Original Article

Incidence of Acute Kidney Injury and its Association with Different Hypoxic-Ischemic Encephalopathy Staging in Birth Asphyxiated Newborns of East Bihar, India

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Abstract

Background: Perinatal asphyxia causes Acute Kidney Injury (AKI) and Hypoxic-Ischemic Encephalopathy (HIE), which is fatal to neonates. The objective of the study was the assessment of birth asphyxiated neonates with AKI having different HIE staging. **Materials and Methods:** Total 100 term neonates (37–42 weeks) born with asphyxia admitted (inborn and outborn) to the neonatal intensive care unit (NICU) and invasive pneumococcal disease (IPD) were selected as Group I and 50 normal-term neonates (37–42 weeks) as Group II. Data were collected from the patients admitted to NICU and IPD, Department of Pediatrics, JLNMCH, Bhagalpur, Bihar, India. In this study, neonates with a serum creatinine level >1.1 mg/dl and urine output <1 ml/kg/h were classified as having AKI. HIE stages were calculated by Sarnat score of all asphyxiated neonates. Birth weight, gestational age, perinatal history of nephrotoxic drug, serum creatinine, and other laboratory findings were analyzed. Blood samples were collected at 48 h, 72 h, and 96 h after birth for biochemical test. **Results:** The incidence of AKI was significantly more in Group I, 76% than Group II, 4%. Among all asphyxiated neonates, 25 (32%) had oliguric and 51 (68%) had nonoliguric AKI, while in Group II, only 2 neonates had prerenal and nonoliguric AKI. The incidence of AKI correlated well with HIE staging. The percent incidence of AKI with HIE stage III neonates (100%) was more than AKI with HIE stage II (85%) and stage I (50%), respectively. Among 76 patients of Group I, 63 (82.8%) improved clinically after fluid therapy while 11 (14.4%) died. **Conclusion:** Birth asphyxia is common cause for AKI in neonates. Prerenal and nonoliguric AKI is dominant and controlled by fluid therapy. The percent incidence of AKI with HIE stage III had highest among all, showing the association of HIE with AKI.

Keywords: AKI, hypoxic-ischemic encephalopathy, neonates, perinatal asphyxia

Introduction

In India, about 0.6 million neonates died in 2018 due to birth asphyxia, preterm birth, neonatal infections and congenital malformations, whereas most of these deaths were preventable.[1,2] Birth asphyxia is a critical condition that poses risks not only during delivery but also in the long term. This condition is defined by impaired respiratory gas exchange, leading to hypoxemia, hypercapnia, and metabolic acidosis.[3] Birth asphyxia occurs in approximately 1%–1.5% of cases across various medical centers and is influenced by the newborn's birth weight and gestational age.[4]

Children under 4 weeks (28 days) of age are neonates, and these 28 days are most important for survival. Perinatal asphyxia often results in Hypoxic-Ischemic Encephalopathy (HIE) in neonates, frequently progressing to multiorgan failure that affects various organ systems. HIE is a common disease in neonates and constitutes a major etiology of morbidity and mortality in Neonatal Intensive Care Unit (NICU). Among 1000 births, about 1–10 newborns develop HIE, influenced by various factors.[5] HIE leads to an altered distribution of cardiac output, impairing tissue perfusion and triggering multiorgan dysfunction. Kidney is one of the organs which directly affected by HIE due to the high sensitivity of glomerular and

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renal tubular tissues to hypoxemia, renal dysfunction can develop within a day of HIE onset. If hypoxia is prolonged in time and irreversible, Acute Kidney Injury (AKI) can result in electrolyte imbalance, fluid and acidbase disturbance.[6] AKI is suspected when a newborn fails to pass urine for 48 h after birth or develops oliguria, edema, or hypertension at any time after birth. A rising trend in creatinine, with an increase of at least 0.3 mg/dl within 48 h, along with electrolyte and acid-base disturbances, indicates AKI. Diagnosing renal failure in neonates is problematic due to the presence of numerous incorrect clinical and biochemical indicators.[7,8] Here, we aim to study the risk factor and incidence of AKI with different stages of HIE in neonates. Early identification of renal failure is crucial in newborns with HIE, as it allows for the administration of appropriate fluid and electrolyte therapy to maintain a stable biochemical balance and save the life.

