Research Article

Association of Cord Blood Glucose and Electrolyte Levels With Birth Asphyxia And Hie Severity in Late-Preterm and Term Neonates: A Hospital-Based Cross-Sectional Study

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ABSTRACT

Background: Birth asphyxia may be accompanied by metabolic disturbances associated with hypoxic-ischaemic injury. This study compared cord blood glucose and electrolyte concentrations between asphyxiated and non-asphyxiated neonates and assessed their association with hypoxic-ischaemic encephalopathy (HIE) severity.

Methods: This hospital-based cross-sectional study included 96 inborn neonates with gestational ages greater than 34 and up to 42 completed weeks, comprising 48 neonates with birth asphyxia and 48 controls. Approximately 2 mL of umbilical venous cord blood was collected immediately after delivery. Glucose, calcium, sodium and potassium were measured using standard laboratory methods. HIE severity among cases was graded using Sarnat staging. Between-group comparisons and correlations with HIE severity were analysed, with $p \leq 0.05$ considered statistically significant.

Results: Compared with controls, asphyxiated neonates had lower mean glucose (48.6±12.4 vs 69.3±11.8 mg/dL; $p<0.001$), sodium (131.8±5.6 vs 135.2±4.3 mEq/L; $p=0.002$) and calcium (7.9±0.8 vs 9.1±0.7 mg/dL; $p<0.001$), whereas potassium was higher (5.8±0.9 vs 4.7±0.7 mEq/L; $p<0.001$). Reported frequencies of severe hypoglycaemia, hyponatraemia, hyperkalaemia and hypocalcaemia were 26.7%, 46.7%, 53.3% and 50.0%, respectively. Increasing HIE severity was associated with lower glucose ($r=-0.62$), sodium ($r=-0.41$) and calcium ($r=-0.48$), and higher potassium ($r=+0.53$); all reported associations were statistically significant.

Conclusion: Birth asphyxia was associated with significant differences in cord blood glucose and electrolyte concentrations. These biochemical parameters were also associated with HIE severity and may provide supportive information alongside clinical assessment. Further studies are required to validate their clinical utility.

Keywords: Birth asphyxia; hypoxic-ischaemic encephalopathy; cord blood; glucose; sodium; potassium; calcium; neonates.

INTRODUCTION

Perinatal asphyxia remains an important cause of neonatal death and neurological morbidity, particularly in settings where timely intrapartum care and neonatal resuscitation may be difficult to access. Hypoxic-ischaemic injury can initiate a cascade of energy failure, excitotoxicity, oxidative stress and secondary cellular injury, with consequences extending beyond the central nervous system to multiple organs. The clinical expression of neonatal encephalopathy varies, and structured staging systems such as the Sarnat classification are used to describe its severity. [1-3]

Reduced oxygen delivery and impaired perfusion can disrupt cellular energy metabolism and membrane ion transport. Consequently, glucose and electrolyte disturbances—including hypoglycaemia, hyponatraemia, hyperkalaemia and hypocalcaemia—may accompany birth asphyxia. These changes may reflect the severity of the underlying insult and may themselves complicate neurological and cardiovascular function. However, biochemical values can also be influenced by the timing and type of specimen, postnatal adaptation, fluid administration and treatment. [4-7]

Several observational studies have reported lower sodium and calcium and higher potassium concentrations in asphyxiated neonates, with some also describing lower glucose concentrations and worsening biochemical abnormalities across increasing grades of encephalopathy. Basu et al. and Jayaprakash et al. reported associations between electrolyte disturbances and asphyxia, while studies by Thakur et al. and Allam Bhat et al. described a relationship between the magnitude of selected electrolyte abnormalities and clinical severity. [8-11] More recent work has also examined cord blood biochemical measurements as early indicators of HIE severity. [12-14]

Cord blood sampling immediately after delivery offers an opportunity to assess biochemical status before many postnatal interventions alter measured concentrations. Nevertheless, findings across studies are not fully consistent, and variation in asphyxia definitions, sample timing, gestational-age groups and laboratory methods limits direct

comparison. Evidence focused on late-preterm and term neonates from South Rajasthan remains useful for describing local patterns and for generating hypotheses for further validation.

