

ELECTROLYTE ABNORMALITIES IN ASPHYXIATED NEWBORNS AND ITS ASSOCIATION WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY

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Abstract

Background: Birth asphyxia continues to be a leading cause of neonatal mortality and long-term morbidity worldwide despite advancements in perinatal care. It is a state of impaired gaseous exchange characterised by hypoxemia, hypercarbia and metabolic acidosis. Any deviation in the serum levels of electrolytes can aggravate brain injury in an already asphyxiated neonate. To determine the occurrence of major electrolyte abnormalities (sodium, potassium, calcium and magnesium) in asphyxiated newborns of gestational age 32 weeks or more. To determine the association of major electrolyte abnormalities with the severity of hypoxic ischemic encephalopathy. **Materials and Methods:** This was a prospective observational study comprising 105 asphyxiated newborns who met the inclusion criteria. Prestructured proforma was used to collect relevant details. Newborns with hypoxic ischemic encephalopathy were classified using Modified Sarnat and Sarnat Staging. Serum electrolyte levels were measured in all neonates. Comparison of electrolyte levels with presence of HIE was done by independent t test. ANOVA test was used for knowing association of electrolyte levels with the severity of encephalopathy in all HIE babies. **Result:** Out of the total study population, 32.3% developed HIE. The mean sodium and potassium values were 137 and 5.1 respectively while that of calcium and magnesium were 8.9 and 2. The most prevalent abnormality was hyponatremia (32%) followed by hyperkalemia (21%). Mean sodium values were lower for stage 3 compared to other two stages of HIE. Hypocalcemia and hypermagnesemia showed a significant association with presence of HIE. No statistically significant association was obtained on comparing serum electrolyte levels with the severity of hypoxic ischemic encephalopathy. **Conclusion:** Hyponatremia, hyperkalemia, hypermagnesemia and hypocalcemia were the prevalent abnormalities in electrolytes among newborns with birth asphyxia in our study. Although the derangements were not proportionate with the severity of hypoxic ischemic encephalopathy, the study emphasise the need of early and serial monitoring of electrolytes, as the imbalances are known to be detrimental to the developing brain.

INTRODUCTION

Perinatal asphyxia continues to be a leading cause of neonatal mortality and long term morbidity worldwide despite advancements in neonatal care. As evident from the National Neonatal Perinatal Database, the prevalent primary cause of neonatal death was perinatal asphyxia accounting for about 28.8% of total mortality.^[1]

The World Health Organisation (WHO) defines perinatal asphyxia as a state of failure to establish or sustain regular breathing at birth.^[2] An impaired

gaseous exchange or decreased blood flow to the foetus during late pregnancy, intrapartum period or immediate postnatal period can result in a setting of progressive hypoxia, hypercapnea and acidemia, thus initiating systemic disturbances.^[3] The end result is hypoxic injury culminating in either epileptic encephalopathy, intellectual disability, cognitive impairment, autistic spectrum disorders, attention deficits, cerebral palsy or even psychiatric illnesses.^[4,5]

Hypoxic ischemic encephalopathy (HIE) is the neurological sequelae of asphyxia and still remains a

concern globally. It is known to increase the socio economic and emotional burden on families. Though there has been tremendous growth in the field of obstetrics and perinatology over the past few years, conveying the complex issues related to perinatal asphyxia continues to be relevant.^[6,7]

Though a vast proportion of derangements in metabolism cannot be corrected in toto, a few parameters are subjectable to modification hence reducing severity of ischemic insult and improving the outcome. A few among them include glucose levels, temperature regulation and normal electrolyte concentrations. Any deviation in the serum levels of electrolytes can lead to seizures, cardiac dysfunction, shock or metabolic disturbances, consequently aggravating brain injury in an already asphyxiated neonate. Maintaining levels of major electrolytes such as sodium, potassium, calcium and magnesium within normal range is hence of considerable importance in an asphyxiated newborn. There has to be a detailed understanding of pathophysiology and management of imbalances in the fluid and electrolytes in perinatal asphyxia.^[8]

In order to formulate a definite treatment plan in an asphyxiated neonate, early diagnosis is of great importance. Timely correction of these electrolyte abnormalities can prevent further clinical deterioration.