Objective

The objective of this study was to investigate the incidence of AKI in neonatal asphyxia and to correlate between severity of AKI and HIE staging.

Materials and Methods

Study design – Cohort study

Study location

This study was conducted at the NICU, Department of pediatrics, J.L.N.M.C.H., Bhagalpur, Bihar. Bhagalpur district is situated in East region of Bihar, and all the patients studied were from Bhagalpur and different districts of East Bihar.

Inclusion criteria

Term neonates (37–42 weeks) with or without asphyxia admitted to the NICU or invasive pneumococcal disease were included.

Exclusion criteria

Neonates with septicemia, necrotizing enterocolitis, significant birth defects, or respiratory distress syndrome, along with those receiving intravenous nephrotoxic medications, those with a maternal history of drug consumption or fever, and those born prematurely (<37 weeks) or postterm (>42 weeks), were excluded from the study.

Sample size

A convenient sample of 100 term (37–42 weeks) neonates born with asphyxia admitted to the NICU were selected in Group I and 50 normal-term (37–42 weeks) neonates without asphyxia in Group II.

Birth weight, gestational age, relevant perinatal history, and laboratory findings were analyzed, and data were collected. The goal of this monitoring was to identify any abnormalities in the metabolic, clinical, and hemodynamic environments in order to facilitate timely treatment. The use of a plastic collecting bag allowed for the monitoring of urine output (UOP) at every 12 h.[9] After getting parents' written consent for this study, blood samples were taken under aseptic conditions at 48 h, 72 h, and 96 h after delivery. The samples were tested for blood urea by colorimetry,[10] serum creatinine on molecular basis,[11] and serum electrolytes using the calorimetric method.[12,13] In this study, neonates with a serum creatinine level > 1.1 mg/dl and a blood urea level > 20 were classified as having acute kidney injury (AKI). Initially, they received a 10 ml/kg saline infusion over a duration of 20 min as part of a fluid challenge. Their UOP and clinical parameters were then examined. If the UOP remained below 1 ml/kg/h, a diuretic (furosemide injection at an administrated 1 mg/kg) was administered. If the UOP still remained below 1 ml/kg/h, the neonates were diagnosed with intrinsic renal failure and peritoneal dialysis was scheduled according to the guidelines.[14]

The neurologic state was evaluated every 12 h. This evaluation comprised the Sarnat and Sarnat staging for HIE, as well as tone, seizures, anterior fontanel, pupil size, and response.[15] All newborns were carefully observed and treated in accordance with established protocols.

Statistical analysis

Descriptive statistical analysis was conducted using SPSS statistic (version 15.0), Chicago, Illinois, USA and Microsoft Excel. The results on continuous measurements are presented in mean ± standard deviation (SD). Student *t*-test (two-tailed, independent) has been used to find out the significance of study parameters on continuous scale between two groups. Significance is assessed at 5% level of significance.

Results

In our study, 76 (78.8%) out of 100 asphyxiated neonates had AKI in which 65 (85.3%) had prerenal AKI and 11 (14.6%) had intrinsic AKI. In 76 AKI patients of Group I, 25 (32.8%) had oliguric and 51 (67.1%) had nonoliguric AKI, while in Group II, only 4% neonates had prerenal and nonoliguric AKI [Table 1]. The percent incidence of AKI with HIE stage III neonates (100%) was more than HIE stage II AKI (85%) and HIE stage I AKI (50%), respectively [Table 2]. AKI incidence was strongly associated with the progression of HIE. Table 2 shows that 62.5% nonoliguric AKI and 37.5% oliguric neonates had HIE I staging. Out of 56 neonates of HIE II, 48 (85%) had AKI developed in which 97.9% had prerenal AKI while only 2.1% had intrinsic renal failure. Maximum numbers of AKI neonates were diagnosed in HIE II staging in which 35 were nonoliguric and 13 oliguric. All neonates (12 out of 12) of HIE III neonates had AKI [Table 2]. Table 3 presents the biochemical analysis of blood samples obtained from infants with acute kidney injury. While estimated Glomerular Filtration Rate (eGFR) decreased with HIE staging, the creatinine level and blood urea increased with HIE staging (HIE III > HIE II > HIE I). Our results showed significant difference in the mean values of creatinine, blood urea, and eGFR, with HIE staging at the 5% level of significance [Table 3]. Sixty-three out of 76 improved clinically while 11 did not improve, 2 newborns were taken discharge against medical advice, 3 had peritoneal dialysis but were unable to recover, while 8 had related morbidities and refused perinatal dialysis and died

