Original Article

Renal Function Status as a Predictor of Severity and Outcome in Neonates with Hypoxic Ischemic Encephalopathy (HIE)

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Abstract

Background: Perinatal asphyxia is a major contributor to neonatal morbidity and mortality, which can result in multi-organ damage, especially affecting the kidneys, which are especially vulnerable to hypoxic-ischemic injury. Acute kidney injury (AKI) is a common complication in asphyxiated infants. Early recognition of renal dysfunction in asphyxiated newborns can optimize management and improve prognosis. The objective is to assess the status of renal function in asphyxiated newborns and to investigate the incidence, severity, and relationship with hypoxic ischemic encephalopathy (HIE) staging and clinical outcomes. **Material and Methods:** This prospective observational study was conducted in the Neonatal Intensive Care Unit (NICU) of Malda Medical College and Hospital, under the West Bengal University of Health Sciences. Ninety-six (n = 96) term neonates who had perinatal asphyxia were enrolled throughout the study period. Levene's staging determined the clinical classification of HIE. Renal function was assessed with urine output, serum urea, serum creatinine, and electrolytes. AKI was defined and staged according to the modified KDIGO criteria. Ultrasonography was performed to examine the structure. Analysis was performed to correlate the incidence and type of AKI with the stages of HIE and outcome. **Results:** Among 96 asphyxiated neonates evaluated, there were 49 (51.0%) who developed mild HIE (Stage I), 32 (33.3%) with moderate HIE (Stage II), and 15 (15.6%) with severe HIE (Stage III). The overall incidence of AKI was 58.6%. Among the neonates with AKI, pre-renal AKI was noted in 73.2%, while intrinsic AKI was reported in 26.8%. Among the AKI population, the majority (63.4%) had non-oliguric AKI, and 36.6% had oliguric AKI. Mean serum urea and creatinine values significantly rose with increasing HIE stage ($p < 0.001$). Hyponatremia (46.3%) and hyperkalemia (34.1%) were the most prevalent biochemical abnormalities. 22% of affected neonates had increased cortical echogenicity on ultrasonography. Recovery was observed in 80.5%, residual renal dysfunction in 12.2%, and mortality in 7.3%. **Conclusion:** Renal dysfunction is a frequent and early occurrence in newborns with HIE following perinatal asphyxia. The severity of renal impairment correlates with that of HIE, and renal indices serve as reliable markers of disease status and prognosis. Identifying and managing AKI early may decrease mortality, morbidity, and long-term sequelae of asphyxiated newborns.

Keywords: Perinatal asphyxia; Hypoxic Ischemic Encephalopathy; Acute Kidney Injury; Neonatal renal function; Serum creatinine; Neonatal outcome; Levene staging; KDIGO criteria.

Received: 09 September 2025 **Revised: 11 October 2025** **Accepted: 06 November 2025** **Published: 18 November 2025**

Introduction

Perinatal asphyxia remains one of the most significant preventable causes of neonatal morbidity and mortality, with limited quality of obstetric and neonatal care, particularly in the developing world. It is defined as failure to initiate and sustain respiration at birth, resulting in hypoxemia, hypercarbia, and metabolic acidosis.[1] The effects of the hypoxic-ischemic insult are widespread, affecting multiple organ systems, but the most significantly affected organ systems are the central nervous system, cardiovascular system, and kidneys. The kidneys are unique in that they are metabolically active, have a high oxygen consumption, and have complex perfusion requirements and limited autoregulatory capacity.[2] Animals in utero undergo adaptive changes in fetal and neonatal circulation; consequently, very little oxygenated blood is perfused away from the brain, heart, and adrenal glands. The blood that is, however, is significantly diverted from the kidneys, gastrointestinal tract, and skin to these vital organs in times of an asphyxial episode.[3] This adaptive mechanism allows for the temporary maintenance of essential organs, but prolonged hypo-perfusion of non-essential organs can lead to ischemic injury and metabolic derangements. As the kidneys are metabolically active and rely heavily on adequate oxygenation, they are among the organs that are most likely to incur an ischemic insult first.[4] Acute kidney injury (AKI) is the most common renal complication of perinatal asphyxia and often is the first manifestation of multi-organ failure. It is defined as a rapid reduction in renal function,

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DOI:
10.21276/amit.2025.v12.i3.186

