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INCIDENCE, RISK FACTORS AND OUTCOMES OF ACUTE KIDNEY INJURY IN PRETERM NEWBORNS

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Abstract

Acute kidney injury is a sudden loss of renal function that results in deterioration of the renal's ability to excrete urine in sufficient quantity and adequate composition. The aim of the study was to determine the incidence, risk factors and outcomes of acute kidney injury in preterm newborns.

The study was conducted at the University Clinic of Pediatrics–Skopje. It was a clinical, epidemiological prospective study. In the period of two years, 40 preterm newborns hospitalized at the Intensive Care Unit (ICU) with documented kidney injury were analyzed. Medical data records of hospitalized preterm infants with kidney injury were processed. The material was statistically analyzed using methods of descriptive statistics.

We evaluated 40 preterm newborns with documented acute kidney injury, who at the period of 2 years were treated in the ICU. The prevalence of kidney injury was 6.9%. Most of the involved preterm newborns were male (72%), and born at 32 to 37 weeks with low birth weight (58%). Prerenal injury was evaluated in 79.5% of the cases. The mortality rate was 36% and it was significantly higher in the group of preterm infants born under 28 weeks, with Extremely Low Birth Weight Newborns ELBW. (P=0.01).

Acute kidney injury is a life threatening condition with a still high mortality rate. Appropriate treatment of kidney injury in newborns with ELBW improves the outcomes and reduces the mortality of the disease.

Key words: acute kidney injury, preterm newborns, ELBW.

Introduction

Acute kidney injury (AKI) is a sudden loss of renal function that results in deterioration of the renal's ability to excrete urine in sufficient quantity and adequate composition, rendering it unable to maintain normal homeostasis of body fluids and electrolytes. It is a common clinical condition associated with poor outcomes in newborns [1-5].

Neonatal kidneys, especially premature infant kidneys, are particularly sensitive to the reduction of renal function, because of the immaturity. Characteristics of neonatal kidneys are: high renal vascular reserve, high plasma rennin activity, low glomerular filtration rate, low sodium reabsorption in the proximal tubule, fondness for tubular/cortical necrosis.

Neonatal glomerular filtration rate (GFR) is 25% compared to adults, so any reduction in renal function leads to kidney damage. The incidence of acute kidney injury in newborns is 8 to 24%, and the mortality rate ranges up 10% to 61% [6-9].

Acute kidney injury could present with normal urine output (UO), especially in preterm newborns. It is generally believed that preterm newborns have non oliguric AKI, but this can be a misconception due to the lack of knowledge about normal UO in critically ill neonates.

The total body water content is greater in newborns than in pediatric patients. Especially in preterm newborns, the total body water could be as high as 80% of the bodyweight. This difference in water content, in addition to immature tubular development, can explain why UO in newborns is normally greater than in others. So, it was demonstrated that urine output less than 0.5mL/kg per hour is a non-sensitive marker of kidney injury and this level must be increased to 1.0 mL/Kg per hour. This urine output level can be even higher (up to 1.5 mL/Kg per hour) in preterm newborns, because of immature tubular development [10-11].

Risk factors of neonatal kidney injury development include very low birth weight (less than 1500 g), low 5-minutes Apgar score, intubation at birth and respiratory distress syndrome [12].

It is difficult to conclude which is the pathophysiological mechanism responsible for the occurrence of kidney injury in newborns. The causes of kidney injury are multiple and can be divided

into prerenal, renal, and post renal categories. Prerenal injury is the most common type of kidney injury in newborns and could account for up to 80% of all cases.

Prerenal injury is characterized by inadequate renal perfusion, which, if promptly treated, is followed by improvements in renal function. In general, newborns with prerenal injury who receive prompt treatment for hypoperfusion have an excellent prognosis.

Renal (intrinsing) injury may occur due to parenchymal kidney damage and has significant risk of death.

The poor prognosis depends on the occurrence of residual renal failure (reduced glomerular filtration rate, tubular dysfunction or backlog growth of the kidney) or permanent loss of renal function with crossing terminal renal insufficiency.

The post-renal kidney injury is a consequence of urinary tract obstruction with inappropriate urine elimination. Newborns with post-renal injury related to congenital urinary tract obstruction have a variable outcome, which depends on the degree of associated renal dysplasia [13-15].

The aim of the study was to determine the incidence, risk factors and outcomes of acute kidney injury in premature infants.

Methods

This is a clinical, epidemiological prospective study that was performed at the Intensive Care Unit (ICU) at the University Clinic of Pediatrics–Skopje.