We aim to address a clinical condition with complex pathophysiology and adverse neurological consequences that is preventable through effective physical as well as therapeutic treatment. The study is therefore being conducted to find out the major electrolyte abnormalities occurring in birth asphyxia and its association with different stages of Hypoxic Ischemic Encephalopathy, whereby preventive measures can be implemented to combat neonatal deaths.

MATERIALS AND METHODS

It was a Prospective observational study conducted at Inborn and outborn Neonatal Intensive Care Units (NICU) of Government Medical College Kottayam between January 2023 to December 2023.

Sample size: Sample size was calculated using the formula $N = 4pq/d^2$

where p is the prevalence

q is 1 - p

d is relative precision, calculated as 15% of p

In the study done by Bhat et al⁹ in Haryana among asphyxiated newborns, the prevalence of electrolyte abnormalities was 78.7% and the severity of hypoxic ischemic encephalopathy had a significant association with hyponatremia, hypocalcemia and hyperkalemia.

Hence on applying the values

p = 78.7

q = 21.3

d = 8

Sample size N = 104.7

Therefore, the minimum sample size required for present study was 105

Convenient sampling technique was used. . All inborn and outborn asphyxiated newborns admitted in the NICUs of Government Medical College Kottayam, who fits the inclusion criteria were included in the study, till the sample size was met. Newborns with a gestational age of 32 weeks or more who are appropriate for gestational age with birth asphyxia.

Inclusion Criteria

Newborns with a gestational age of 32 weeks or more, with birth asphyxia defined as a failure to initiate and sustain breathing at birth² (as per WHO), and based on the Apgar score as five minute Apgar less than 7 even after receiving resuscitation as per Neonatal Resuscitation guidelines, who are appropriate for gestational age (AGA) and born at Government Medical College, Kottayam or admitted within first twenty four hours of life at our outborn NICU were included in the study.

Exclusion Criteria

1. Babies with lethal congenital anomalies
2. Babies born to mothers on antiepileptics or drugs causing neonatal depression, mothers with electrolyte abnormalities, gestational diabetes/overt diabetes and those treated with magnesium sulphate
3. Babies born via cesarean section done under general anesthesia
4. Post term babies (>42weeks gestation)

Study Procedure

All inborn and out born asphyxiated AGA (birth weight falling between 10th and 90th percentile for gestational age) babies with gestational age more than or equal to 32 weeks requiring admission within the first twenty four hours of life in the NICUs as per our institution protocol were included in the study. An informed written consent was obtained from their parents. The study population comprised of moderate preterm (32weeks to 33weeks 6days), late preterm (34weeks to 36weeks 6days) and term babies.^[10]

Prestructured proforma was used to collect relevant details including antenatal history, gestational age, mode of delivery, perinatal events, birth weight and details of new born resuscitation. New Ballard Scoring system was used to confirm gestational age. The findings on physical examination soon after admission were recorded followed by daily assessment for progression or development of symptoms and signs. Special emphasis was put while examining nervous system. Newborns with HIE were classified into one of the three stage (Stage 1, 2 and 3) using Modified Sarnat and Sarnat Staging, done within first 24 hours of life and there after daily till postnatal day 14.

1-2 ml of Venous blood samples was drawn between 24 to 36 hours of life under aseptic precautions for estimation of serum sodium, potassium, calcium and magnesium levels, considering the fact that the internal milieu of new born will be similar to mother in the initial few hours of life. Ion selective electrode

method was used in estimation of electrolyte levels using Acculyte 3P electrolyte analyzer. The values of electrolytes drawn at 24-36 hours of life were compared against the presence as well as severity of HIE.

Statistical analysis: Data was entered in Microsoft excel spreadsheet and further statistical analysis done using SPSS software, Version 20.0 .Quantitative variables were expressed in mean with standard deviation. Qualitative variables were expressed in proportion. One way ANOVA test was used in comparison of mean electrolyte values with severity of HIE. Unpaired t test was used for comparison of

electrolyte levels with presence of HIE. For all these interpretations p value less than 0.05 was considered as statistically significant.

