

Decoding the Myth of Severity in HIE - A Study to Find Correlation of Serum Sodium and Calcium Levels with HIE Severity in Asphyxiated Neonates with Convulsion

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Abstract

Background: Hypoxic ischemic encephalopathy is a significant cause of neonatal morbidity and mortality and can lead to severe long term neurodeficits. There is a complex interaction of released neurotransmitters, altered electrolytes level and enzymatic activation. Without proper evaluation of biochemical changes, it is difficult to control its progression. The objective is to give an insight into correlation of severity with hypocalcemia and hyponatremia among HIE cases. **Subjects and Methods:** To conduct this cross sectional observational study serum sodium and calcium levels were measured in asphyxiated newborns who presented with seizure i.e HIE stage 2 and stage 3. Measured electrolytes levels were compared with severity of encephalopathy. **Results:** Results showed negative linear correlation of severity with both sodium and calcium levels but strength of association was more with sodium ($r = -.631$) than calcium ($r = -.247$). Also delay in presentation was more strongly associated with hyponatremia than hypocalcemia. **Conclusion:** Biochemical disturbances are very common in newborn with perinatal asphyxia. Among those who are presenting with seizures, hyponatremia is possibly more detrimental than hypocalcemia.

Keywords: HIE, Neonatal seizure, Hyponatremia, Hypocalcemia.

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Received: 18 December 2020

Revised: 30 January 2021

Accepted: 07 February 2021

Published: 30 March 2021

Introduction

WHO has defined perinatal asphyxia as a 'failure to initiate and sustain breathing at birth.'^[1] Hypoxic Ischemic Encephalopathy refers to the CNS dysfunction associated with perinatal asphyxia.^[2] Worldwide, hypoxic - ischemic encephalopathy is the leading cause of neonatal brain injury and neonatal mortality with neurodevelopmental impairment.^[3] 36.4% of neonatal seizures are due to hypoxic ischemic encephalopathy.^[4] According to Sarnat staging system newborn with HIE can be grouped into HIE stage 1, stage 2, stage 3.^[5] Of which convulsion is seen in stage 2 and stage 3 cases. In stage 1 seizures don't happen. Along with multi organ involvement electrolyte abnormalities are commonly seen in asphyxiated babies.^[6] SIADH is a very common complication resulting in hyponatremia and seizure.^[7] Hypocalcemia also promotes seizure activity. It is difficult to postulate seizure activity due to asphyxia or hyponatremia, hypocalcemia.^[8] There are previous studies suggesting strong correlation of sever-

ity of asphyxia with both hyponatremia and hypocalcemia.^[9] Rachna Pasi and others in a recent study to find out correlation of neonatal seizures and hyponatremia found significant hyponatremia among neonates with HIE.^[10] In a cohort study by Sakeer et al showed significant hypocalcemia among HIE babies prior to therapeutic hypothermia.^[11]

Subjects and Methods

Study design: Cross sectional observational study.

Study timeline: 6 months starting from August 2019 to January 2020.

Place of Study: Department of Pediatrics, Malda Medical College and Hospital.

Study Population: Asphyxiated inborn and outborn babies admitted to NICU.

Sample Size: 224

Inclusion Criteria: HIE stage 2 and stage 3 cases.

Exclusion criteria: HIE stage 1.

Laboratory investigations: Serum Sodium and Calcium levels. Hospital laboratory reference for hyponatremia was < 135 mEq/l (Mild: 125-134 mEq/l, Moderate: 110-124 mEq/l, Severe <110 mEq/l) and for hypocalcemia was < 9mg/dl (Severe < 7 mg/dl)

Ethical Clearance: Was taken from Institutional ethical committee.

Outcome measured: Data were analysed using SPSS Statistics 23.

Results

Correlation were also obtained between age on presentation and severity of birth asphyxia, serum sodium and calcium levels.

Among 224 cases taken 145 (64.7%) were boy and 79 (35.3%) were girl babies, 67 (29.9%) was inborn and 157 (70.1%) were outborn, 109 cases (48.7%) were delivered by LUCS and 115 (51.3%) were delivered by NVD. Mean gestational age of our sample size was 38.86 in weeks, mean birth weight was 2744 grams, mean age on presentation was 19.5 hours after birth. Of the 224 cases enrolled 114 (50.9%) were Sarnat HIE stage 2 and 110 (49.1%) were HIE stage 3.

Mean sodium level of total study population was 110.46 ± 7.92 mEq/l. Of which HIE 2 cases had mean sodium of 115.36 ± 6.5 mEq/l and HIE 3 cases had means sodium of 105.38 ± 5.78 mEq/l. Mean calcium level of total study population was 8.32 ± 0.59 mg/dl. Of which HIE 2 cases had mean calcium of 8.46 ± 0.49 mg/dl and HIE 3 cases had 8.17 ± 0.64 mg/dl. Significant difference was observed on comparing the mean values of sodium and calcium using ANOVA (p-value <0.001). To find correlation between severity of asphyxia and electrolytes level, bivariate analysis was done and pearson test was used to find correlation coefficient. Both calcium and sodium had negative correlation with severity of HIE but strength of association was more with sodium than with calcium level.