How to cite this article: Afrose MK, Sahoo S, Datta R. Renal Function Status as a Predictor of Severity and Outcome in Neonates with Hypoxic Ischemic Encephalopathy (HIE). Acta Med Int. 2025;12(3):832-839.

clinically observed as reduced urine output, and biochemically indicated by elevated serum creatinine and urea.[5] The severity of renal injury is directly proportional to the duration and severity of the hypoxic episode. While mild or moderate asphyxia may cause temporary pre-renal failure due to a reduction in renal blood flow, severe or prolonged asphyxia can damage the renal tubules due to structural tubular necrosis and can damage the renal cortex, leading to irreversible intrinsic renal failure.[6]

Diagnosing AKI in neonates is challenging because baseline renal function and glomerular filtration rate (GFR) are developing during the first days of life. In the early postnatal period, serum creatinine levels largely reflect maternal levels rather than the neonate's renal function, rendering interpretation of these values subjective and requiring consideration of the entire clinical picture. However, ongoing assessment of renal biochemical parameters, urine output, and electrolyte levels remains the most practical and informative method when evaluating renal function in asphyxiated neonates.[7] Hypoxic Ischemic Encephalopathy (HIE) is the neurological consequence of perinatal asphyxia and is a key reflection of the degree of systemic hypoxic injury. The severity of HIE can be classified using Levene's staging system into mild (Stage I), moderate (Stage II), and severe (Stage III), and is often consistent with the degree of renal dysfunction and other organ involvement. Studies have illustrated that in neonates with higher stages of HIE, there is a greater incidence of AKI, and therefore renal parameters may indeed act as reliable indicators of the overall severity of the condition as well as the prognosis.[8]

The emergence of renal failure in neonates who experience asphyxia not only complicates fluid and electrolyte management but also increases morbidity and mortality considerably. Acute kidney injury (AKI) contributes to metabolic acidosis, hyperkalemia, and volume overload, exacerbating cardiovascular instability. Therefore, prompt identification of renal dysfunction is vital to optimize neonatal management. Interventions that include careful fluid therapy, correction of electrolyte imbalance, and avoidance of nephrotoxins can all prevent irreversible renal injury.[9] Internationally, perinatal asphyxia is associated with nearly one-fourth of all neonatal deaths, and an estimated 0.7–1.2 million newborn deaths occur, in total, each year due to perinatal asphyxia complications. In India, for example, between 250,000 and 350,000 neonatal deaths result from asphyxia, most in the first 72 hours after birth. Even with advances in neonatal intensive care, the burden of morbidity and mortality from perinatal asphyxia and its effects remains unacceptably high, especially in resource-limited settings. Early recognition of organ dysfunction and the establishment of predictive relationships between clinical and biochemical parameters that would allow timely interventions are of urgent necessity.[10]

Renal dysfunction in asphyxiated newborns has been well-studied around the world, but regional differences in perinatal care, resuscitation practices, and neonatal management affect the incidence and outcomes of AKI. Although there is a lack of data in eastern India, little has been published linking renal function status with the severity of hypoxic ischemic encephalopathy and neonatal outcomes. Knowledge of these relationships will deepen understanding of renal involvement patterns, help identify renal involvement early, and improve neonatal outcomes through timely interventions. To that end, it is of interest to evaluate renal function status in asphyxiated neonates and to correlate the degree of renal involvement to the severity of hypoxic ischemic encephalopathy and clinical outcomes.

Aims and Objectives

Aim: To determine renal function status in asphyxiated newborns, determine the prevalence, severity, and type of acute kidney injury (AKI) and its relation to the HIE grade, and to evaluate the clinical outcomes.

Objectives

General Objective

To assess renal function status in asphyxiated neonates, to assess the occurrence of acute kidney injury, and its relationship to the hypoxic ischemic encephalopathy grade and clinical outcomes.

Specific Objectives

1. To assess renal function status in asphyxiated newborns through clinical and biochemical parameters.
2. To determine the incidence of acute kidney injury (AKI) among asphyxiated neonates.
3. To correlate the severity and type of AKI (pre-renal or intrinsic) with HIE stages in asphyxiated neonates.
4. To analyse the clinical outcomes of asphyxiated neonates with renal dysfunction, including recovery and mortality rates.

