Effect of Perinatal Asphyxia with Hypoxic-Ischemic Encephalopathy on Blood Glucose and Calcium Level in Term Neonates

Razaul Haque,[1] Prof. Bikash Kumar Majumder,[2] Sufia Khatun,[3] Ayasha Sultana,[4] Akter Banu,[4] Monika Mazumder,[5] Abu Rayhan Md. Suja-Ud-Doula,[6] Jahidur Rahman,[6] Md. Golam Mostafa Kamal[7]

Abstract:
Perinatal asphyxia is a major cause of neonatal death and disability worldwide. Asphyxiated newborn are vulnerable to develop hypoglycaemia and hypocalcaemia. The objective of the study was to determine the effect of birth asphyxia with hypoxic- ischemic encephalopathy on blood glucose and calcium level in term neonates. This cross-sectional observational study was conducted at department of Pediatrics of Rangpur Medical College Hospital from January 2017 to December 2018. After ethical clearance, total 87 eligible hospitalized term neonates fulfilling the inclusion and exclusion criteria were enrolled into the study. Estimation of blood glucose and calcium were done within one hour of admission. Data were analyzed through SPSS software (version 23.0). Minimum level of significance was predetermined as $p<0.05$. Analysis revealed that frequency of hypocalcaemia ($p=<0.001$) and hypoglycaemia ($p=<0.05$) were significant. Hypocalcaemia was significant ($p=<0.001$) among three grades of Sarnat and Sarnat HIE staging. Present study concluded that hypoglycaemia and hypocalcaemia were significant findings in perinatal asphyxia with hypoxic-ischemic encephalopathy in term neonates.

Indexing words: Neonates, Perinatal asphyxia, Hypoxic ischemic encephalopathy, Hypoglycaemia, Hypocalcaemia.

Introduction:

Perinatal asphyxia is an insult to the fetus or newborn infant due to lack of oxygen and perfusion to various organs and manifests as difficulty in establishing spontaneous respiration evident by delayed cry after birth, at least one minute.[1] Hypoxic- ischemic encephalopathy (HIE) is characterized by clinical and laboratory evidence of acute or sub-acute brain injury due to asphyxia. Perinatal asphyxia is the second leading cause of neonatal mortality in Bangladesh.[2]

1. Lecturer, Dept. of Pharmacology Rangpur Medical College, Rangpur.
2. Professor and Head, Dept. of Pediatrics, Rangpur Medical College, Rangpur
3. Consultant, Dept. of Gynae & Obs. Upazilla Health Complex, Mithapukur, Rangpur.
4. Assistant Professor, Dept. of Pediatrics Rangpur Medical College, Rangpur
5. Junior Consultant, Dept. of Pediatrics Rangpur Medical College Hospital, Rangpur
6. Associate Professor, Dept. of Pediatrics Rangpur Medical College, Rangpur.
7. Assistant Professor, Dept. of Opthalmology Rangpur Medical College, Rangpur.

Neonatal hypocalcaemia is defined as a total blood calcium concentration less than 7.0 mg/dl in preterm infants, and <8.0 mg/dl in term infants and an ionized calcium concentration of less than 4.0 mg/dl (1.0 mmol/L).[3,4] Neonatal hypoglycaemia is defined as the level of glucose in whole blood below 40 mg/dl (2.2 mmol/L).[5] In asphyxiated infant , clinically it is difficult to distinguish the effects of hypoglycaemia and hypocalcaemia from hypoxic ischemic encephalopathy (HIE). Therefore, it is essential to monitor blood calcium and blood glucose level to evaluate hypoglycaemia and hypocalcaemia for prompt and proper management of perinatal asphyxia to reduce neonatal mortality and morbidity.