Table 1: Different types of acute kidney injury in Group I and Group II

	Total AKI neonates, *n* (%)	Prerenal, *n* (%)	Intrinsic renal, *n* (%)	Oliguria, *n* (%)	Nonoliguria, *n* (%)
Group I (*n*=100)	76 (76)	65 (85.5)	11 (14.4)	25 (32.8)	51 (67.1)
Group II (*n*=50)	2 (4)	2 (100)	0	0	2 (100)

AKI: Acute kidney injury

Table 2: Percent incidence of acute kidney injury and type of acute kidney injury and its association among different stages of HIE in Group I

HIE staging	Total number of neonates (Group I)	Number of AKI, *n* (%)	Number of patients with Pre-renal AKI, *n* (%)	Number of patients with intrinsic AKI, *n* (%)	Number of oliguric, *n* (%)	Number of nonoliguric, *n* (%)
HIE I	32	16 (50)	16 (100)	0	6 (37.5)	10 (62.5)
HIE II	56	48 (85)	47 (97.9)	1 (2.1)	13 (27)	35 (72.9)
HIE III	12	12 (100)	2 (16.6)	10 (83.3)	6 (50)	6 (50)
Total	100	76 (76)	65 (85.5)	11 (14.4)	25 (32.8)	51 (67.1)

AKI: Acute kidney injury, HIE: Hypoxic-ischemic encephalopathy

Table 3: Distribution of renal parameters among different stages of hypoxic-ischemic encephalopathy

HIE staging	Mean creatinine	Mean blood urea	Mean (eGFR)	Mean Na^+	Mean K^+	Mean Cl^-
HIE I	1.31	29.21	19.18	138.31	4.94	100.43
HIE II	1.72	57.36	13.64	138.31	5.01	98.75
HIE III	2.48	142.91	9.34	143.33	5.24	102.58
Mean±SD	1.84±0.48	76.5±48.34	14.03±4.0	139.98±2.36	5.06±0.12	100.59±1.56
P	<0.001	<0.002	<0.001	0.053	0.235	0.820

HIE: Hypoxic-ischemic encephalopathy, SD: Standard deviation, eGFR: Estimated glomerular filtration rate

in Group I while 2 out of 2 (100%) patients with AKI was clinically improved in Group II [Table 4].

Discussion

In our study, the average blood urea value was 76.5 ± 48.34. In contrast, Jayashree et al. reported an average of 94 ± 32.7, with 30 newborns, 55.5% of whom had Hypoxic-Ischemic Encephalopathy (HIE) Stage III.[16] Additionally, Aggarwal *et al*. conducted research with 25 patients and 25 controls, reporting a mean blood urea value of 33.6 ± 11.5 in the cases.[17] The majority of oliguric newborns had sonographic abnormalities, which were associated with a poorer prognosis. In our study, 82.8% improved clinically after fluid therapy (i.e., they had prerenal failure), while 14.4% did not improve (had intrinsic renal failure), while 100% Group II patients were recovered (they had prerenal failure). Our results are also in line with those of Mohan and Pai, who found a mortality rate of 36.1%, attributed to the high prevalence of co-morbid illnesses, 46.15% of which were nonoliguric among their patients.[18] Gupta *et al*. revealed that 47.14% of newborns who experienced asphyxiation suffered acute kidney damage.[19] Out of the 70 newborns that suffocated, 32 cases did not show any signs of hypoxic-ischemic encephalopathy. Specifically, a baby was considered to have renal failure if their UOP was < 0.5 ml/kg/h, their blood urea levels were >40 mg/dl, their serum creatinine levels were more than 1 mg/dl, and there was noticeable hematuria or proteinuria. Phuljhele *et al*. reported that 415 neonates were hospitalized with HIE after prenatal hypoxia, 52 (12.5%) of these instances were HIE-I; 242 (58.0%) were HIE-II; 121 (20.1%) were HIE-III,[1] whereas in our research, AKI with HIE III (100%) was more than HIE II (85%) and HIE I (50%), respectively.