Accordingly, this study compared cord blood glucose, sodium, potassium and calcium concentrations between neonates with and without birth asphyxia and examined the relationship of these parameters with HIE severity among asphyxiated neonates.

Materials and Methods

Study design and setting

This hospital-based observational cross-sectional study was conducted in the Department of Pediatrics at Ananta Institute of Medical Sciences, Rajasthan, over 18 months period following institutional ethics approval and clearance from Rajasthan University of Health Sciences.

Participants

A total of 96 inborn neonates with gestational age >34 to ≤42 completed weeks were included: 48 neonates with birth asphyxia and 48 controls without clinical evidence of asphyxia. Cases met the study criteria of an Apgar score <7 at 1 minute and requirement for positive-pressure ventilation for more than 1 minute. Controls cried immediately after birth and had an Apgar score ≥7 at 1 minute. Neonates with congenital malformations and those born to mothers with pre-gestational or gestational diabetes were excluded. Eligible neonates were enrolled consecutively after written informed consent from parents/guardians.

Sample collection and biochemical analysis

Approximately 2 mL of umbilical venous cord blood was collected aseptically immediately after delivery into plain sterile containers and transported to the laboratory within 15 minutes. Samples were centrifuged at 3000 rpm for 10 minutes within 30 minutes of collection, and serum was separated for analysis. Glucose was estimated using the glucose oxidase-peroxidase method, total calcium using the Arsenazo III method, and sodium and potassium using ion-selective electrode methods on a VITROS 5600 autoanalyser. Internal quality-control procedures and routine calibration were followed.

Clinical assessment and outcomes

Perinatal and demographic information, mode of delivery, birth weight, gestational age, Apgar scores and resuscitation details were recorded. HIE among cases was graded using Sarnat staging. The present manuscript focuses on group differences in biochemical parameters and their association with HIE severity; detailed discharge outcomes and receiver operating characteristic analyses are intentionally reserved for a separate, non-overlapping analysis.

Statistical analysis

Data were entered in Microsoft Excel and analysed using SPSS version 25. Continuous variables were summarised as mean±standard deviation and categorical variables as frequency and percentage. Independent-samples t-tests were used for comparison of means, and correlation coefficients were used to assess relationships between biochemical parameters and HIE severity. Statistical significance was set at $p \leq 0.05$.

Ethical considerations

Written informed consent was obtained from the parents/legal guardians of all participating neonates. Ethical approval was granted by the Institutional Ethics Committee (IEC), Ananta Institute of Medical Sciences and Research Centre (Approval No. AIMS/Ananta IEC/2024/283; dated 28 June 2024).

RESULTS

TABLE 1: Comparison of cord blood biochemical parameters

Parameter	Asphyxiated (n=48)	Controls (n=48)	P value
Glucose (mg/dL)	48.6 ± 12.4	69.3 ± 11.8	<0.001
Sodium (mEq/L)	131.8 ± 5.6	135.2 ± 4.3	0.002
Potassium (mEq/L)	5.8 ± 0.9	4.7 ± 0.7	<0.001
Calcium (mg/dL)	7.9± 0.8	9.1 ± 0.7	<0.001

Mean glucose, sodium and calcium concentrations were lower in cases than controls, whereas mean potassium was higher. The differences were statistically significant for all four biochemical parameters

TABLE 2: Frequency of biochemical abnormalities among cases

Abnormalities	Cases (%)	Operational threshold reported
Severe Hypoglycemia	26.7	Glucose <40 mg/dL
Hyponatremia	46.7	Sodium <135 mEq/L
Hyperkalemia	53.3	Potassium >5.5 mEq/L
Hypocalcaemia	50.0	Calcium <8.5 mg/dL

