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FOLLOW-UP OF CHILDREN WITH KIDNEY INJURY IN NEONATAL AGE

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Abstract

Long-term follow-up of patients with acute kidney injury (AKI) has shown that glomerular filtration and tubular function are still normal. Renal blood flow remains permanently impaired, suggesting that there is still some irreversible loss of nephrons and that glomerular filtration is maintained by hypertrophy of the remaining nephrons.

The aim of the study was to identify signs of chronic kidney diseases in children with kidney injury in neonatal age.

The study was designed as a prospective investigation conducted in the period of two years, which included 50 neonates with kidney injury hospitalized in NICU, University Clinic for Pediatric Diseases in Skopje. Due to the potential risk of developing chronic renal failure by the end of the first year of life, in 26 children with kidney injury in neonatal age were evaluated growth and development, arterial tension, and renal function. The material was statistically analyzed using methods of descriptive statistics.

Of the total of 50 neonates with documented AKI, we followed 26 neonates because of the risk of disease progression to chronic renal failure. According to the results from the percentage growth curves, 85% of children had a normal finding, while 15% were obese children, with weighing between 85 and 95 percentiles. 96% of children had arterial tension with reference values according to age group, and only one child had prehypertension. We registered microproteinuria in 7.6% of children, and there were no hematuria findings.

Most of the monitored children had proper renal function, which was probably due to the predominance of prerenal AKI, associated with a better prognosis. The follow-up period of one year was short and in order to obtain more reliable results, long-term controlled monitoring is required, which would last several years.

Keywords: neonates, acute kidney injury, follow-up

Introduction

Acute kidney injury (AKI) is a common problem in neonates in the Neonatal Intensive Care Unit (NICU) [1,2]. There are several pathophysiological mechanisms responsible for the development of kidney injury in neonates such as changes in renal perfusion, changes in glomerular permeability, as well as the increased reabsorption through the tubular damaged cells [3,4].

The most common type of AKI in neonatates is prerenal AKI, which occurs in 70 to 80% of cases. It is caused by a variety of hemodynamic disorders that attack the immature neonatal kidneys. Namely, the kidneys in neonates are less able to compensate for the change in renal arterial pressure, so hypovolemia and hypotension often lead to hypoperfusion of the kidneys and reduced glomerular filtration [5]. Renal kidney injury may occur due to parenchymal kidney damage and post-renal kidney injury as a consequence of urinary tract obstruction with inappropriate urine elimination [6,7].

Prerenal AKI (if treatment is started on time) and postrenal AKI (if distal urinary tract obstruction is removed in time) have a good prognosis. Renal AKI with residual renal failure (decreased glomerular filtration, tubular dysfunction, or stunted renal growth) or permanent loss of renal function and development of terminal renal failure has a poor prognosis [8,9].

Glomerular filtration is determined by the filtering capacity of each individual nephron. When kidney injury occurs, the number of nephrons decreases, resulting in compensatory hypertrophy of the remaining nephrons. They operate under increased intracapillary hydraulic pressure, which in turn leads to damage to the capillary wall. This inevitably leads to progressive glomerulosclerosis, proteinuria, hypertension, and terminal renal failure. This hyperfiltration hypothesis explains the

occurrence of terminal renal failure which is a severe disability that impairs the quality of patients life. On the other hand, the expensive and long-term treatment financially depletes health funds and families of affected children [10,11].

Follow-up of infants with significant AKI should be considered. At any follow-up appointments growth and development, blood pressure and urine for proteinuria should be checked. Long-term follow-up of patients with AKI has shown that glomerular filtration and tubular function are still normal. However, renal blood flow remains permanently impaired, suggesting that there is still some irreversible loss of nephrons and that glomerular filtration is maintained by hypertrophy of the remaining nephrons [12,13].

Children with AKI are at risk of developing chronic renal failure in the future, especially extremely premature babies who may develop kidney injury during the first year of life [14,15]. The aim of the study was to identify signs of chronic kidney diseases in children with kidney injury in neonatal age.

Methods

The study was designed as a prospective investigation conducted in the period of two years, which included 50 neonates with kidney injury hospitalized in NICU, University Clinic for Pediatric Diseases in Skopje.