All preterm newborns admitted from the period of two years with documented kidney injury were included.

AKI was defined by elevated serum creatinine greater than 130 umol/L in premature newborns younger than 33 weeks and greater than 90 umol/L in premature newborns older than 33 weeks. The presence of oliguria was defined as urinary output less than 1.0 ml/kg/h. According to our criteria, all premature newborns who had major congenital abnormalities and were under 25 weeks of gestation and older than 28 days of age were excluded from the study.

Medical data records of hospitalized premature newborns with AKI were analyzed. The newborns were analyzed according to gender, birth weight and gestational age.

The laboratory examinations of serum creatinine values were done in the biochemical laboratory of the clinic, 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

During the study period, 580 newborns were hospitalized at the ICU due to various pathological conditions and 40 preterm newborns with acute kidney injury were selected. The calculated prevalence of AKI in preterm newborns was 6.9%. The average age of gestation was 31.12 ± 3.1 weeks, while the average birth weight was 1750.8 ± 686.1 g.

Figure 1 shows according to the distribution by gender, it reflects the predominance of males in 29 (72%), compared to females in 11(28%). The male to female ratio was 2.6:1

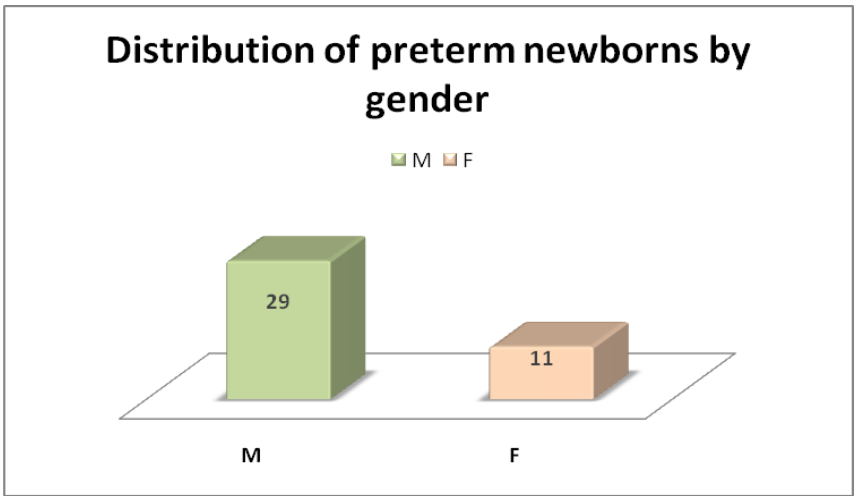

Figure 1. Distribution of preterm newborns by gender

Demographic characteristics of preterm newborns are summarized in Table 1.

Table1. Demographic characteristics of preterm infants with AKI

	Mean ± SD	Min	max
Age (days)	4.93 ± 3.5	2	28
Gestational age (wk)	31.12 ±3.1	25	37
Weight (g)	1750.80±686.12	780	2450
Duration of stay (days)	12.82±8.42	5	28

Most of the involved preterm newborns were born between 32 to 37 weeks, with low birth weight (LBW) 23/40v(58%). Seven of the preterm newborns 7/40(17%), were born under 28 weeks, with extremely low birth weight (ELBW).

Table 2 shows the distribution of preterm newborns of AKI according to gestation and birth weight.

Table 2. Distribution of preterm infants with AKI according to gestation and birth weight

	Number of patients (n)	Percent (%)
32-37 weeks, LBW	23	58
28-31 weeks, VLBW	10	25
<28 weeks, ELBW	7	17

The prevalence of prerenal, renal and postrenal AKI was 79.5%, 18.0% and 2.5%. The most common cause of AKI in newborns was prerenal AKI, which may result in intrinsic kidney injury if not treated promptly. Table 3 shows the distribution of types of AKI.

Table 3. Distribution of the type of AKI

	Number of patients (n)	percent
Prerenal AKI	32	79.5
Renal AKI	7	18.0
Post renal AKI	1	2.5

The mortality among hospitalized preterm newborns with AKI was 36%. It was significantly higher in the group of preterm newborns born under 28 weeks with ELBW. (P=0.01).

Discussion

This paper presents a clinical epidemiological study that evaluated preterm newborns that have been treated in the ICU at the University Clinic of Pediatrics–Skopje.

During the period of two years, large number of neonates (580) with various pathological conditions and AKI development were hospitalized. However, this study covered 40 preterm newborns with documented kidney injury. From here, the calculated prevalence of AKI in preterm newborns was 6.9%.