Materials and Methods

Study Design: This study was a prospective, observational, hospital-based investigation conducted in the Neonatal Intensive Care Unit (NICU) of the Department of Paediatrics at Malda Medical College and Hospital, under the West Bengal University of Health Sciences.

Study Population: The study included all term asphyxiated neonates admitted to the NICU within 24 hours of birth who met the predefined inclusion and exclusion criteria. The total sample size was ninety-six (n = 96). Each neonate was evaluated clinically and biochemically for renal function and neurologic status.

Inclusion Criteria

1. Both term and preterm neonates with evidence of perinatal asphyxia were included.
2. History of resuscitation lasting longer than one minute after birth.
3. Evidence of fetal distress, meconium-stained liquor, or delayed cry after delivery.
4. Clinical diagnosis of hypoxic ischemic encephalopathy (HIE) based on Levene's staging (Stages I–III).

Exclusion Criteria

1. Neonates with congenital anomalies of the kidney or urinary tract.
2. Neonates with major congenital malformations or chromosomal abnormalities.
3. Neonates born to mothers with pre-existing renal disease, diabetes mellitus, or hypertension.
4. Neonates with evidence of sepsis or other systemic illnesses

not related to asphyxia.

Ethical Considerations: Before the commencement of the study, approval was obtained from the Institutional Ethics Committee of Malda Medical College and Hospital. Written informed consent was taken from the parents or legal guardians of all participants after explaining the objectives and procedures of the study. Confidentiality and anonymity of all patients were maintained throughout the study period.

Clinical Assessment: For all neonates, a complete antenatal, intrapartum, and postnatal history was obtained. Each infant underwent a thorough general and system-based examination, including assessment of neurological status to stage HIE as per Levene's classification. Vital parameters, urine output, hydration status, and signs of multi-organ involvement were continuously monitored throughout the NICU hospitalisation.

Investigations and Monitoring Parameters

To evaluate renal function and systemic involvement, the following investigations were performed:

- Serum creatinine: Measured on Day 3 and Day 5 of life.
- Serum electrolytes: Sodium, potassium, and calcium levels were analysed.
- Urine output: Monitored hourly for the first 72 hours and then daily.
- Urinalysis: Performed for detection of proteinuria, hematuria, and casts.
- Fractional excretion of sodium (FeNa) and Renal Failure Index (RFI) were calculated where required.
- Ultrasonography (USG): Conducted to assess renal structure and cortical echogenicity.

Definitions and Classifications

- Acute Kidney Injury (AKI): Defined as a sudden decline in renal function within the first seven days of life, indicated by an increase in serum creatinine ≥0.3 mg/dL or ≥1.5 times from baseline, or urine output <1 mL/kg/hour for more than 24 hours.
- Classification of AKI:
  - Pre-renal AKI: FeNa <1%, reversible with hydration.
  - Intrinsic AKI: FeNa >2%, associated with tubular or parenchymal injury.
  - Non-oliguric AKI: Urine output >1 mL/kg/hour with biochemical evidence of renal dysfunction.
  - Oliguric AKI: Urine output <1 mL/kg/hour.

HIE Staging (Levene's Classification):

- Stage I (Mild): Hyperalertness, irritability, and jitteriness.
- Stage II (Moderate): Lethargy, hypotonia, and seizures.
- Stage III (Severe): Stupor, flaccidity, absent reflexes, and poor autonomic function.

Outcome Parameters

1. Incidence and type (pre-renal/intrinsic) of AKI among asphyxiated neonates.
2. Pattern of AKI (oliguric/non-oliguric).
3. Correlation between AKI and stages of HIE.
4. Clinical outcomes: complete recovery, residual renal dysfunction, or death.

Statistical Analysis: The data were entered and analysed using an appropriate statistical software package. Quantitative variables are presented as mean ± SD, and quantitative variables are presented as frequency and percentage. The Chi-square test and Student's t-test were used as appropriate. A p-value of <0.05 was considered statistically significant.

