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Original Research Article

A Hospital-Based Study Assessing Renal Functions in Perinatal Asphyxia and Various Stages of Hypoxic-Ischemic Encephalopathy (HIE) in Term Neonates

Kannu Priya[1], Nupur Kumari[2], Alka Singh[3], Bir Prakash Jaiswal[4]

[1]Senior Resident, Department of Pediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India
[2]Senior Resident, Department of Pediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India
[3]Professor, Department of Pediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India
[4]Professor, Department of Pediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India

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Corresponding author: Dr Nupur Kumari
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Abstract

Aim: The aim of the present study was to assess renal functions in perinatal asphyxia and various stages of Hypoxic-Ischemic Encephalopathy (HIE) in term neonates.

Material & Methods: This observational study included 150 full-term perinatally asphyxiated neonates admitted in Neonatal Intensive Care Unit (NICU) of Department of Pediatrics. Serum urea, creatinine and urine output were assessed on 1st, 3rd and 10th day of admission. A total of 75 newborns with normal Renal Function Test (RFT) and urine output were kept in Group A, while 75 newborn with abnormal RFT and urine output were kept in Group B.

Results: There was no significant difference between studied groups as regarding gestational age, weight, sex, maternal age and parity. There was statistically significant difference among Apgar score at 1 and 5 minutes between cases and controls. Assisted vaginal delivery and emergency caesarean section were more common among cases (13.34%, 41.33%) as compared to controls (8%, 16%). Urine parameters like creatinine clearance, urine output, urinary creatinine, Ph, urinary sodium, fractional excretion of sodium, renal failure index and osmolality all showed statistically significant difference between cases and controls except urine potassium and urine specific gravity. In this study as HIE stage progressed from stage-I to stage-III there was increase in values of blood urea, serum creatinine, urinary sodium, FeNa, RFI, along with fall in creatinine clearance and this difference was statistically significant ($p<0.001$).

Conclusion: Renal dysfunction correlates well with increasing severity of asphyxia in terms of HIE staging and it can be used as a marker to assess the severity of perinatal asphyxia.

Keywords: Hypoxic ischemic encephalopathy, Renal dysfunction, Serum creatinine, Serum urea

Introduction

Perinatal asphyxia is one of the most common causes of neonatal mortality and morbidity in developing countries. The world health organizations has defined birth asphyxia as "failure to initiate and sustain breathing at birth" and based on APGAR score as an Apgar score of <7 at one minute of life. [1] According to the 2000 report of National Neonatal Perinatal Database of India, [2] perinatal asphyxia occurred in 9 per cent of institutional deliveries. Its incidence is about 1-10% per 1000 live births. [3] Asphyxia can cause multiorgan dysfunction due to redistribution of cardiac output. Perfusion to more vital organs like heart, brain and adrenals is maintained at the expense of kidneys, gut and skin. [4]

As a result of prenatal hypoxia, the kidney is one of the organs that is frequently damaged. Renal insult may occur within 24 hours of a hypoxic ischemic episode, which if extended, may still cause irreversible cortical necrosis. [5] because kidneys are particularly sensitive to oxygen shortage; it is possible for this to happen. [6] Renal injury in birth asphyxia is a potential consequence of an adaptive mechanism. [7] Amongst the recognised complications, Acute Renal Failure (ARF) is the most common and carries a poor prognosis and even 40% of survivors may develop permanent renal damage. [8] The presence of perinatal asphyxia and its severity appears to correlate with the increasing incidence of AKI. [6,9]

Asphyxia is an important cause of AKI and transient kidney impairment with adverse effects, especially in initial five days of birth.[5] Early recognition of renal injury is important for maintenance of fluid

and electrolyte homeostasis. [6] The current diagnostic method for AKI is based on an abrupt fall in GFR, which is manifested by an acute rise in serum creatinine levels and/or a decline in urine output over a specified period of time. Current diagnostic approach of AKI is based on an acute decrease of GFR, as reflected by an acute rise in serum creatinine (SCr) levels and/or decline in urine output over a given time interval. [10,11,12] The novelty of this study is that it compared renal dysfunction in different stages of HIE (Levene staging) and also assessed the renal function on postnatal day 1, 3 and 10.