Methods:

This cross sectional observational study was conducted at inpatient department of Paediatrics of Rangpur Medical College Hospital from January 2017 to December 2018. Main outcome variables were blood calcium and blood glucose level, stages of HIE. All asphyxiated term neonates, hospitalized within 72 hours of birth, fulfilling the selection criteria were enrolled into

the study. Inclusion criteria were-term neonates of both sex, age-within 72 hours of birth, birth weight 2500 to 4000 gm, history of perinatal asphyxia evident by failure to initiate and sustain breathing at birth or delayed cry after birth at least for one minute, term neonates showing the neurobehavioral signs of HIE. Exclusion criteria were- congenital anomaly, early onset neonatal sepsis, congenital infection, infant of diabetic mother, clinically suspected inborn error of metabolism. 2 ml of venous blood was collected within one hour of admission for estimation of blood glucose and blood calcium and for sepsis screening. The level of significance of 0.05 was used for this study.

Results:

A total of 87 asphyxiated neonates were enrolled into the study.

Table 1: Distribution of the term neonates by Sarnat and Sarnat HIE staging (n=87)

Sarnat and Sarnat staging	Number of patient	Percentage
HIE stage I	10	11.49
HIE stage II	38	43.87
HIE stage III	39	44.82

Table 1 shows that 90% term neonates belonged to HIE stage II and HIE stage III divided into two equal halves.

Table 2: Frequency of hypoglycaemia in PNA with HIE (n=87)

Glycaemic status	Sarnat and Sarnat staging						p value
	HIE stage I (n=10)		HIE stage II (n=38)		HIE stage III (n=39)		
	N	%	N	%	N	%	
Hypoglycaemia	01	10	10	26.3	18	46.2	0.046 (S)
Normoglycemia	09	90	28	73.7	21	53.8	

n: Number of neonates, **%:** Percentage, **S**: Significant in Chi-square test of significance of difference.
Table 2 shows frequency of hypoglycaemia was significant in HIE stage III (p= 0.046)

Table 3: Severity of hypocalcaemia in PNA with HIE staging (n=87)

Blood calcium (mg/dl)	Sarnat and Sarnat HIE staging						p value
	HIE stage I (n=10)		HIE stage II (n=38)		HIE stage III (n=39)		
	N	%	n	%	n	%	
<04	0	00	0	00	3	7.7	<0.001 (S)
04-08	0	00	10	26.3	23	59	
>08	10	100	28	73.7	13	33.3	

n: Number of neonates, **%:** Percentage, **S**:significant, in Chi-square test of significance of difference.
Table 3 shows severity of hypocalcaemia escalated with progressive severity of HIE

Table 4: Severity of hypoglycaemia in PNA with HIE staging (n=87)

Blood glucose (mg/dl)	Sarnat and Sarnat HIE staging						p value
	HIE stage I (n=10)		HIE stage II (n=38)		HIE stage III (n=39)		
	N	%	n	%	N	%	
<20	0	00	1	2.6	3	7.7	0.165 (NS)
20-40	1	10	9	23.7	15	38.4	
>40	9	90	28	73.7	21	53.9	

PNA: Perinatal asphyxia, **HIE:** hypoxic ischemic encephalopathy **n** : Number of neonates, **%:** Percentage, **NS**: Non-significant, in Chi-square test of significance of difference
Table 4 shows severity of hypoglycaemia increased with severity of HIE.

Table 5: Frequency of hypocalcaemia in PNA HIE staging (n=87)

Status of serum calcium	Sarnat and Sarnat staging						p value
	HIE stage I (n=10)		HIE stage II (n=38)		HIE stage III (n=39)		
	N	%	n	%	n	%	
Hypocalcaemia	0	00	10	26.3	26	66.7	<0.001 (S)
Normocalcemia	10	100	28	73.7	13	33.3	

n: Number of neonates, **%:** Percentage, **S**: Significant in Chi-square test of significance of difference
Table 5 shows hypocalcaemia was most frequent in HIE stage III (p<0.05)

Discussion:

This study was carried out with an aim to evaluate the effect of perinatal asphyxia with hypoxic ischemic encephalopathy on blood glucose and calcium level in term neonates. In this study, it was found that 11.49% of neonates were in Sarnat and Sarnat's HIE stage I, 43.87% in stage II, and 44.82% in stage III.