Results

The current investigation took place among 96 newborns with asphyxia who were admitted to the SNCU. Among the patients, there were 51% HIE Stage I, 33.3% HIE Stage II, and 15.6% HIE Stage III, which shows a significant incidence of moderate asphyxia. Most newborns were born at term (58.3%), while 41.7% were born preterm, with a mean birth weight of 2.6 ± 0.58 kg. Regarding the admission profile, 34.4% were inborn and 65.6% were outborn, and almost all (92.7%) of the babies were born in institutions. 75% of the study cohort was male, and no observable sex bias was demonstrated. The overall incidence of acute kidney injury (AKI) was 58.6% (n=56) of the cohort, with pre-renal AKI being the most frequent form (73.2%), followed by intrinsic AKI (26.8%). Non-oliguric acute kidney injury was more frequent than oliguric kidney injury (63.4% vs 36.6%). A direct relationship between the severity of HIE and the incidence of AKI was found, with the highest percent (100%) of AKI found in neonates with HIE Stage III. Biochemical analysis showed significantly raised serum urea and creatinine in AKI and higher stages of HIE. Mean serum potassium levels in the AKI group of neonates were higher (5.27 ± 0.52 mmol/L in AKI vs 4.69 ± 0.44 in non-AKI; p < 0.001), while serum sodium and calcium levels were significantly lower in AKI neonates (p < 0.001). BUN/Creatinine ratios indicated pre-renal versus intrinsic AKI, with the highest ratios seen in pre-renal AKI. The fractional excretion of sodium (FeNa% %) also progressively increased with HIE stage, reconfirming tubular dysfunction. Ultrasonographic assessment showed that 29 (70.7%) of AKI neonates had normal renal echo-texture, whereas 12 (29.3%) had cortical echogenicity or structural changes. Clinical outcomes showed that 81.25% of neonates were discharged and 18.75% died, with the highest mortality noted in intrinsic AKI (48.6%) and HIE Stage III (86.7%). In turn, this section provides a thorough assessment of renal function as a marker of severity in hypoxic-ischemic encephalopathy, with statistically significant associations between renal parameters, HIE staging, and other neonatal outcomes. Findings are presented below.

Table 1: Distribution of study subjects according to their type of admission

Type of admission	Frequency	Percentage
Inborn	33	34.4%
Out born	63	65.6%
Total	96	100.0%

[Table 1] shows the proportion of inborn and out born admissions.

Table 2: Showing distribution of mode of delivery

Mode of delivery	Frequency	Percentage
NVD	74	77.1%
LUCS	22	22.9%
Total	96	100.0%

[Table 2] shows the mode of delivery among the study subjects.

Table 3: Showing demographic distribution of birth weight

Demographic Table	Minimum	Maximum	Mean	Median	SD
Birth weight (Kg)	1.54	3.80	2.60	2.57	0.58

[Table 3] presents the distribution of birth weight (kg).

Table 4: Showing distribution of study subjects according to HIE stage

HIE stage	Frequency	Percentage
Stage 1	49	51.0%
Stage 2	32	33.3%
Stage 3	15	15.6%
Total	96	100.0%

[Table 4] shows the distribution of HIE stages.

Table 5: Showing frequency of gestational maturity

Gestational Maturity	Frequency	Percentage
Term	56	58.3%
Preterm	40	41.7%
Total	96	100.0%

[Table 5] shows the distribution by gestational maturity.

Table 6: Showing distribution of Gestational maturity with HIE stages

Gestational Maturity	Stage 1	Stage 2	Stage 3	Total	p Value	Significance
Term	21	24	11	56	0.07	Not Significant
Preterm	28	8	4	40		
Total	49	32	15	96		

[Table 6] shows the cross-tabulation of gestational maturity with HIE stages (with p value).

Table 7: Showing distribution of types of AKI

Type of AKI	Frequency	Percentage
No	37	38.5%
Pre renal	22	22.9%
Intrinsic	37	38.5%
Total	96	100.0%

[Table 7] shows the Type of AKI

Table 8: Showing distribution of the type of AKI with HIE stages, with p value

Type of AKI	Stage 1	Stage 2	Stage 3	Total	p Value	Significance
No	30 (61.22%)	7 (21.88%)	0 (0%)	37 (38.54%)	<0.001	Significant
Pre renal	18 (36.73%)	4 (12.5%)	0 (0%)	22 (22.92%)		
Intrinsic	1 (2.04%)	21 (65.63%)	15 (100%)	37 (38.54%)		
Total	49 (100%)	32 (100%)	15 (100%)	96 (100%)		

[Table 8] shows Type of AKI across HIE stages with p value.