Discussion

Both Sodium and calcium are among the major electrolytes in the body. Alteration from their normal level contributes to convulsion and aggravate CNS injury in patients with HIE.^[12] Overall mean values for sodium and calcium was 110.46 ± 7.92 mEq/l and 8.32 ± 0.59 mg/dl. Now if we look at the mean values for HIE stage 2 and 3 separately then it is as follows: Mean sodium in HIE 2 was 115.36 ± 6.5 mEq/l and in HIE 3 it was 105.38 ± 5.78 mEq/l. So when

we compare the mean values of sodium among two stages of HIE using ANOVA there was significant difference between them (p- value <0.001). In a study conducted by Basu P et al the mean value for sodium was 122.1 ± 0 mEq/l.^[13] Reason for much lower mean sodium in our study may be due to timing of sample collection. Most (70.1%) cases were outborn babies, so mostly they presented late to us due to longer transportation time from rural areas of Bengal eventually worsening the severity. Presence of SIADH explains why so much hyponatremia in these newborns. Vijayalaxmi et al. in their study also showed presence of SIADH in HIE cases.^[14] Mean calcium in HIE 2 was 8.46 ± 0.49 mg/dl and in HIE 3 it was 8.17 ± 0.64 mg/dl. Again if we compare the mean values of calcium among different stages of HIE, there is statistically significant difference. So with worsening of HIE both hyponatremia and hypocalcemia worsened. In a study conducted in Tamil Nadu in 2018 by Satheesh et al showed similar findings.^[15] But ANOVA test showed mean decrease in sodium was statistically more significant than mean decrease in calcium. Now bivariate analysis was done between stages of HIE with sodium and calcium level. Sodium level had a negative correlation with severity of asphyxia ($r = -.631$) and also the calcium level had negative correlation ($r = -.247$). Now if we see at the strength of association definitely hyponatremia was more strongly correlated with severity of asphyxia than hypocalcemia. If we look at the correlation of HIE severity with age on presentation then there was obvious positive correlation as severity worsens with delay. Now if we look at the correlation of serum sodium with age on presentation significant negative correlation ($r = -.165$) was found but not that much with calcium ($r = -.079$). In perinatal asphyxia many other parameters like hypoglycemia, hypomagnesemia, acidosis comes into play when the baby is having seizures.^[16] And it is also true that no single factor can be postulated to be the most important in causing seizures. Researches will be always there to evaluate different factors. But in view of this study we can definitely postulate that serum sodium, may it be cause or effect, is definitely of concern in worsening severity of hypoxic ischemic encephalopathy.

Conclusion

Biochemical disturbances are very common in newborn with perinatal asphyxia. Among those who are presenting with seizures, hyponatremia is possibly more detrimental than hypocalcemia.

References

1. Moshiro R, Mdoe P, Perlman JM. A Global View of Neonatal Asphyxia and Resuscitation. *Front Pediatr.* 2019;7:489. ;Available from: <https://dx.doi.org/10.3389/fped.2019.00489>.

Table 1: Correlations of HIE stage and sodium level

		HIE stage	Serum sodium
HIE stage	Pearson Correlation	1	-.631**
	Sig. (2-tailed)		.000
	N	224	224
Serum sodium	Pearson Correlation	-.631**	1
	Sig. (2-tailed)	.000	
	N	224	224

** Correlation is significant at the 0.01 level (2-tailed).

Table 2: Correlations of HIE stage and calcium

		HIE stage	Serum calcium
HIE stage	Pearson Correlation	1	-.247**
	Sig. (2-tailed)		.000
	N	224	224
Serum calcium	Pearson Correlation	-.247**	1
	Sig. (2-tailed)	.000	
	N	224	224

** Correlation is significant at the 0.01 level (2-tailed).

Table 3: Correlations of age on presentation and HIE

		Age on presentation	HIE stage
Age on presentation	Pearson Correlation	1	.411**
	Sig. (2-tailed)		.000
	N	224	224
HIE stage	Pearson Correlation	.411**	1
	Sig. (2-tailed)	.000	
	N	224	224

** Correlation is significant at the 0.01 level (2-tailed).

Table 4: orrelation of age on presentation and sodium level

		Age on presentation	Serum sodium
Age on presentation	Pearson Correlation	1	-.165*
	Sig. (2-tailed)		.014
	N	224	224
Serum sodium	Pearson Correlation	-.165*	1
	Sig. (2-tailed)	.014	
	N	224	224