By this way, we can recognise early derangements of renal function in asphyxiated neonates according to their HIE stage which can be helpful in management of perinatal asphyxiated neonates, so we can reduce the mortality and morbidity in perinatally asphyxiated term neonates.

Hence, the present study was conducted with an aim to study renal functions in perinatal asphyxia and various stages of HIE in term neonates

Material & Methods

This prospective observational study was conducted in the NICU, Department of Pediatrics, NMCH, Patna, Bihar, India, India for a period of one year.

All the patients fulfilling the inclusion criteria within this time frame of the study were considered eligible. Parents gave their written, informed consent for the enrollment of their children in the study.

Inclusion Criteria:

All full-term asphyxiated neonates (n=146), determined by any of the following criteria, i.e., Failure to initiate and sustain breathing at birth (WHO criteria) or Apgar score <7 at 1 minute of age {National Neonatal Perinatal Database (NNPD) criteria}, born in the hospital and admitted in NICU of the department of Pediatrics of NMCH, Patna, Bihar, India, India during the study period were enrolled. [6]

Exclusion Criteria:

Neonates whose parents were not willing to give consent for participation, preterm (<37 weeks of gestation), out born, congenital malformations and congenital infections, confirmed or suspected clinical meningitis, nonvigorous meconium stained liquor, maternal USG during pregnancy showing any structural abnormality of fetal kidney, surgical conditions like necrotising enterocolitis and tracheoesophageal fistula, structural disease of kidney confirmed by ultrasonography, neonates with sepsis (positive sepsis screen and or positive blood culture) and neonates with primary disease of kidney were excluded from the study.

Methodology

Neonates with deranged baseline RFT as per age reference values in presence of normal maternal RFT were assumed to have primary disease of kidney. RFT was assessed from patient's serum, on the Randox Imola auto-analyser available in the central biochemistry lab of the institute. The reference values of serum urea and creatinine for term neonates were taken as 3-12 mg/dL and 0.3-1.0 mg/dL, respectively. [13] A total of 50 neonates were excluded and total 100 neonates were analysed for final results. Complete antenatal, perinatal and postnatal history was recorded in a predefined study proforma.

Full medical history especially the history of anaesthesia during caesarean section and drug intake by mother or infant were recorded. Complete physical and systemic examination including detailed neurological examination was done at the time of admission. Gestational age, birth weight, findings on physical examination and systemic examination were recorded on a predesigned pretested study proforma. Gestational age of newborn was assessed by the New Ballard score. [14] All asphyxiated neonates were also graded into HIE stages by the Levene staging system for HIE.

The classification system modified by Levene has three stages-mild HIE (I), moderate HIE

(II), severe HIE (III) based on clinical observation. [15]

In HIE stage I, no seizures are experienced and the neonate is irritable, tone is decreased and sucking is poor. In HIE stage II, neonate is lethargic, marked hypotonic, unable to suck and seizures are usually seen within 12 hours after birth. In HIE stage III, neonate is comatose, severely hypotonic, unable to maintain spontaneous respiration and seizures are prolonged. Maternal renal functions (serum urea and serum creatinine) prior to delivery were also measured.

After admission in NICU, baseline venous blood samples were withdrawn under aseptic conditions. Venous Blood samples were collected in appropriate vials for routine base line investigation like Complete blood count, Random blood sugar, C-reactive proteins, Serum electrolytes, blood culture and RFT at the time of NICU admission (Day 1). All blood samples were sent to the central laboratory of the hospital within 30 minutes of collection for estimation of biochemical parameter. RFT were again repeated on day 3 and day 10. USG abdomen of all enrolled neonate was done to rule out the suspected primary disease of kidney, i.e., any structural abnormality of fetal kidney. Kidney size, echo texture and corticomedullary differentiation were noted on ultrasonography. Urine output monitoring was done daily since admission to 10th

day of life. Oliguric renal failure was defined as urine output <1 mL/kg/hr for past 12 hours in a baby more than 24 hours of age. [6]

Asphyxiated babies with normal kidney functions (n=50) were grouped as A and asphyxiated babies with abnormal kidney functions (n=50) were grouped as B. Asphyxiated newborn (with our without deranged renal function) were managed conservatively as per the standard NICU protocols.