RESULTS

Among 105 newborns with perinatal asphyxia, 59 were males (56.2%) and 46 were females (43.8%) with a male: female ratio of 1.2:1. In the study there were 63 term neonates with perinatal asphyxia (60%) while late preterm babies comprised 26.7% and the rest 14 newborns (13.3%) were moderate preterms.

Table 1: Gender distribution of newborns among all stages of HIE.

HIE stage	Male N (%)	Female N (%)	Total
Stage 1	7 (87.5)	1(12.5)	8
Stage 2	12(57.1)	9 (42.9)	21
Stage 3	3 (60)	2(40)	5

87.5% of stage 1 and 57.1% of stage 2 babies were males. In stage 3 60% were males while 40% were females. Out of all stage 1 babies, 50% were moderate preterm, 25% were late preterms and rest 25% were term babies. Among 21 babies in stage 2, 80.9% were term babies. In stage 3, 40 % were late preterms and 60% were term babies.

Table 2: Distribution of mean electrolyte levels at 24- 36 hours of life based on HIE stage

Electrolyte	HIE Stage							
	Stage I		Stage II		Stage III		No HIE	
	Mean	S.D	Mean	S.D	Mean	S.D	Mean	S.D
Sodium	135	10.31	137	8.72	130	2.61	138	4.71
Potassium	5.0	1.12	5.2	0.68	4.5	1.36	5.1	0.67
Calcium	8.2	1.43	8.4	1.38	8.4	1.69	9.1	0.82
Magnesium	1.9	0.20	2.3	0.42	2.0	0.46	1.9	0.28

In those babies without HIE, mean sodium levels at 24-36 hours were 138, potassium 5.1 ,calcium 9.1 and that of magnesium was 1.9. The mean sodium levels at 24-36 hours of life in stage 1 HIE was 135 ± 10.31 , stage 2 was 137 ± 8.72 and stage 3 was 130 ± 2.61 . Mean values of serum potassium was 5 ± 1.12 in stage 1, 5.2 ± 0.68 in stage 2 and 4.5 ± 1.36 in stage 3 subjects. In stage 1 HIE the mean calcium levels were 8.2 ± 1.43 , stage 2 was 8.4 ± 1.38 and in stage 3 was 8.4 ± 1.69 . The magnesium levels had a mean value of 1.9 ± 0.2 in stage 1, 2.3 ± 0.42 in stage 2 and 2 ± 0.46 in stage 3.

Table 3: Abnormalities in serum sodium at 24-36 hours based on severity of HIE

Status of serum sodium	HIE Stage					
	Stage 1		Stage 2		Stage 3	
	N	%	N	%	N	%
Hyponatremia	5	62.5	11	52.3	4	80
Normal	1	12.5	5	23.8	1	20
Hypernatremia	2	25	5	23.8	0	0
Total	8	100	21	100	5	100

Among all babies with stage 1 HIE, 62.5% had hyponatremia and 25% had hypernatremia .In stage 2 babies, 52.3% had low sodium while 23.8% had high sodium. In stage 3 babies, only 80% had hyponatremia and none had hypernatremia.

Table 4: Abnormalities in serum potassium at 24-36 hours of life based on severity of HIE

Status of serum potassium	HIE Stage					
	Stage 1		Stage 2		Stage 3	
	N	%	N	%	N	%
Hypokalemia	1	12.5	0	0	1	20
Normal	4	50	15	71.4	3	60
Hyperkalemia	3	37.5	6	28.6	1	20
Total	8	100	21	100	5	100

Among stage 1 babies, 12.5% had hypokalemia and 37.5 % had hyperkalemia. In stage 2 babies 71.4 % had normal levels while rest had hyperkalemia. Potassium was normal in 60% of stage 3 babies. In the remaining 40% there was an equal proportion of hypokalemia and hyperkalemia.