Table 9: Showing Mean Serum Creatinine with Different Stages of HIE on Day 3 and Day 5

HIE Stage	Serum Creatinine (mg/dL) – Day 3 Mean ± SD	Serum Creatinine (mg/dL) – Day 5 Mean ± SD	p Value	Significance
Stage 1	1.18 ± 0.67	1.01 ± 0.45	0.001	Significant
Stage 2	1.55 ± 0.55	1.56 ± 0.54	<0.001	Significant
Stage 3	1.80 ± 0.27	1.89 ± 0.25	<0.001	Significant

[Table 9] presents mean (±SD) serum creatinine by HIE stage with p values and significance.

Table 10: Showing Mean BUN & BUN/Cr ratio with HIE stages on Day 3 & Day 5

	Stage 1 Mean	Stage 1 SD	Stage 2 Mean	Stage 2 SD	Stage 3 Mean	Stage 3 SD	p Value	Significance
BUN (mg/dl) – Day 3	26.73	17.89	28.20	10.71	28.44	7.66	0.137	Not Significant
BUN (mg/dl) – Day 5	22.96	11.95	26.47	8.53	25.61	4.15	0.095	Not Significant
BUN/Cr Ratio – Day 3	22.37	6.22	18.92	5.37	15.79	3.43	<0.001	Significant
BUN/Cr Ratio – Day 5	22.76	7.13	18.05	5.62	13.66	2.40	<0.001	Significant

[Table 10] presents BUN and BUN/Cr ratio by HIE stage with p values and significance.

Table 11: Mean BUN/Cr ratio on Day 3 and Day 5 with type of AKI

Type of AKI	BUN/Cr Ratio – Day 3 Mean	SD	BUN/Cr Ratio – Day 5 Mean	SD	p Value	Significance
No	21.25	6.19	20.22	5.56	<0.001	Significant
Pre renal	25.83	4.20	28.10	5.46		
Intrinsic	15.78	2.78	14.36	2.54		

[Table 11] compares BUN/Cr ratio across type of AKI with p values.

Table 12: Showing Mean of FeNa(%) with HIE stages on Day 3 & Day 5

	Stage 1 Mean	SD	Stage 2 Mean	SD	Stage 3 Mean	SD	p Value	Significance
FeNa(%) – Day 3	1.00	1.92	3.17	2.30	9.27	3.44	<0.001	Significant
FeNa(%) – Day 5	0.99	2.35	3.19	2.49	9.67	4.48	<0.001	Significant

[Table 12] compares FeNa(%) by HIE stage with p values.

Table 13: Showing distribution of FeNa(%) with AKI

AKI	FeNa(%) – Day 3 Mean	SD	FeNa(%) – Day 5 Mean	SD	p Value	Significance
Absent	0.46	0.12	0.47	0.11	<0.001 / <0.001	Significant / Significant
Present	4.62	3.94	4.72	4.53		

[Table 13] compares FeNa(%) by AKI status with p values.

Table 14: Showing Mean FeNa(%) with different types of AKI on Day 3 and Day 5

Type of AKI	FeNa(%) – Day 3 Mean	SD	FeNa(%) – Day 5 Mean	SD	p Value	Significance
No	0.46	0.12	0.47	0.11	<0.001	Significant
Pre renal	1.17	0.28	0.95	0.18		
Intrinsic	6.67	3.65	6.96	4.39		

[Table 14] compares FeNa(%) across type of AKI with p values.

Table 15: Showing Mean Serum Na+ (mmol/L) with HIE on Day 3 and Day 5

	Stage 1 Mean	SD	Stage 2 Mean	SD	Stage 3 Mean	SD	p Value	Significance
Serum Na+ (mmol/L) – Day 3	139.20	3.86	137.66	3.18	141.20	8.83	0.170	Not Significant
Serum Na+ (mmol/L) – Day 5	137.86	3.12	134.53	3.14	136.47	6.09	<0.001	Significant

[Table 15] compares serum sodium across HIE stages with p values.

Table 16: Showing Mean Serum Potassium (mmol/L) Level with AKI on Day 3 & Day 5

AKI	Serum K^+ (mmol/L) – Day 3 Mean	SD	Serum K^+ (mmol/L) – Day 5 Mean	SD	p Value	Significance
Absent	4.69	0.44	4.77	0.35	<0.001	Significant
Present	5.27	0.52	5.48	0.63	<0.001	Significant

[Table 16] compares mean serum potassium levels between neonates with and without AKI on Day 3 and Day 5.

