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Original Research Article

Clinical Profile and Outcome of Newborns with Hypoxic Ischemic Encephalopathy in a Teaching Hospital of Bihar

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Abstract:

Introduction: Perinatal asphyxia is a serious condition in neonatology which has a significant effect on neonatal morbidity and mortality. It affects the neurological and intellectual development of the infant. Hypoxia refers to a decrease in oxygen supply to cells or organs, while ischemia is insufficient blood flow to maintain normal function. Hypoxic-ischemic encephalopathy (HIE) is a condition that can cause permanent damage to the central nervous system. It is estimated that around four million babies are born asphyxiated and among those one million die and an equal number of babies develop serious neurological consequences ranging from cerebral palsy and mental retardation to epilepsy. This study was done to study the clinical profile and, immediate outcome of perinatal asphyxia in Nalanda Medical College and Hospital, Patna, Bihar, India.

Methods: It was a prospective case controlled study involving 80 neonates as case and 45 as control fulfilling the inclusion criteria conducted during June 2022 to May 2023. Inclusion criteria included new-borns with: a) APGAR score equal to or less than seven at five minutes, b) requirement of more than one minute of positive pressure ventilation.

Results: Out of total 125 neonatal intensive care unit (NICU) admissions, 80 (64%) cases were of perinatal asphyxia, 56 inborn and 24 referred cases. The rest 45 babies served as controls. Of those 80 cases, HIE stage I had good outcome with survival rate of 95% and HIE stage III had poor outcome with survival rate of only 30%. Mean urinary output was less in cases as compared to controls. Out of 80 asphyxiated babies 33 developed acute renal failure (ARF) of which predominant type was oliguric type ARF. Out of 33, 10 babies died (8 oliguric and 2 non-oliguric renal failure).

Conclusion: Acute renal failure was common in asphyxiated babies its incidence being 41% and incidence of ARF increases with severity of asphyxia. Majority of ARF cases were of oliguric type thus showing correlation between asphyxia and type of renal failure.

Keywords: Asphyxia, NICU, Encephalopathy, Renal Failure, Oliguria.

Introduction

Perinatal asphyxia is a severe condition with significant impacts on neonatal health and development [1]. It is characterized by a lack of oxygen and blood perfusion to the organs, particularly the brain. Most cases occur during the antepartum and intrapartum periods due to placental insufficiency, while a smaller portion occurs postpartum due to various abnormalities [2]. Severe metabolic acidosis at birth, along with early signs of encephalopathy, is the key indicator of intrapartum hypoxic-ischemic events.

Perinatal asphyxia has a profound global impact, with millions of affected babies each year. It is a major contributor to neonatal mortality, stillbirths, and long-term neurological consequences such as cerebral palsy, mental retardation, and epilepsy [3]. While neonatal mortality has decreased, the morbidity associated with birth asphyxia has remained the same or even increased due to improved survival rates. Asphyxia occurs when the fetus or new-born experiences a lack of oxygen and/or perfusion to the organs. The extent of damage depends on the duration and severity of the insult. Hypoxia can lead to permanent damage in the central nervous system, resulting in neonatal death or long-term mental deficiencies [2].

The incidence of birth asphyxia is around 1 to 1.5%, higher in preterm infants and babies of diabetic or toxemic mothers. It contributes to approximately 40% of neonatal admissions and is a major cause of neonatal morbidity and mortality. Inadequate oxygenation of maternal blood,

placental complications, low maternal blood pressure, maternal infection, and fetal/neonatal factors such as shock, anaemia, infections, and growth retardation contribute to fetal hypoxia [4].

Asphyxia can initiate a chain of physiological disturbances affecting various organs, resulting in diverse clinical symptoms in new-borns. Circulatory responses cause blood flow redistribution, prioritizing vital organs like the brain, heart, and adrenals while compromising others. Renal involvement is common in birth asphyxia and may lead to renal failure, though it is often overshadowed by neurological symptoms [5].

Neonatal encephalopathy (NE) is a clinical syndrome of neurological dysfunction, with hypoxic-ischemic encephalopathy (HIE) being NE following a perinatal hypoxic-ischemic event [1]. HIE severity ranges from mild to severe, affecting consciousness, tone, reflexes, autonomic function, and causing seizures soon after birth. The outcome varies based on the severity, with mild HIE having a good prognosis, moderate HIE having a higher risk of poor outcomes, and severe HIE often leading to death or disability [7].