Chiabi et al found 51.0% of neonates were in Sarnat and Sarnat's stage I, 26% in stage II, and 23% in stage III.[6] This is in contrast with the findings of current study. Current study revealed that 90% neonates belonged to HIE stage II and HIE stage III divided into two equal halves. On initial neurological evaluation Memon et al found 15.0% were normal while clinical signs of HIE were present in 85.0%, with 30.0% in stage I, 35.0% in Stage II and 20.0% in stage III of HIE.[7] Olusegun J et al found that out of 563 asphyxiated neonates 50.3% had moderate asphyxia and 49.7% had severe asphyxia (Apgar score ≤3), which resemble with the present study.[8]

In this current study, almost two third 58(66.66%) of the patients had blood glucose level >40 mg/dl, 4(4.59%) neonates had <20 mg/dl in HIE and 25(28.73%) had 20-40 mg/dl in HIE. This significant decrease in blood glucose was directly associated with degree of asphyxia. This is similar to the study by Kiyani et al who observed temporary hyperinsulinism contributing to hypoglycaemia in asphyxiated neonates.[9] Olusegun et al also reported hypoglycaemia in severe asphyxia.[8] Shinghal et al. concluded that among hypoglycemic babies, birth asphyxia contributed to 24.2% of cases.[10]

In this study majority 51(58.62%) of the patients had blood calcium level >8 mg/dl, 3(3.44%) had <4 mg/dl and 33(37.93%) had 4-8 mg/dl. There was significant decrease in calcium level in the asphyxiated babies and the decrease was directly proportionate to the degree of asphyxia. This is similar to observations reported by MacDonald who estimated hypocalcaemia in asphyxiated neonates and concluded that the decrease in blood level of total calcium was more profound in asphyxiated newborns than non-asphyxiated newborns.[11] Ria et al also observed high incidence of low blood calcium in asphyxiated infants.[12] A study conducted by Perlamn et al among asphyxiated infants exhibited significantly low plasma calcium concentrations than their controls.[13] These findings closely resemble with the findings of present study.

It was observed that 9(90%) of the patients had blood glucose level >40 mg/dl in HIE state I, 28(73.7%) in HIE stage II and 21(53.9%) in HIE stage III. There was association between severity of Sarnat and Sarnat staging with low blood glucose level.

Study findings revealed that 10(100.0%) patients who had blood calcium level >8 mg/dl were in HIE stage I, 28(73.7%) in HIE stage II and 13(33.3%) in HIE stage III. There was a significant association between Sarnat and Sarnat staging with blood calcium level.

Regarding association between hypoglycaemia of asphyxiated newborn with Sarnat and Sarnat staging it was observed in this study that 1(10%) of the patients had hypoglycaemia in HIE state I, 10(26.3%) in HIE stage II and 18(46.2%) in HIE stage III. The difference was statistically significant ($p<0.05$) among three groups.

Association between hypocalcaemia with Sarnat and Sarnat staging revealed that none in HIE stage I had hypocalcaemia, 10(26.3%) in HIE stage II and 26(66.7%) in HIE stage III were hypocalcaemic. Hypocalcaemia was significantly ($p<0.05$) associated with HIE stage III. Vamne et al observed hypocalcaemia in hypoxic Ischemic encephalopathy, 30.0% in stage I, 56.0% in stage II and 14.0% in stage III cases.[14]

Conclusion:

This study concluded that there was significant positive association between severity of perinatal asphyxia with hypoglycemia and hypocalcaemia in term neonates.

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Correspondence :
Dr. Razaul Haque
Lecturer, Department of Pediatrics
Rangpur Medical College
Rangpur.