Statistical Analysis

All the data was collected, compiled, analysed using SPSS (Statistical Package for Social Sciences) Version 22.0 statistical analysis software and inter-operated statistically through relevant statistical methods like student's test (unpaired t-test) to compare renal function in various HIE stages.

Results

Table 1: Baseline characteristics in asphyxiated and non-asphyxiated babies

Variables	Cases (N=75)	Controls (N=75)	P value
	Mean±SD	Mean±SD	
Maternal age (years)	24.26±4.66 (18-36)	26.48±4.16 (20-37)	0.01
Gravida	1.66±0.84 (1-4)	1.62±0.76 (1-5)	0.82
APGAR score at 1 minute	3.47±1.36 (1-6)	7.0±0.0 (7-7)	<0.001
APGAR score at 5 minutes	6.64±1.56 (2-9)	9.0±0.0 (9-9)	<0.001
Length of baby	49.64±1.54 (47.5-52)	49.75±1.58 (47-53)	0.79
Birth weight (kgs)	2.90±0.36 (2.5-3.7)	2.92±0.32 (2.5-3.5)	0.88
Gestational age (weeks)	38.18±1.02	38.72±0.96	0.07

There was no significant difference between studied groups as regarding gestational age, weight, sex, maternal age and parity. There was statistically significant difference among Apgar score at 1 and 5 minutes between cases and controls.

Table 2: Mode of delivery in asphyxiated and non-asphyxiated babies

Mode of delivery	Cases (N=75)		Controls (N=75)	
	N	%	N	%
Normal vaginal delivery	34	45.34	54	72
Assisted vaginal delivery	10	13.33	6	8
Emergency LSCS	31	41.33	12	16
Elective LSCS	0	0.0	3	4

Assisted vaginal delivery and emergency caesarean section were more common among cases (13.34%, 41.33%) as compared to controls (8%, 16%).

Table 3: Renal function tests in asphyxiated and non-asphyxiated babies

Variables	Cases (N=75)	Controls (N=75)	P value
	Mean±SD	Mean±SD	
Creatinine clearance (ml/min/1.73m^2)	18.52±4.66 (8.3-28.6)	23.37±6.01 (12-39)	<0.001
Urine output (ml/kg/hr)	1.18±0.64 (0.2-3.5)	1.58±0.22 (1.24-2.1)	<0.001
Urine creatinine (mg/dl)	16.34±6.04 (8-33)	15.55±1.92 (10-28)	<0.001
Urine pH	5.07±0.19 (4.9-6)	6.05±0.39 (5-7)	<0.001
Urine specific gravity	1.018±0.007 (1.01-1.03)	1.023±0.007 (1.01-1.05)	0.01
Urine K^+ (m mol/l)	16.34±3.07 (10-25)	17.53±3.56 (11-26)	0.06
Urine Na^+ (m mol/l)	46.4.±14.6 (16-88)	18.72±2.56(13-23)	<0.001
FeNa (%)	2.10±0.88 (1-4.1)	1.24±0.42 (0.58-2.70)	<0.001
RFI	3.1±1.53(1.1-8)	1.73±0.58 (0.8-3.6)	<0.001
Urine osmolality	432.88±106.84 (249-610)	604.76±40.32 (520-680)	<0.001

Urine parameters like creatinine clearance, urine output, urinary creatinine, Ph, urinary sodium, fractional excretion of sodium, renal failure index and osmolality all showed statistically significant difference between cases and controls except urine potassium and urine specific gravity.