HIE has significant global burdens, with a substantial number of infants surviving with neurological impairment. It remains a leading cause of term/near-term neonatal deaths, and the outcomes have emotional, financial, and societal implications. Early identification and intervention for renal dysfunction associated with birth asphyxia can help reduce mortality and long-term morbidity [8].

In conclusion, perinatal asphyxia is a critical issue in neonatology, impacting neonatal mortality, morbidity, and neurodevelopmental outcomes. Understanding its clinical profile, identifying risk factors, and implementing appropriate interventions are crucial for improving outcomes and reducing the burden of this condition on infants, families, and healthcare systems worldwide.

Methodology

The present study was the prospective case control study conducted in the tertiary care centre of Patna which is also a major referral centre during the year June 2022 to May 2023.

All the babies who are born in this institute during the study period having apgar score of less than 7 at 5 minute were included in the study. Those babies delivered at Obstetrics and Gynecology Department of NMCH were attended by Junior Resident and whose Apgar score was seven at 5 minutes were selected as a case. Uniformity in the neonatal resuscitation protocol and grading of asphyxia according to Apgar at 5 minutes was assured by eliminating observes bias. Non-asphyxiated babies with no known confounding factor believed to alter the renal functions such as septicemia, respiratory distress syndrome, necrotising enterocolitis, major congenital malformations were randomly picked up to serve as a control. The enrolled babies are thus divided in two groups. The group A comprises of asphyxiated babies and group B comprises of non-asphyxiated babies as control.

The asphyxiated neonate on the basis of apgar score were further classified into mild (score 6 or 7), moderate (score 5 to 4) and severe (score 3 to less). All neonate with clinical feature of HIE were staged by sarnat and sarnat staging system. All the enrolled babies were subjected to Ultrasonography to rule out any congenital malformation. Gestational age estimation was done and babies were classified in Preterm, term and post-term. Birth weight, relevant Perintal history finding on physical examination and system sign were recorded on a Performa. Urine examination and 24 hours urine output was monitored.

Results

Most of the Babies in the study and control group were term babies which constitute 80 (64%) of study group and 45 (36%) in control group respectively. 56 asphyxiated babies were inborn while 24 were referred. Most of the babies (47.5%) under study group were in the severe asphyxia group with apgar score at 5 minute less than 3. The maximum number of asphyxiated babies were in the stage II of HIE (40 cases) i.e. 50%. Then 30 cases (37.5%) were in stage I while only 10 cases (12.5%) were in stage III of HIE. Out of 80 asphyxiated babies under study 33 (47.1%) developed ARF. The mean urinary output in the asphyxiated babies (A) was 1.12 ml/kg/hr. less than the control group (B) i.e. 1.67 ml/kg/hr. 12 cases out of 33 cases of ARF show proteinuria in the routine urine examination.

Out of 33 cases of ARF developed secondary to birth asphyxia 16 cases had abnormal urinary microscopic findings. The higher level of blood urea 48.3 mg/dl and serum creatinine 1.4mg/dl were noted with stage III of HIE. The predominant type of ARF was of oliguric type which constituted 20 out of 33 cases of ARF. The maximum number of ARF cases i.e. 28 out of 38 were from severe Birth Asphyxia (lower score of Apgar 0-3).While chances of renal involvement was minimal in mild birth asphyxia (higher score of Apgar 6-7).

This was shown that in severe Birth Asphyxia (Apgar 0-3) the predominant type of ARF was oliguric type 67.87% while in mild birth asphyxia (Apgar 6-7) the predominant type of ARF was non-oliguric. Almost all the referred cases were of severe birth asphyxia with stage III HIE. In stage III there were highest chances of renal failure i.e. 75%. With stage III 85% cases were of oliguric

type of ARF, while in stage I only 16.6% of ARF cases were of oliguric type.

While non-oliguric type of ARF were more prevalent in lower stage of HIE. In 33 cases of ARF 10 cases expired which is about 30% of ARF cases. 8 cases expired out of 10 cases suffered with the oliguric type of ARF which constituted maximum cases of mortality group. While only 2 cases that expired were of non-oliguric type of ARF.

All 8 cases which expired were referred from different centers to our hospital.

Table 1: Distribution of Gestation of Babies in The study (A) & Control (B) group

Birth Weight	Study Group (N=80)		Control Group (N=45)	
	No. of case	%	No. of case	%
Pre-term	15	18.75	10	22.22
term	60	75	31	68.89
Post-term	5	6.25	4	8.89

Table 2: The urea and creatinine level correlated with HIE Stage

HIE Stage of Group A	N	Blood Urea		Serum Creatinine	
		Mean	Range	Mean	Range
Stage I	30	31.36	18-68	1.1	0.61-1.47
Stage II	40	41.20	19-68	1.3	0.68-1.96
Stage III	10	48.30	22-69	1.4	0.83-2.43
Control Group (B) Non-asphyxiated	45	18.6	15-23	0.79	0.68-0.92

This table shows as the stages of the HIE increases the mean Blood urea and serum creatinine also increases. The higher level of Blood urea 48.3 mg/dl and serum creatinine 1.4mg/dl were noted with stage III of HIE.