Due to the potential risk of developing chronic renal failure by the end of the first year of life, in 26 children with kidney injury in neonatal age were evaluated:

- Growth and development, estimated by growth curves (for height and weight). The finding of the height or weight growth curve below 5 percentile or above 95 percentile in relation to age deviates from the finding that we consider normal / age appropriate (5-95 percentile). In addition, we classified the respondents under the 5th percentile of the weight curve as children with stunted growth; respondents weighing between 85th and 95th percentile as obese children, while respondents weighing over 95th percentile as obese, obese overweight children.
- Measurement of blood pressure. Arterial hypertension was defined as a condition in which systolic blood pressure and / or diastolic blood pressure were above 90 percent or at / above 95 percent for the appropriate age group in at least three measurements. Hypertension was classified in three groups: prehypertension (arterial tension between 90 and 95%), stage 1 (arterial tension between 95 and 99% plus 5 mmHg) and stage 2 hypertension (arterial tension above 99% plus 5 mmHg).
- Renal function. Assessment through certain laboratory parameters (urea and creatinine in serum and urine analysis of the first urine with calculated protein / creatinine ratio) and ultrasonographic examination of the kidneys. As a reference value for the calculated protein / creatinine ratio we took the value 0.5 mg/mm.

Medical data records of admitted 26 neonates with AKI (without lethal outcome) were analyzed according to gender and weight. The laboratory examinations of serum creatinine and urea values and urine creatinine and protein values were done in the biochemical laboratory of the University Clinic for Pediatric Diseases using Kodak camera dry biochemistry.

The material was statistically analyzed using the methods of descriptive statistics. To determine the significance of differences in the parameters, the tests for independent samples were analyzed. Statistical significance was determined for the values of $p<0.05$.

Results

Of the total of 50 neonates with documented AKI, 16 had a lethal outcome. We monitored the remaining 34 (without lethal outcome) for one year after the initial kidney injury. Of these, another 6 neonates, due to complications in the infant period ended up fatally before the end of the first year. Of the remaining 28 neonates, we followed only 26 because of the risk of disease progression to chronic renal failure. The condition was not monitored in 2 children, because they did not respond to the call for control examination.

As part of the pediatric examination, body growth and development and renal function were assessed in children called for follow-up. According to the results obtained from the percentage growth curves, 22/26 (85%) children had a normal finding, while 4/26 (15%) were obese children,

weighing between 85 and 95 percentiles. We did not register any findings in overweight or obese children (weighing over 95%) and children with stunted growth (weighing less than 3-5%). The results of percentage growth curves are shown in Figure 1.

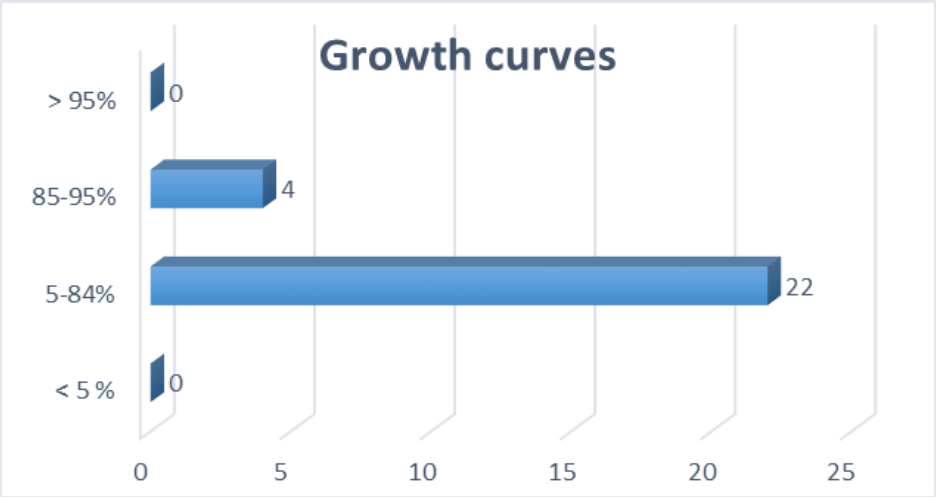

Figure 1. The results of percentage growth curves

According to blood pressure measurement, 25/26 (96%) children had pressure with reference values in line with the age group. Only in one child a condition of prehypertension was recorded, with a blood pressure level between 90 and 95%, as well as an increase in body weight over 85% of the growth curve. Otherwise, this child was born as large for gestational age (LGA) with a birth weight over 4000 g. The results of the blood pressure level are shown in Figure 2.

In all children, the serum waste products showed normal values, with an average value of creatinine of 46.38 ± 20.6 mmol / l and of urea 2.00, ± 0.6 mmol / l. We registered microproteinuria in 2/26 (7.6%) children in the urine, with values of protein / creatinine ratio within the reference limits (<0.5 mg / mmol).

Hematuria as well as pathological echotomographic findings of the urogenital tract were not registered in the group of children that we followed up. The results of biochemical investigation in serum and in urine are shown in Table 1.