The occurrence of AKI in newborns is influenced by various factors, such as gestational age, birth weight and co-morbid conditions, present during and immediately after birth [16-20].

A similar finding has been published in the study of Vachvanichsanong et al. where the incidence of AKI in preterm newborns was 6.3%, while in study of Bolat et al. it was 8.0%. However, there are opposite findings.

Thus, in the study of Momtaz et al. the incidence of AKI was 1.5%, in the study of Mortazavi et al. 2.7% and at the Agras it was 3.4%. We assume that these differences can be due to differences in the criteria for diagnosing kidney injury in preterm newborns [21-24].

According to the distribution by gender, male preterm newborns dominated. The high prevalence of AKI in boys is probably a result of some predisposing factors, such as respiratory distress syndrome, which are more common in males than females.

A different finding was presented in the study of Momtaz et al., where females predominated in 87.7% of cases [25-27].

According to the distribution of gestational age and weight, the majority of preterm newborns (58%) were born with LBW between 32 to 37 weeks. Abu-Haweleh et al. and Mortazavi et al. published similar findings in their studies as well. Abu-Haweleh reported that 52% and Mortazavi 59% of preterm newborns with AKI were born as LBW newborns [28-29].

Prerenal injury was registered in 79.5% of preterm infants as a result of inappropriate renal perfusion. This finding correlates with the data presented in the studies of Ottonello et al. and Gopal et al. Namely, Ottonello found prerenal injury in 85% of premature newborns with AKI, while Gopal in 80% of cases.

Due to the immaturity of the kidneys in newborns, especially in preterm newborns, poor renal perfusion may result in a secondary decrease in renal function, and finally in acute kidney injury. Hence, the importance of timely and adequate treatment of premature newborns with kidney injury arises, including optimal hydration, treating contributing conditions, reducing nephrotoxic medications and invasive procedures [30-32].

The mortality rate was 36% and it correlates to the data presented in the studies of Gharehbaghi et al. and Mortazavi et al. In our study, the mortality was significantly higher in premature newborns born under 28 weeks with ELBW, in which invasive therapeutic procedures were applied, such as umbilical catheterization, intubations and assisted ventilation. Special attention needs to be paid in the application of invasive procedures in preterm newborns due to the association of these procedures with the risk of AKI [33-35].

Conclusion

Acute kidney injury is a serious condition with a still high mortality rate. Appropriate treatment of kidney injury in preterm newborns with ELBW improves the outcomes and reduces the mortality of the disease. This approach leads to a substantially improved renal function, as well as prognosis of the kidney injury.