Table 3: The Biochemical Parameter on Day I and Day II in Study and Control Group

Group	Group A Asphyxiated				Group B			
	Day I		Day II		Day I		Day II	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range
Blood urea in mg/dl								
Pre-term	36.06	18-58	42.09	22.69	20.3	18-24	19.3	17-23
Term	33.50	16-53	38.72	18.68	19.0	16-24	18.0	15-20
Post-term	31.85	15-24	37.20	20.63	19.4	17-23	18.6	16-21
Serum Creatinine in mg/dl								
Pre-term	1.12	0.62-1.82	1.34	0.72-2.43	0.90	0.82-0.98	0.83	0.75-0.92
Term	0.94	0.53-1.49	1.18	0.61-1.96	0.82	0.78-0.86	0.80	0.68-0.88
Post-term	0.98	0.53-1.37	1.12	0.65-1.79	0.81	0.75-0.90	0.74	0.70-0.78
Serum Sodium (Na) in mg/dl								
Pre-term	132.04	126-136	129.72	124-134	137.8	133-142	135.7	131-139
Term	131.75	127-140	130.55	125-139	138.22	135-142	135.4	130-139
Post-term	133.20	130-136	131.40	127-136	139.01	137-141	136.6	131-141
Serum Potassium in mg/dl								
Pre-term	4.62	4.16-4.8	4.87	4.23-5.64	4.82	4.0-5.1	4.67	4.30-5.30
Term	4.26	4.06-4.96	4.36	3.83-5.56	4.70	3.8-5.3	4.76	4.3-5.2
Post-term	4.32	4.17-4.8	4.65	4.09-5.62	4.63	3.9-5.2	4.52	4.1-5.1

Table 4: Blood Urea and Serum Creatinine correlated with Apgar score

Apgar Score of Group A	N	Blood Urea		Serum Creatinine	
		Mean	Range	Mean	Range
Apgar 6-7 (Mild Asphyxia)	14	27.75	20-54	0.8	0.61-1.39
Apgar 4-5 (Moderate Asphyxia)	28	31.22	19-68	1.1	0.65-2.09
Apgar 0-3 (Severe Asphyxia)	38	44.43	18-69	1.9	0.79-2.43
Group (B) Control Group	45	18.60	15-23	0.79	0.68-0.92

This table shows higher level of Blood Urea and Serum Creatinine with the lower Apgar score (0-3) while relatively lower of Blood Urea and Serum Creatinine were seen with higher Apgar score (6-7).

Table 5: Correlation of severity of Birth Asphyxia (Apgar score) and Type of Renal Failure (ARF)

Severity of Birth Asphyxia Apgar Score	No. of cases	No. of cases of ARF	Non-oliguric (ARF)		Oliguric (ARF)	
			No. of Cases	%	No. of Cases	%
6-7 (Mild Asphyxia)	14	1	1	100	0	0
4-5 (Moderate Asphyxia)	28	4	3	75	1	25
0-3 (Severe Birth Asphyxia)	38	28	9	32.2	19	67.8

This table shows in severe Birth Asphyxia (Apgar 0-3) the predominant type of ARF was oliguric type 67.8% while in mild birth asphyxia (Apgar 6-7) the predominant type of ARF was non-oliguric.

Table 6: Correlation of Type of Acute Renal Failure (ARF) with Hypoxic Ischemic encephalopathy (HIE) stages in the study group A

HIE Stages	No. of cases of HIE (n=80)	No. of Cases of (ARF) (n= 33)	Non-oliguric (ARF)		Oliguric (ARF)	
			No. of Cases	%	No. of Cases	%
HIE Stages I	30	6	5	83.3	1	16.6
HIE Stages II	40	20	7	35	13	65
HIE Stages III	10	7	1	14.3	6	85.7

This table shows as the stage of HIE increases oliguric type of ARF increase. With stage III 85.7% cases were of oliguric type of ARF. While in stage I only 16.6% of ARF cases were of oliguric type. While non-oliguric type of ARF were more prevalent in lower stage of HIE.