The prevalence of acute kidney damage (AKI) in neonates exposed to hypoxia was 76% in our research. This rate is higher compared to other studies due to two main reasons. At first, our first inclusion criteria were all infants with HIE symptoms across all three phases. Second, we employed precise criteria to establish acute kidney injury in neonates, which encompassed either a UOP of <0.5 ml/kg/h or a serum creatinine level that surpasses 1.9 ± SD above the average value for gestational age (1 mg/dl). These parameters were unique to this study and effectively guided the management of neonates in the early stages of prerenal failure. The neonates reacted well to the fluid challenge, leading to a complete recovery rate of 100%. This information is important because it shows that the kidney is the organ that is most susceptible to harm caused by a lack of oxygen in episodes of low oxygen and blood flow, even though it receives the highest amount of oxygen. This occurs as a result of the unique blood supply to the renal medulla in the kidneys, leading to a transient decrease in the ability to concentrate urine. Prolonged injury causes extensive impairment of the tubules, ultimately resulting in intrinsic renal failure. Neonates that have experienced asphyxiation need to be resuscitated during the prerenal failure stage and administered sufficient fluids to avert the significant mortality associated with advancing renal failure.

Table 4: Outcome among Group I and Group II with acute kidney injury incidence

Outcomes	Number of neonates (%)	
	Group I ($n=76$)	Group II ($n=2$)
Clinically improved after fluid therapy (prerenal failure)	63 (82.8)	2 (100)
Clinically did not improve after fluid therapy (intrinsic renal failure)	11 (14.4)	0
Number of neonates who had associated morbidities and refused peritoneal dialysis and who died	8 (10.5)	0
Neonates in whom peritoneal dialysis was planned but went DAMA	2 (2.6)	0
Neonates who underwent peritoneal dialysis and died	3 (3.9)	0
Total number of neonates who died	11 (14.4)	0

DAMA: Discharge against medical advice

The predominant type observed in our study was nonoliguric, which can be attributed to a reduced sensitivity of the kidneys to vasopressin or a decrease in the release of vasopressin by the pituitary gland. Furthermore, there is a diverse response among individual nephrons and varying levels of damage to the tubular epithelium, leading to structural impairment in the majority of nephrons. This, in turn, hampers the flow of fluid through the tubules and reduces the amount of reabsorption taking place. Thus, it is important to note that acute kidney injury (AKI) can occur not only in newborns with low UOP (oliguric), but also in those with normal UOP (nonoliguric). This nonoliguric presentation is more common in Group I of delivery asphyxia and should not be disregarded.

Limitation

Although the study sheds light on the relationship between various HIE stages and the birth asphyxiated patient, it should be emphasized that it has several limitations. Data on maternal history of outborn patients, APGAR score, dietary habits, Kegel exercises, and birth time could not be noted. The study was limited to a hospital in JLNMCH with a convenient sample, and two groups were of unequal sample. However, the study provides an important basis for further investigation and treatment, clinical symptoms, and characteristics of birth asphyxiated neonates correlated with different HIE staging.

Conclusion

This study suggests the actual situation of East Bihar for incidence of AKI with different stages of HIE. Perinatal hypoxia is a significant contributing risk factor to neonatal renal insufficiency whereas shock and hypovolemia were additional risk factors for AKI. AKI and HIE staging exhibit a strong positive association in Group I of birth asphyxia.

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Conflicts of interest

There are no conflicts of interest.