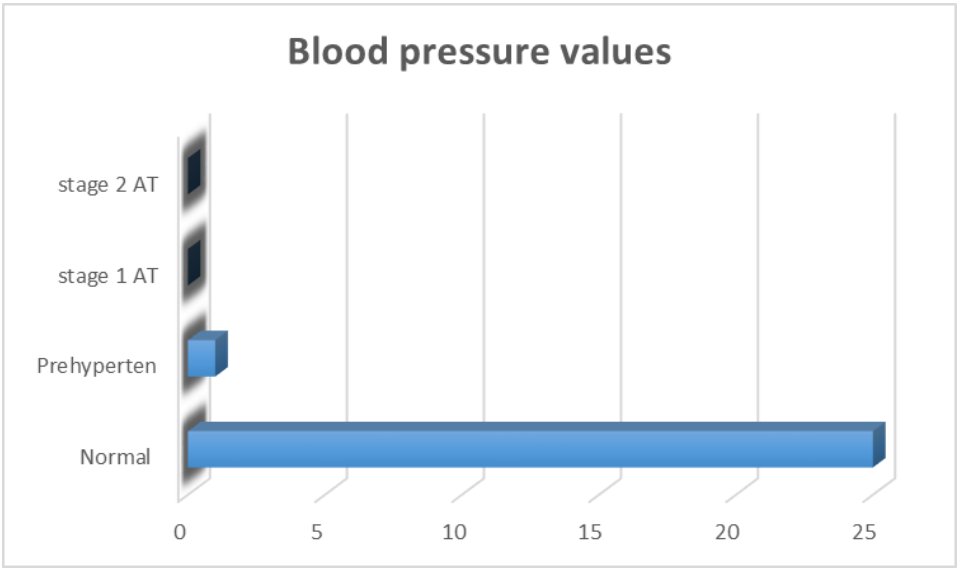

Figure 2. The results of blood pressure level

Table 1. The results of biochemical investigation

Findings	
Creatinine	46.38 ± 20.6 mmol
Urea	2, ± 0.6 mmol / l.
Microproteinuria	in 7.6%
Protein/Cr	<0.5 mg / mmol
Hematuria	none
Echo UGT	normal

Discusion

Children who have had AKI in neonatal age are at risk of developing chronic kidney disease in the future. This is due to damage to the endothelial vascular cells which subsequently progresses to fibrosis, or glomerulosclerosis, resulting in loss of renal function. This risk is particularly pronounced in children born with a very low birth weight, in whom progression of renal disease is possible during the first years of life [16,17].

In our study, follow-up was performed one year after the initial kidney injury. Only 52% children were followed up, which was due to the reduction of the group, partly due to the unfavorable outcome in the neonatal or infant period, and partly due to the rejection of the call for control. Most of the monitored children had normal body growth and development; arterial tension within the reference values and normal renal function [18].

The prerenal AKI was registered in more than 90% of the babies who were born at term, and which injury is known to be associated with a better prognosis of the disease, if adequate treatment is started in a timely manner. But, at the same time, these findings do not exclude the possibility of chronic kidney disease in the coming period, because the follow-up so far was realized in a short period of only one year. Therefore, it is necessary for these respondents to be monitored in the coming years in order to timely identify children with possible development of chronic kidney disease [19,20].

In 2/26 (7.6%) neonates we registered microproteinuria and waste products at the upper limits of the reference values. These findings, which are an important indicator of chronic kidney disease, suggest that these children are at risk for early progression of kidney disease [21,22].

Long-term (multi-year) monitoring of these children is necessary in order to timely recognize the occurrence of chronic renal disease and take appropriate therapeutic measures to prevent further loss of renal function and transition to terminal renal failure [23].

Terminal renal failure is a severe disability that impairs the quality of life of patients and their families, and expensive and long-term treatment financially depletes both health funds and families of affected children [24,25].

The neonates in whom we registered a condition of prehypertension also had an increased body weight. Thus, further monitoring is needed, but not because of the possible progression of kidney disease, but because of the risk of developing metabolic syndrome which is significantly associated with high blood pressure and increased body weight.This follow-up has to be the subject of another study [26,27].

Conclusion

Twenty-six of 50 neonates with AKI manifested in the neonatal period were monitored one year after the initial impairment, due to a possible disease progression during the first years of life. In our group, most of the children had proper renal function, which was probably due to the predominance of prerenal AKI in 90% of the monitored children, which is known to be associated with a better prognosis. But, given that the progression of chronic kidney disease is a long process, it is clear that our results are not definitive.

The follow-up period of one year was short and in order to obtain more reliable results, long-term controlled monitoring is required, which would last several years. Thus, it would contribute to the clarification of the true prognosis of the disease.

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