Discussion

The babies in the study group fall in the three groups on the babies of apgar score at 5 minutes. The numbers of babies with the Apgar score at 5 minutes between 6-7 are 14 and number of babies with apgar score at 5 minutes between 4-5 are 28 and lastly the number of babies with apgar score below 3 are 38. So 17.5% babies are of mild asphyxia, 35% of moderate asphyxia and 47.5% of severe asphyxia. A similar study by B.D. Gupta et al. (2005) showed the distribution of cases in mild, moderate and severe asphyxia as 32%, 42% and 24% respectively. Since Patna Medical College is a referral Hospital. Most of the babies under study in our cases fall in moderate and severe asphyxia. The number of babies in HIE – I is 30, in HIE II are 40 and in HIE III are 10. In the study of B.D. Gupta et al.2005 only 38 case out of 70 cases under study have HIE. The percentage in different stages of HIE are 12.5, 28.5 and 12.5 in stage I, II and III respectively [9].

The Biochemical profile of study and control group on Day 1st and day 3rd. The mean Blood Urea (mg/dl) level in the Pre-term, Term and Post-term asphyxiated Baby was 36.06 (Range 18-38), 33.5 (Range 16-33) and 31.85 (Range 15-54) respectively which increased to 42.09 (22-69), 38.72 (18-68) and 37.20 (20-63) in Preterm, Term and Post-term respectively on Day 3rd. In the control group the Blood Urea level on the Day 1st in the Pre-term 20.3 mean, (range 18-24) Term 19.0 mean, (range 16-21) and in the Post-term 19.4 mean (range 17-23). Which decreased slightly on the Day 3rd which was in the Pre-term 19.3 mean (range 17-23), Term 18 mean, (range15-20), and in the Post-term 18.6 mean, (range 16-21). Mishra et al. (1991) observed a serum urea level of 62.8 ± 15.37 on Day I and 72.42 ± 16.59 later on, in asphyxiated ARF cases. This is well correlated with this study. The slight fall of Blood Urea level in the control group of cases is due to increased maturity of renal function during the first week of life.

The serum creatinine which was taken as criteria to diagnose ARF in this study was consistently raised in asphyxiated group of ARF cases. The mean serum creatinine in mg/dl in the preterm wad on the day 1, 1.12 range (0.62-1.82), in term 0.94 (range 0.53-1.49) and in the post-term 0.98 (range 0.54-1.37). Which increased on Day 3rd as in Preterm 1.34 (range 0.72-2.43), in term 1.18 (range 0.61-1.96) and in the post-term as 1.12 (range 0.65-1.79) respectively.

In the control group the mean serum creatinine on Day 1 in the pre-term 0.90 (range 0.82-0.98), in term 0.82 (range 0.78-0.86), and in the post-term 0.81(range 0.75-0.90) which decrease further on Day 3rd as in the pre-term 0.83 (range 0.75-0.92) in term 0.80 (range 0.68-0.78) and in the post-term 0.74 (range 0.70-0.78). We notice a higher level of serum creatinine in ARF cases on Day 1 which further increased on the day 3rd suggesting renal dysfunction. Since at the time of Birth, the serum creatinine level is the non-asphyxiated control group is well explained. Mishra et al. (1991) found a mean creatinine level of 3.13 ± 0.14 on the day 2 in ARF. This high level may again be due to inclusion of only severely asphyxiated babies in their study.

Serum Sodium level (m.eg/L) was on the Day 1st. In pre-term means 132.20 (range 130.136). The serum Sodium level in the study Group was lower on Day 3rd i.e. in pre-term 129.72 (range 124-134), in Term 130.55 (range 125-139) and in post-term 131.40 (range 127-136). The serum sodium level was almost unaffected in the control group of babies on Day 1st and day 3rd. The lower level of

serum sodium were found in the asphyxiated ARF babies where ischemic injury might have affected proximal renal tubules leading in impaired sodium reabsorption and thus lower blood level. A rising trend in Blood Urea and serum creatinine was observed as the HIE staging of neonate progressed.

The Mean Blood Urea in the stage I was 31.36 (range 18-68) and creatinine was 1.1(range 0.61-1.47), in the stage II was Blood Urea mean 41.20 (range 19-68) and serum creatinine 1.3 (range 0.68-1.96) and in the stage III urea mean 48.3 (range 22-60) and serum Creatinine 1.4 (range 0.83-2.43). In contrast the control group blood Urea and serum Creatinine 18.6 (range 15-23), 0.79 (range 0.68-0.92) respectively. The findings in the present study were similar to other studies done in recent times. Mortality was high in ARF as the referred cases were very sick and presented late to the health facility at our side.

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