Table 5: Abnormalities in serum calcium at 24-36 hours of life based on severity of HIE

Status of serum calcium	HIE Stage					
	Stage 1		Stage 2		Stage 3	
	N	%	N	%	N	%
Hypocalcemia	2	25	3	14.2	1	20
Normal	6	75	18	85.7	4	80
Hypercalcemia	0	0	0	0	0	0
Total	8	100	21	100	5	100

Among stage 1 HIE babies 25% had hypocalcemia, rest had normal levels. 14.2 % of stage 2 and 20% of stage 3 babies had low calcium

Table 6: Abnormalities in serum magnesium at 24-36 hours of life based on severity of HIE

Status of serum magnesium	HIE Stage					
	Stage 1		Stage 2		Stage 3	
	N	%	N	%	N	%
Hypomagnesemia	0	0	0	0	1	20
Normal	8	100	16	76.1	4	80
Hypermagnesemia	0	0	5	23.8	0	0
Total	8	100	21	100	5	100

All babies in stage 1 HIE had normal magnesium levels. In stage 2 babies, 23.8% had hypermagnesemia and rest had normal levels. Among stage 3 babies, 20 % had low levels of magnesium

Table 7: Association of serum sodium with severity of HIE

Electrolyte	HIE stage	N	Mean	S.D	95% Confidence Interval for Mean		F	P value
					Lower Bound	Upper Bound		
Sodium	Stage I	8	135.00	10.309	126.38	143.62	1.293	0.289
	Stage II	21	137.19	8.716	133.22	141.16		
	Stage III	5	130.40	2.608	127.16	133.64		

On comparing mean sodium levels with different stages of HIE using one way ANOVA test, f value was 1.293 and p value was 0.289. Hence no significant association existed between serum sodium levels and severity of HIE.

Table 8: Association of serum potassium with severity of HIE

Electrolyte	HIE stage	N	Mean	S.D	95% Confidence Interval for Mean		F	P value
					Lower Bound	Upper Bound		
Potassium	Stage I	8	5.025	1.124	4.085	5.965	1.147	0.331
	Stage II	21	5.162	0.675	4.854	5.469		
	Stage III	5	4.480	1.359	2.793	6.167		

The serum potassium levels were compared with different stages of HIE using one way ANOVA test the f value was 1.147 and p value was 0.331, thus no statistically significant association was present.

Table 9: Association of serum calcium with severity of HIE

Electrolyte	HIE stage	N	Mean	S.D	95% Confidence Interval for Mean		F	P value
					Lower Bound	Upper Bound		
Calcium	Stage I	8	8.225	1.433	7.027	9.423	0.061	0.941
	Stage II	21	8.433	1.3829	7.804	9.063		
	Stage III	5	8.360	1.686	6.266	10.454		

The mean values of serum calcium compared with different stages of HIE using one-way ANOVA test yielded a f value of 0.061 and p value of 0.941 and which was statistically not significant.

Table 10: Association of serum magnesium with severity of HIE

Electrolyte	HIE stage	N	Mean	S.D	95% Confidence Interval for Mean		F	P value
					Lower Bound	Upper Bound		
Magnesium	Stage I	8	1.913	0.195	1.749	2.076	2.732	0.081
	Stage II	21	2.252	0.4155	2.063	2.442		
	Stage III	5	1.980	0.4604	1.408	2.552		

On comparing mean magnesium values with different stages of HIE using one way ANOVA test, f value was 2.732 and p value obtained was 0.081 and was not statistically significant.

DISCUSSION

Demographic characteristics showed a slight male preponderance with a male: female ratio of 1.2:1. Among 105 newborns, 60% were term babies, 26.7% were late preterms and 13.3% were moderate preterms. 51.4% were delivered via caesarean section, 38.1% by vaginal delivery and rest were instrument assisted deliveries. Though all were AGA (appropriate for gestational age), 46.7% weighed below 2.5 kg. Five minute Apgar score was less than 4 in 10.5% of study population.

Out of total 34 neonates with HIE, majority belonged to stage 2 and the least was from stage 3 of HIE, being similar to results from the study done by Acharya et al.^[11] On taking into account the electrolyte changes, our study yielded comparable results to that conducted by Bhat et al⁹ where the total prevalence of electrolyte derangements in asphyxiated babies was 78.7%.