References

1. Phuljhele DS, Dewangan DS, Rathi DY. Incidence of acute kidney injury in birth asphyxia and its correlation with severity of hypoxic ischemic encephalopathy (HIE) in newborns with perinatal asphyxia in SNCU at DR. BRAM Hospital, Raipur (CG). Pediatric Rev Int J Pediatr Res 2024;6:304-9.
2. Raina R, Nada A, Shah R, Aly H, Kadatane S, Abitbol C, *et al.* Artificial intelligence in early detection and prediction of pediatric/neonatal acute kidney injury: Current status and future directions. Pediatr Nephrol 2024;39:2309-24.
3. Gopal G. Acute Kidney Injury (AKI) in perinatal asphyxia. Indian J Pharm Biol Res 2014;2:60.
4. Keerio K, Memon S, Memon F, Jamil F, Syed FS. Frequency of Acute kidney injury with hypoxic ischemic encephalopathy staging in neonates with perinatal asphyxia: An observational study (Descriptive Case Series). Pak J Med Health Sci 2023;17:511.
5. Khandokar S, Naher BS, Albani SA, Sahidullah S, Jahan YT, Malaker P, *et al*. Impairment of renal function in perinatal asphyxia with hypoxic ischemic encephalopathy in term neonates. KYAMC J 2024;14:198-205.
6. Dincer E, Topçuoğlu S, Keskin Çetinkaya EB, Yatır Alkan Ö, Özalkaya E, Sancak S, *et al.* Acute kidney injury in neonatal hypoxic-ischemic encephalopathy patients treated with therapeutic hypothermia: Incidence and risk factors. Ther Hypothermia Temp Manag 2024;14:31-5.
7. Rajesh KC, Kanodia P, Sah SN, Adhikari S. Acute renal failure in newborns with Birth Asphyxia. J Nepalgunj Med Coll 2022;20:1-3.
8. Iribarren I, Hilario E, Álvarez A, Alonso-Alconada D. Neonatal multiple organ failure after perinatal asphyxia. An Pediatr (Engl Ed) 2022;97:280.e1-8.
9. Turner MJ, Rumpel JA, Spray BJ, Stence N, Neuberger I, Frymoyer A, *et al.* Urine biomarkers of acute kidney injury and association with brain MRI abnormalities in neonatal hypoxic-ischemic encephalopathy. J Perinatol 2024;44:1203-7.
10. Langenfeld NJ, Payne LE, Bugbee B. Colorimetric determination of urea using diacetyl monoxime with strong acids. PLoS One 2021;16:e0259760.
11. Narimani R, Esmaeili M, Rasta SH, Khosroshahi HT, Mobed A. Trend in creatinine determining methods: Conventional methods to molecular-based methods. Anal Sci Adv 2021;2:308-25.
12. Laurenciano CJ, Tseng CC, Chen SJ, Lu SY, Tayo LL, Fu LM. Microfluidic colorimetric detection platform with sliding hybrid PMMA/paper microchip for human urine and blood sample analysis. Talanta 2021;231:122362.
13. Molla MD, Degef M, Bekele A, Geto Z, Challa F, Lejisa T, *et al.* Assessment of serum electrolytes and kidney function test for screening of chronic kidney disease among Ethiopian Public Health Institute staff members, Addis Ababa, Ethiopia. BMC Nephrol 2020;21:494.
14. Karlowicz MG, Adelman RD. Nonoliguric and oliguric acute renal failure in asphyxiated term neonates. Pediatr Nephrol 1995;9:718-22.

15. El-Gamasy MA, Alarabawy R. Relation of serum creatinine to sarnat scoring and brain computerized tomography of neonates with hypoxic ischemic encephalopathy. A single-center experience. J Pediatr Neurosci 2018;13:437-42.
16. Jayashree G, Dutta AK, Sarna MS, Saili A. Acute renal failure in asphyxiated newborns. Indian Pediatr 1991;28:19-23.
17. Aggarwal A, Kumar P, Chowdhary G, Majumdar S, Narang A. Evaluation of renal functions in asphyxiated newborns. J Trop Pediatr 2005;51:295-9.
18. Mohan PV, Pai PM. Renal insult in asphyxia neonatorum. Indian Pediatr 2000;37:1102-6.
19. Gupta BD, Sharma P, Bagla J, Parakh M, Soni JP. Renal failure in asphyxiated neonates. Indian Pediatr 2005;42:928-34.