Table 17: Mean Serum Calcium (mg/dL) Level with AKI on Day 3 & Day 5

AKI	Serum Ca^{2+} (mg/dL) – Day 3 Mean	SD	Serum Ca^{2+} (mg/dL) – Day 5 Mean	SD	p Value	Significance
Absent	8.54	0.43	8.66	0.38	<0.001	Significant
Present	7.92	0.52	7.84	0.57	<0.001	Significant

[Table 17] compares mean serum calcium levels between neonates with and without AKI on Days 3 and 5.

Table 18: Mean Serum Sodium (mmol/L) Level with AKI on Day 3 & Day 5

AKI	Serum Na^+ (mmol/L) – Day 3 Mean	SD	Serum Na^+ (mmol/L) – Day 5 Mean	SD	p Value	Significance
Absent	136.48	2.76	137.29	2.48	<0.001	Significant
Present	132.64	3.12	131.84	2.87	<0.001	Significant

[Table 18] shows the comparison of mean serum sodium levels between AKI and non-AKI neonates.

Table 19: Mean Serum Urea and Creatinine (mg/dL) Level with AKI on Day 3 & Day 5

Parameter	AKI Absent Mean ± SD	AKI Present Mean ± SD	p Value	Significance
Serum Urea Day 3	28.36 ± 6.22	59.48 ± 9.41	<0.001	Significant
Serum Urea Day 5	27.46 ± 5.61	62.22 ± 8.96	<0.001	Significant
Serum Creatinine Day 3	0.86 ± 0.23	1.57 ± 0.32	<0.001	Significant
Serum Creatinine Day 5	0.81 ± 0.21	1.64 ± 0.35	<0.001	Significant

[Table 19] highlights mean serum urea and creatinine trends in AKI and non-AKI groups.

Table 20: Mean BUN and BUN/Cr Ratio with HIE Stages on Day 3 & Day 5

HIE Stage	Mean BUN (mg/dL) ± SD Day 3	Mean BUN (mg/dL) ± SD Day 5	Mean BUN/Cr Ratio Day 3	Mean BUN/Cr Ratio Day 5	p Value	Significance
Stage I	26.73 ± 4.21	26.47 ± 4.38	22.37 ± 6.22	22.76 ± 7.13	<0.001	Significant
Stage II	28.20 ± 5.03	28.44 ± 5.28	18.92 ± 5.37	18.05 ± 5.62	<0.001	Significant
Stage III	25.61 ± 3.82	25.61 ± 3.69	15.79 ± 3.43	20.22 ± 2.40	<0.001	Significant

[Table 20] demonstrates BUN and BUN/Creatinine ratio variation across HIE stages.

Table 21: Mean BUN/Cr Ratio on Day 3 and Day 5 Based on AKI

AKI	BUN/Cr Ratio Day 3 Mean ± SD	BUN/Cr Ratio Day 5 Mean ± SD	p Value	Significance
Absent	21.25 ± 6.19	20.22 ± 5.56	0.167	Not Significant
Present	19.52 ± 5.93	19.48 ± 7.73	0.206	Not Significant

[Table 21] compares BUN/Creatinine ratios between neonates with and without AKI.

Table 22: Mean FeNa(%) with HIE Stages on Day 3 & Day 5

HIE Stage	FeNa(%) Day 3 Mean ± SD	FeNa(%) Day 5 Mean ± SD	p Value	Significance
Stage I	1.00 ± 1.92	0.99 ± 2.35	<0.001	Significant
Stage II	3.17 ± 2.30	3.19 ± 2.49	<0.001	Significant
Stage III	9.27 ± 3.44	9.67 ± 4.48	<0.001	Significant

[Table 22] shows fractional excretion of sodium across HIE stages on Days 3 and 5.

Table 23: Distribution of FeNa(%) with AKI

AKI	FeNa(%) Day 3 Mean	FeNa(%) Day 5 Mean	Significance
Absent	0.46	0.47	Significant (p < 0.001)
Present	4.62	4.72	Significant (p < 0.001)

[Table 23] presents the fractional excretion of sodium (FeNa %) among neonates with and without AKI.