The major electrolyte abnormalities noted in the study were hyponatremia, hyperkalemia, hypocalcemia and hypermagnesemia, the most frequent being hyponatremia (32%). Results were closer to other studies as done by Rahman et al,^[12] and Singhi et al,^[13] where 30.1% and 30% of population respectively, had low sodium levels.

Rahman et al,^[12] in their study on dyselectrolytemia in perinatal asphyxia yielded the proportion of hyperkalemia as 21.1% with majority having normal levels of serum potassium which too was similar to our findings.

Jajoo et al,^[14] Rai et al,^[15] in their studies observed low levels of calcium in babies with perinatal asphyxia, and was consistent with our findings. None of the subjects in present study showed hypercalcemia.

As per the study by Ilves P et al,^[16] newborns with perinatal asphyxia who did not develop HIE and those with milder features showed high magnesium levels while hypomagnesemia was common in severe stages of HIE. This was in contrary to the findings from our study where majority of asphyxiated subjects without HIE had normal magnesium levels. Out of all stage 1 babies, 62.5% had hyponatremia while 25% had hypernatremia. Also the proportion of hyponatremia (52.3%) was higher than hypernatremia (23.8%) in stage 2 babies. None of stage 3 babies had high sodium, instead 80% were having hyponatremia in initial sampling.

The proportion of hyperkalemia was more than hypokalemia in initial two stages of HIE, but the distribution was almost equal in stage 3 of HIE. 25% stage 1 babies, 14.2 % of stage 2 babies and 20 % of stage 3 babies had low serum calcium. None had hypercalcemia. 20% of stage 3 population had hypomagnesemia and 23.8% of stage 2 babies had hypermagnesemia. On repeating the sampling at 48 hours of life for rechecking the deranged values, we found that proportion of hyponatremia and hypernatremia reduced in all stages except stage

3. Similar to this proportion of abnormalities in potassium levels also reduced.

A previous study by Kumar Singh et al,^[17] couldn't draw any association between serum sodium and calcium levels with birth asphyxia. Similarly, no statistically significant differences were obtained on comparing mean values of sodium, potassium and calcium with different stages of HIE in present study. This was in contrast to findings reported by Gupta J et al,^[18] where a definite association between hyponatremia and hyperkalemia with severity of HIE was found.

However we found a significant difference between calcium levels among asphyxiated babies with HIE and those without, babies with HIE had lower calcium levels. Hasan et al,^[19] reported no significant difference in serum calcium levels among asphyxiated babies and control group. This was not relatable to results obtained from our study.

Serum concentration of magnesium was found to be higher in those with HIE than the asphyxiated population without HIE and was statistically significant in the current study. Khalessi et al,^[20] reported significantly low levels of serum magnesium in asphyxiated babies compared to control group, similar to our study results.

Our study has few limitation- Preterm infants have developmental differences in primitive reflexes, tone and posture and can thus affect the interpretation of Sarnat score. As the study was conducted in a single centre and sample size was limited, findings may not be applicable to a large population.

CONCLUSION

The prevalent abnormalities noted were hyponatremia, hyperkalemia, hypocalcemia and hypermagnesemia. From the study we couldn't obtain any significant association between abnormalities in serum electrolyte levels and severity of HIE. However, the serum calcium level was significantly lower and that of magnesium was significantly higher in asphyxiated babies with HIE compared to those without HIE. Despite appreciable advancements in the field of medicine, birth asphyxia continues to remain as a cause of concern for medical professionals all over the world. Considering the consequences especially those affecting central nervous system the entity needs great attention. A timely and apt intervention undertaken in the first minute of life or the so called golden minute, helps prevent the grave outcome.

Existing literature stresses the importance of routine monitoring of blood parameters including electrolytes in asphyxiated babies. Dyselectrolytemia worsens the hypoxic insult and multiorgan failure. Early determination of serum electrolyte levels and appropriate corrective measures are of immense help in improving the quality of survival and reducing the deaths associated with birth asphyxia.

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