References

1. Selewski DT, Charlton JR, Jetton JG, et al. Neonatal acute kidney injury. Pediatrics. 2015; 136(2): 463-73.
2. Jetton JG, Askenazi DJ. Update on acute kidney injury in the neonate. Curr Opin Pediatr. 2012; 24(2): 191-6.
3. Askenazi DJ, Ambalavanan N, Goldstein SL. Acute kidney injury in critically ill newborns: What do we know? What do we need to learn?. Pediatr Nephrol. 2009; 24(2): 265-74.
4. Andreoli SP. Acute renal failure in the newborn. Semin Perinatol 2004;8:112-23.
5. Schrier W., Wang W., Poole B. et al. Acute renal failure: Definitions, diagnosis, pathogenesis, and therapy. J Clin Invest. 2004; 114: 5–14.
6. Subramanian S, Agarwal R, Deorari AK et al. Acute renal failure in neonates. Indian J Pediatr. 2008:75(4):385-91.
7. Weintraub AS, Carey A, Connors J, et al. Relationship of maternal creatinine to first neonatal creatinine in infants <30 weeks gestation. J Perinatol. 2015; 35:401.
8. Bateman DA, Thomas W, Parravicini E, et al. Serum creatinine concentration in very-low-birth-weight infants from birth to 34-36 wk postmenstrual age. Pediatr Res. 2015; 77:696.
9. Vieux R, Hascoet JM, Merdariu D, et al. Glomerular filtration rate reference values in very preterm infants. Pediatrics. 2010:125:e1186.
10. Libório AB, Branco CM, Bezerra CT. Acute kidney injury in neonates: from urine output to new biomarkers. BioMed Research International. 2014;601568.
11. Bezerra CT, Vaz Cunha LC, Libório AB. Defining reduced urine output in neonatal ICU: importance for mortality and acute kidney injury classification. Nephrol Dial Transplant. 2013;28(4):901-9.
12. Pandey V, Kumar D, Vijayaraghavan P, et al. Non-dialytic management of acute kidney injury in newborns. J Renal Inj Prev. 2017; 6(1): 1-11. [DOI: 10.15171/jrip.2017.01].
13. Bansal SC, Nimbalkar AS, Kungwani AR, et al. Clinical profile and outcome of newborns with acute kidney injury in a level 3 neonatal unit in Western India. J Clin Diagn Res. 2017; 11:SC01–4.
14. Askenazi D, Ambalavanan N and Goldstein S. Acute kidney injury in critically ill newborns: What do we know? What do we need to learn? Pediatr Nephrol. 2009;24(2): 265–7
15. Cataldi L, Leone R, Moretti U, et al. Potential risk factors for the development of acute renal failure in preterm newborn infants: a case-control study. Arch Dis Child Fetal Neonatal Ed. 2005;90(6):514–9.
16. Doronjski A, Stojanovic V, Spasojevic S, et al. Acute Renal failure in premature neonates. Vojnosanit Pregl.2009;66(11):863–7.
17. Gupta BD, Sharma P, Bagla J, et al. Renal failure in asphyxiated neonates. Indian Pediatr. 2005;42(9):928–34.
18. Vishwanathan S, Manyam B, Azhibekou T, et al. Risk factors associated with acute kidney injury in extremely low birth weight (ELBW) infants. Pediatr Nephrol. 2012;27(2):303–11.
19. Youssef D, Abd-Elrahman H, Shehab N, et al. Incidence of acute kidney injury in the neonatal intensiven care unit. Saudi J Kidney Dis Transpl.2015;26(1):67-72.
20. Kapoor K., Jajoo M., Dabas V et al. Predictors of mortality in neonates with acute renal failure. Iran J Pediatr. 2013; 23(3): 321–6.
21. Mortazavi F, Hosseinpour S, and Nejati N. Acute kidney failure in neonatal period. Iran J Kidney Dis. 2009;3(3):136-40.

22. Vachvanichsanong P, McNeil E, Dissaneevate S, et al. Neonatal acute kidney injury in a tertiary center in a developing country. Nephrol Dial Transplant. 2012;27(3):973-7.
23. Peng YQ, Liang QL, Shi W. Clinical characteristics and outcome evaluation of acute renal failure in critically ill patients in ICU. Chin J Pract Inter Med. 2007; 27: 1753-5.
24. Bresolin N, Silva C, Halllal A, et al. Prognosis for children with acute kidney injury in the intensive care unit. Pediatr Nephrol. 2009;24:537-44.
25. Vachvanichsanong P, Dissaneewate P, Lim A, et al. Childhood acute renal failure: 22-year experience in a university hospital in southern Thailand. Pediatrics.2006;118: 786–91.
26. Youssef D, Abd-Elrahman H, Shehab N, et al. Incidence of acute kidney injury in the neonatal intensiven care unit. Saudi J Kidney Dis Transpl.2015;26(1):67-72.
27. Andreoli SP. Acute kidney injury in children. Pediatr Nephrol. 2009;24:253-63.
28. Mak RH. Acute kidney injury in children: the dawn of a new era. Pediatr Nephrol. 2008;23:2147-9.
29. Abu-Haweleh AF. Acute renal failure in newborn: etiology and mortality rate in Jordan patients. Saudi J Kidney Dis Transpl. 1998;9:18-21.
30. Singbartl K. and Kellum J.A. AKI in the ICU: definition, epidemiology, risk stratification, and outcomes. Kidney International.2012;81:819–25.
31. Ottonello G, Dessi A, Neroni P, et al. Acute kidney injury in neonatal age. J of Pediatric and Neonatal I Medicine. 2014;3(2):030246.
32. Gopal Girish. Acute kidney injury in perinatal asphyxia.Indian J Pharm. Biol Res. 2014;2(2):60-5.
33. Gharehbaghi M. and Peirovifar A. Evaluating causes of acute renal failure in newborn infants. Pak J Med Sci. 2007; 23:877-80.
34. Agras P, Tarcan A, Baskin E, et al. Acute renal failure in neonatal period. Ren Fail. 2004;26(3):305-9.
35. Alkandari O, Eddington K.A., Hyder A. et al. Acute kidney injury is an independent risk factor for pediatric intensive care unit mortality, longer length of stay and prolonged mechanical ventilation in critically ill children: a two-center retrospective cohort study. Critical Care.2011;15:146.