Table 4: Distribution of renal parameters among different stages of HIE

HIE staging	Stage 1	Stage 2	Stage 3	P value
Creatinine clearance	22.88±2.86	18.92±3.14	14.06±3.16	<0.001
Serum Creatinine	1.2±0.131	1.435±0.25	2.01±0.34	<0.001
Blood urea	48±4.6	76.4±8.32	92.8±12.8	<0.001
Urine Na^+	50.22±12.04	72.98±27.23	106.4±23.02	<0.001
FeNa	2.14±0.77%	3.75±2.33%	8.82±2.20%	<0.001
RFI	3.84±2.32	6.44±3.54	14.36±5.03	<0.001

In this study as HIE stage progressed from stage-I to stage-III there was increase in values of blood urea, serum creatinine, urinary sodium, FeNa, RFI, along with fall in creatinine clearance and this difference was statistically significant ($p<0.001$).

Discussion

The condition known as perinatal asphyxia occurs when a foetus or newborn does not receive enough oxygen (hypoxia) or blood flow (ischemia) to cause a variety of organ dysfunction of sufficient magnitude and duration. [16] In India, between 250,000 and 350,000 infant deaths are reported annually, most commonly in the first three days of life. [17] The burden of birth asphyxia in neonates is so high that 104 children pass away from the illness every hour. Nearly every organ in the body is affected by birth asphyxia, however the kidneys, central nervous system, heart, and lungs are the most frequently damaged. [18] It is quite challenging to identify and classify the hypoxia after birth in the absence of a prenatal record. [19,20] The kidneys, gut, and skin are sacrificed in order to maintain perfusion to more essential organs including the heart, brain, and adrenals. As a result of prenatal hypoxia, the kidney is one of the organs that is frequently damaged. Renal insult may occur within 24 hours of a hypoxic ischemic episode, which if extended, may still cause irreversible cortical necrosis [21] because kidneys are particularly sensitive to oxygen shortage; it is possible for this to happen. [22]

There was no significant difference between studied groups as regarding gestational age, weight, sex, maternal age and parity. There was statistically significant difference among Apgar score at 1 and 5 minutes between cases and controls. Assisted vaginal delivery and emergency caesarean section were more common among cases (13.34%, 41.33%) as compared to controls (8%, 16%). Urine parameters like creatinine clearance, urine output, urinary creatinine, Ph, urinary sodium, fractional excretion of sodium, renal failure index and osmolality all showed statistically significant difference between cases and controls except urine potassium and urine specific gravity. Our study nearly exactly matched other research by Aggarwal A et al [23] that discovered impaired renal function in 56% of asphyxiated infants. Similar relationships between metabolic markers and the severity of HIE were discovered in other investigations as well. According to Jayshree G et al [24] stage 2 and stage 3 patients were substantially more likely to have ARF than stage 0 and stage 1 patients. In 40 neonates with varying HIE stages, the kidney functions evaluated by Jayaswal A et al on days 3 and 5 of age revealed a substantial difference. As the HIE stage progressed, metabolic derangement also increased, which is similar to our discovery in their study. [25]

In this study as HIE stage progressed from stage-I to stage-III there was increase in values of blood urea, serum creatinine, urinary sodium, FeNa, RFI, along with fall in creatinine clearance and this difference was statistically significant ($p<0.001$). It is well recognized that many organ dysfunctions can be brought on by neonatal birth asphyxia. In the current investigation, asphyxiated newborns' biochemical markers that may indicate renal dysfunction, urine production, and hemodynamic state were tracked and shown to differ significantly from other HIE phases. It is crucial to understand that non-oliguric neonates can also sustain serious acute kidney injury (AKI). Due to the kidneys' high sensitivity to oxygen deprivation, renal insufficiency can develop within 24 hours of a hypoxic ischemic insult and, if left untreated, can result in irreversible cortical damage. [22]

Conclusion

Renal dysfunction is a common finding present in patients of perinatal asphyxia. Renal derangement increases with severity of disease. Prerenal AKI, which affects infants with birth asphyxia most frequently, responds to fluid resuscitation with a 100% recovery rate. Monitoring of urine production as well as serum and urinary parameters are crucial for the early detection of AKI in newborns that have had birth asphyxia but are still not oliguric.

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