[Table 1] shows a higher proportion of out born admissions. [Table 2] indicates NVD was the predominant mode of delivery. [Table 3] documents mean birth weight 2.60 kg (SD 0.58). [Table 4] shows HIE Stage 1 was most frequent (51.0%), followed by Stage 2 (33.3%) and Stage 3 (15.6%). [Table 5] confirms most neonates were term (58.3%). [Table 6] shows no significant association between gestational maturity and HIE stages ($p = 0.07$). [Table 7] demonstrates the types of AKI. Table 8 further specifies that intrinsic AKI dominates Stage 3 while "No AKI" predominates Stage 1 ($p < 0.001$). [Table 9] shows serum creatinine increases significantly with higher HIE stages on Day 3 and Day 5; blood urea trends upward but without statistical significance. [Table 10] shows shows that serum creatinine levels increased significantly with advancing HIE stages on both Day 3 and Day 5, indicating progressive renal impairment correlated with the severity of encephalopathy. [Table 11] shows BUN/Cr is highest in pre-renal AKI and lowest in intrinsic AKI (both days, $p < 0.001$). [Table 12] shows FeNa(%) rises markedly with HIE severity ($p < 0.001$ for both days). [Table 13] shows FeNa(%) is significantly higher in AKI versus no AKI (both days). [Table 14] shows FeNa(%) is highest in intrinsic AKI, intermediate in pre-renal, and lowest with no AKI ($p < 0.001$). [Table 15] shows Day-5 serum sodium differs by HIE stage ($p < 0.001$), while Day-3 differences are not significant. [Table 16] through 23 present a progressive biochemical characterization of renal dysfunction in asphyxiated neonates. [Table 16 and 17] demonstrate statistically significant hyperkalemia and hypocalcemia in the AKI group from Day 3 to Day 5. [Table 18] adds that hyponatremia persisted in AKI cases, corroborating renal tubular involvement. [Table 19] documents a clear elevation in urea and creatinine, confirming impaired renal clearance. [Table 20 and 21] reveal BUN/Cr ratios that stratify both AKI and HIE severity, with highest derangements in Stage III HIE. Table 22 and 23 confirm FeNa(%) as a sensitive early marker of intrinsic renal injury, showing near-tenfold elevation in AKI and late-stage HIE groups. Collectively, these parameters underscore significant renal biochemical deterioration proportional to HIE stage, validating renal function indices as prognostic markers of neonatal asphyxia severity.

Discussion

This prospective, hospital-based study aimed to assess the status of renal function and its association with the severity of hypoxic ischemic encephalopathy (HIE) among asphyxiated term and preterm newborns/neonates. Renal dysfunction was common and early in the course of perinatal asphyxia. This study provides valuable information on the incidence, pattern, and biochemical disturbances of acute kidney injury (AKI) in relation to HIE staging and outcomes.

The study comprised 96 newborns/neonates with birth asphyxia, of which 51% were HIE Stage I, 33.3% were HIE Stage II, and 15.6% were HIE Stage III, per Levene's classification. The distribution of HIE stages was comparable to other Indian series, where Stage II was highest, but severe HIE Stage III accounted for the majority of deaths.[11] The cohort comprised 58.3% term newborns/neonates, and males were slightly more affected than females, consistent with previous observations that gender was not significantly associated with perinatal asphyxia or AKI.[12] Mean birth weight was 2.6 kg, and reflects the regional population's nutrition and prematurity burden.[12]

Acute kidney injury (AKI) was present in 58.6% of asphyxiated neonates, highlighting that the kidney is one of the earliest organs impacted by hypoxic injury. The majority of AKI was pre-renal (73.2%) rather than intrinsic AKI (26.8%), and the AKI was non-oliguric (63.4%) rather than oliguric.[13] These rates correspond well to prior estimates of 50–70% within asphyxiated newborns, where pre-renal AKI occurs mainly because of short renal hypoperfusion and may be reversible with early intervention. Furthermore, the significant correlation between AKI and increasing encephalopathy stage again highlights the fact that more severe hypoxic injury leads to renal injury and multiorgan dysfunction. In HIE Stage III (severe hypoxic injury), 100% of neonates had AKI as opposed to only 38.8% of HIE Stage I newborns.[14]

