 st. CKD**		**4 st. CKD**
1 group, n=122	abs.	6	18	55	43
	%	4,9	14,7	45,1	35,3
2 group, n=138	abs.	15	49	50	24
	%	10,9*	35,5*	36,2	17,4*
Total, n=260	abs.	21	67	105	67
	%	8,1	25,8	40,4	25,8

Note: * — statistically significant difference between groups ($p < 0.05$).

As shown in the table, in the group of children with cardiovascular disorders (CVD), stage 1 CKD was recorded 2.2 times less frequently compared to the second group (4.9% vs. 10.9%; $p = 0.003$); stage 2 CKD — 2.4 times less frequently (14.7% vs. 35.5%; $p = 0.004$); stage 3 — 1.2 times more frequently (45.1% vs. 36.2%; $p = 0.006$); and stage 4 CKD — 2 times more frequently than in the group of children without CVD (35.3% vs. 17.4%; $p = 0.003$).

Among the factors influencing the development of CVD in children with CKD, we found that congenital anomalies of the urinary system (CAKUT) were less frequently associated with CVD, whereas chronic glomerular diseases were significantly more likely to be predictors of cardiovascular disorders in children. The data are presented in Table 2.

Table 2. Distribution of Examined Children With and Without Cardiovascular Disorders Depending on the Cause of CKD

Causes	1 group, n=122		2 group, n=138	
	abs.	%	abs.	%
Glomerular diseases, n=144	74	60,7	70	50,7
Congenital malformations (CA), n=116	48	39,3	68	49,3

When analyzing the development of cardiovascular disorders in relation to glomerular filtration rate (GFR) (Table 3), we found that children in Group 1 had significantly lower GFR values compared to those in Group 2 — averaging 44.1 ± 2.1 ml/min/1.73 m² versus 56.2 ± 2.1 ml/min/1.73 m², respectively ($p < 0.01$). A consistent pattern was observed: the frequency of cardiovascular disorders increased as GFR declined. For instance, when GFR ranged between 90–120 ml/min/1.73 m², the incidence of CVD was 4.9%, whereas at GFR levels of 15–29 ml/min/1.73 m², the incidence increased by 7.4 times ($p < 0.01$).

Table 3. Frequency of Cardiovascular Pathology Depending on GFR Levels

Degree of kidney impairment by GFR, mL/min/1.73m²	1 group, n=122		2 group, n=138	
	abs.	%	abs.	%
90-120	6	4,9	13	9,4*
60-89	18	14,7	50	36,2**
30-59	54	44,3	51	37,0
15-29	44	36,1	24	17,4*
Total	44,1±2,1		56,2±2,1*	

Note: * — statistically significant difference between groups ($p < 0.05$).

A comparative analysis of hematological parameters (Table 4) showed that in children with cardiovascular disorders (CVD) associated with CKD, mean hemoglobin levels were significantly reduced — by 1.4 times compared to the control group ($p < 0.01$) and by 1.1 times compared to children with CKD without CVD ($p < 0.05$).

Table 4. Complete Blood Count Results in Children With CKD Depending on the Presence of Cardiovascular Pathology

	Parameters	1 group, n=122	2 group, n=138	Control group
1	Hb, g/L	82,6±1,9**	94,3±1,5*^	115,2±4,4
2	Red blood cells (RBCs), x 10^{12}/L	3,1±0,05*	3,7±0,1*	4,4±0,9
3	Color ındex (CI)	0,71±0,08**	0,85±0,07*^	0,9±0,06

Note: * - statistically significant compared to control group (* - $p<0.05$; ** - $p<0.01$); * - statistically significant difference between Group 1 and Group 2 (^ - $p<0.05$).

Red blood cell (RBC) count in children with CKD was significantly reduced compared to the control group — by 1.4 times ($p < 0.05$), and by 1.2 times compared to patients in Group 2 ($p < 0.05$). A decrease in the color index (CI) was also noted in children with CKD. In the presence of cardiovascular disorders, the CI was reduced by 1.3 times compared to the control group ($p < 0.05$) and by 1.2 times compared to Group 2 ($p < 0.05$).

An odds ratio analysis was performed to identify the most significant hematological predictors for the development of cardiovascular disorders in children with CKD — specifically, a reduction in hemoglobin, red blood cells, and color index (Table 4).

Table 5. Results of Factor Analysis of Hematological Predictors for the Development of Cardiovascular Pathology in Children With CKD

Hematological parameters	1 group, n=122		2 group, n=138	
	abs.	%	abs.	%
Decreased hemoglobin	110	90,2	107	77,5
Decreased red blood cells (RBCs)	112	91,8	105	76,1
Decreased color index (CI)	108	88,5	98	71,0

In our study, anemia was found in 217 children with CKD, accounting for 83.5% of cases. Among children with cardiovascular disorders (CVD), the incidence of anemia was 90.2% (110 out of 122 patients). The link between cardiovascular disorders, CKD, and anemia lies in the fact that anemia influences the progression of CKD and the development of cardiovascular pathology. Notably, the severity of anemia tends to be more pronounced in patients with advanced stages of chronic kidney disease.

CONCLUSION AND SUGGESTIONS

Thus, reductions in hemoglobin levels, red blood cell count, and color index are among the most informative indicators for assessing the degree of circulatory impairment. These parameters not only reflect the severity of hemodynamic disturbances in patients with CKD but also play a role in the pathogenesis of cardiovascular damage through hypoxic injury to the myocardium. Restoration of hemoglobin levels is necessary even at the early stages of CKD, as even slight improvements in cardiovascular function following full correction of anemia play a crucial role in preventing cardiovascular complications — the leading cause of death among children and adolescents with CKD.

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