** Correlation is significant at the 0.05 level (2-tailed).

- Lai MC, Yang SN. Perinatal hypoxic-ischemic encephalopathy. *J Biomed Biotechnol.* 2011;2011:609813. ;Available from: <https://dx.doi.org/10.1155/2011/609813>.
- Allen KA, Brandon DH. Hypoxic Ischemic Encephalopathy: Pathophysiology and Experimental Treatments. *Newborn Infant Nurs Rev.* 2011;11(3):125-133. ;Available from: <https://dx.doi.org/10.1053/j.nainr.2011.07.004>.
- Moayed AM, Zakeri S, Moayed F. Neonatal Seizure: Etiology and Type. *Iran J Child Neurol.* 2008;2(2):23–26. Available from: <https://doi.org/10.22037/ijcn.v2i2.458>.
- Robertson CM, Perlman M. Follow-up of the term infant after hypoxic-ischemic encephalopathy. *Paediatr Child Health.*

Table 5: Correlation of age on presentation and sodium level

		Age on presentation	Serum calcium
Age on presentation	Pearson Correlation	1	-.079
	Sig. (2-tailed)		.238
	N	224	224
Serum calcium	Pearson Correlation	-.079	1
	Sig. (2-tailed)	.238	
	N	224	224

** Correlation is significant at the 0.05 level (2-tailed).

- 2006;11(5):278-282.;
- Thakur J, Bhatta NK, Singh RR, Poudel P, Lamsal M, Shakya A. Prevalence of electrolyte disturbances in perinatal asphyxia: a prospective study. *Ital J Pediatr.* 2018;44(1):56. Available from: <https://doi.org/10.1186/s13052-018-0496-7>.
 - Gupta BD, Sharma P, Bagla J, Parakh M, Soni JP. Renal Failure in Asphyxiated Neonates. *Indian Pediatrics.* 2005;42:928–934.
 - Moen V, Irestedt L. Hyponatremia in Birth Asphyxia—Cause or Effect? *Indian J Pediatr.* 2010;77(9):1049–1050. Available from: <https://dx.doi.org/10.1007/s12098-010-0161-7>.
 - Madhusudhan K, Suresh N, Babu T, Rao J, Kumar S. Study of biochemical abnormalities in neonatal seizures with special reference to hyponatremia. *Int J Contemp Pediatr.* 2016;3(3):730–734. Available from: <https://dx.doi.org/10.18203/2349-3291.ijcp20162172>.
 - Pasi R, Roy B, Ravi KS, Chacham S. Profile of Neonatal Seizures and its Correlation with Serum Sodium Levels: A Prospective Cross-sectional Study. *J Clin Diagn Res.* 2019;13(4):4–07. Available from: <https://dx.doi.org/10.7860/jcdr/2019/40485.12760>.
 - Vayaltrikkovil S, Bashir R, Espinoza M, Irvine L, Scott JN, Mohammad K. Serum calcium derangements in neonates with moderate to severe hypoxic ischemic encephalopathy and the impact of therapeutic hypothermia: a cohort study. *J Matern-Fetal Neonatal Med.* 2020;33(6):935–940. Available from: <https://dx.doi.org/10.1080/14767058.2018.1510911>.
 - Thakur J, Bhatta NK, Singh RR, Poudel P, Lamsal M, Shakya A. Prevalence of electrolyte disturbances in perinatal asphyxia: a prospective study. *Ital J Pediatr.* 2018;44(1):56. Available from: <https://doi.org/10.1186/s13052-018-0496-7>.
 - Basu P, Som S, Das H, Choudhuri N. Electrolyte status in birth asphyxia. *Indian J Pediatr.* 2010;77(3):259–262. Available from: <https://doi.org/10.1007/s12098-010-0034-0>.
 - Gagandeep V, S VP. Syndrome of inappropriate antidiuretic hormone secretion in neonates with birth asphyxia at tertiary care centre. *Int J Contemp Pediatr.* 2019;6(6):2549. Available from: <https://dx.doi.org/10.18203/2349-3291.ijcp20194732>.
 - D SK, M T, K. Electrolyte abnormalities in asphyxiated newborns. *Int J Contemp Pediatr.* 2018;5(3):1036. Available from: <https://dx.doi.org/10.18203/2349-3291.ijcp20181537>.
 - Vamne A, Bhimte B. Metabolic Derangement in Birth Asphyxia due to Cellular Injury with Reference to Mineral Metabolism in Different Stages of Hypoxic-ischemic Encephalopathy in Central India. *Indian J Med Biochem.* 2017;21(2):86–90. Available from: <https://dx.doi.org/10.5005/jp-journals-10054-0027>.

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How to cite this article: Sahoo S, Mandal S. Decoding the Myth of Severity in HIE – A Study to Find Correlation of Serum Sodium and Calcium Levels with HIE Severity in Asphyxiated Neonates with Convulsion. *Asian J. Clin. Pediatr. Neonatol.* 2021;9(1):32-35.

DOI: [dx.doi.org/10.47009/ajcpn.2021.9.1.7](https://doi.org/10.47009/ajcpn.2021.9.1.7)

Source of Support: Nil, **Conflict of Interest:** None declared.