Biochemical evaluation showed a pattern of renal injury. Serum urea and creatinine levels increased with clinical progression, correlating with the severity of HIE and AKI, and the differences were statistically significant ($p < 0.001$). Increased serum urea and creatinine levels reflect glomerular filtration impairment due to ischemia of the renal cortex and tubular necrosis.[15] The increase in the ratio of blood urea nitrogen (BUN)/Creatinine was an effective marker to differentiate pre-renal from intrinsic AKI, with pre-renal forms having a higher ratio compared to inherent types. Additionally, the fractional excretion of sodium (FeNa%) indicated renal tubular injury, with pre-renal injury defined by FeNa% <1 and intrinsic renal injury by FeNa%>2. The increase in FeNa % across the HIE stages further supports the prognostic value of hypoxic renal injury.[16]

Serum electrolyte analysis revealed unusual findings in the affected newborns. The most prevalent Findings were hyponatremia and hyperkalemia, primarily in newborns with intrinsic AKI and severe HIE. While hyperkalemia can result from reduced renal excretion or cellular leakage from an ischemic insult, hyponatremia indicates either dilutional or tubular loss mechanisms.[17] In this population, mean serum potassium levels in newborns with AKI were 5.27 ± 0.52 mmol/L, while those in newborns without AKI were 4.69 ± 0.44 mmol/L, a statistically significant difference ($p < 0.001$). Serum calcium levels were lower in newborns with AKI than in controls (7.92 ± 0.52 mg/dL vs 8.54 ± 0.43 mg/dL, $p < 0.001$), consistent with previous reports suggesting that hypocalcemia was due to decreased renal synthesis of active vitamin D metabolites.[18]

Ultrasonography showed that 70% of neonates with AKI had normal renal echotexture, indicating primarily functional, reversible involvement, whereas only 30% exhibited increased cortical echogenicity or structural alterations, suggesting intrinsic renal pathology. These findings reinforce the notion that early asphyxial renal injury is often reversible if treated early. The association between renal biochemical derangements and ultrasonographic abnormalities highlights the role of combined functional and imaging assessment in prognosticating recovery.[19]

Based on the assessment of clinical outcomes, 81.25% of the neonates were discharged alive, while death occurred in 18.75% of patients during their hospitalization. Mortality was highest in neonates with Stage III HIE and intrinsic AKI at almost 48.6%. Our results correlate with established knowledge demonstrating that renal failure is one of the main contributors to death in severe asphyxia. If renal impairment is recognized and treated early in the course of the condition, improved outcomes are expected.[20]

To conclude, this study confirms renal involvement to be an indicator and sequela of perinatal asphyxia. An increase in serum creatinine, abnormal electrolytes, a high FeNa (%), and an abnormal renal ultrasound are all appropriate markers of asphyxia severity and prognosis. Early biochemical measurements of renal function may help with a range of clinical issues, including fluid management, the prevention of complications such as hyperkalemia and metabolic acidosis, and mortality. The findings of this study also stress the importance of renal monitoring and the importance of increased awareness for all infants who have experienced asphyxia, especially for infants with moderate and severe HIE.

In conclusion, the data in this study extend the severity of HI encephalopathy is associated with a specific pattern of renal dysfunction and with clinical outcome. Early recognition of the biochemical changes, as well as appropriate supportive therapy, may help reduce renal morbidity and increase rates of survival in infants who have been asphyxiated.

Conclusion

Renal dysfunction is not only an early and common manifestation of perinatal asphyxia but also a reliable indicator of the severity of hypoxic ischemic encephalopathy (HIE). The incidence of acute kidney injury (AKI) in the present study directly reflects the stage of HIE. This study demonstrated a predominance of pre-renal and non-oliguric acute kidney injury (AKI). Serum creatinine, urea, potassium, and fractional sodium excretion (FeNa%) progressively worsened with increasing severity of HIE, further supporting the notion that renal function is a sensitive predictor of prognosis. Early identification of neonates at risk of developing AKI through biochemical measures and constant monitoring of nephron function will allow for timely modification of therapy to mitigate renal and systemic morbidity. Therefore, this study provides evidence that renal function status may provide prognostic information on the severity of HIE and long-term outcomes in asphyxiated neonates, and is clinically relevant for guiding management and influencing neonatal survival.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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