Multiple biochemical abnormalities were present in a subset of cases; 16.7% were reported to have abnormalities in three or more parameters

TABLE 3: Association with HIE Severity

Parameter	Correlation Coefficient (r)	P value	Direction
Glucose	-0.62	<0.001	Decreased with increasing HIE stage
Sodium	-0.41	0.002	Decreased with increasing HIE stage
Potassium	0.53	<0.001	Increased with increasing HIE stage
Calcium	-0.48	<0.001	Decreased with increasing HIE stage

Glucose showed the strongest negative correlation with HIE stage among the reported parameters, followed by potassium in the positive direction. Sodium and calcium also showed significant negative correlations with increasing HIE severity.

Discussion

The principal finding of this study was a consistent pattern of biochemical disturbance in neonates with birth asphyxia: lower cord blood glucose, sodium and calcium concentrations and higher potassium concentrations than in controls. All four comparisons were statistically significant. The pattern is biologically plausible because hypoxia and impaired perfusion can compromise cellular energy production and membrane transport, while associated organ dysfunction and endocrine responses may alter electrolyte balance. [4-7]

The glucose difference is clinically relevant. In the present cohort, mean glucose was 48.6±12.4 mg/dL among cases and 69.3±11.8 mg/dL among controls, and severe hypoglycaemia was reported in 26.7% of cases. Liu et al. described changes in glucose during early postnatal life following birth asphyxia, while Jayaprakash et al. and other comparative studies also reported lower glucose in more severely affected neonates. [9,12] Low glucose may coexist with hypoxic-ischaemic injury and can potentially compound neuronal energy failure; however, the cross-sectional design does not establish whether the biochemical change preceded, caused or simply reflected the severity of injury.

Mean sodium was lower in cases, and sodium showed a moderate negative correlation with HIE stage (r=−0.41). This agrees with reports describing hyponatraemia or declining sodium concentrations with increasing severity of asphyxia. Basu et al. reported significantly lower sodium in asphyxiated newborns, and Thakur et al. found progressively lower sodium values across increasing grades of asphyxia. [8,10] Possible contributors include altered water handling and antidiuretic hormone responses, as well as systemic organ dysfunction.

Potassium was higher among cases and rose with HIE severity (r=+0.53). This is consistent with studies by Basu et al. and Allam Bhat et al., which described higher potassium concentrations and an association between hyperkalaemia and more severe encephalopathy. [8,11] Acidosis, cellular injury and impaired renal excretion may contribute, although the present study did not directly test these mechanisms.

Calcium concentrations were lower in asphyxiated neonates and declined with increasing HIE severity (r=−0.48). This finding is consistent with reports of hypocalcaemia in neonatal asphyxia, including studies by Rai et al. and Acharya et al. [9,13] Calcium disturbances may arise from altered parathyroid responses, metabolic stress and associated organ dysfunction. Differences between studies may partly reflect whether total or ionised calcium was measured, the timing of sampling and the threshold used to define hypocalcaemia.

The observed correlations suggest that cord blood biochemical parameters track clinical severity, but none should be treated as a substitute for a structured neurological assessment. The Sarnat stage remains a clinical classification, and biochemical values should be integrated with perinatal history, examination, resuscitation details and other investigations. Studies of cord blood markers, including those by Kavya et al. and Goyal et al., similarly support further evaluation of early biochemical measurements as adjuncts to severity assessment. [12,14]

An important strength of this study is the immediate collection of cord blood, reducing the influence of some postnatal interventions on the initial biochemical measurements. Inclusion of late-preterm as well as term neonates also makes the findings relevant to a group that may be under-represented in studies restricted to term infants. Limitations include the single-centre design, modest sample size, potential limitations in the operational definition of birth asphyxia, and lack of long-term neurodevelopmental follow-up. The reported thresholds and correlations should be validated in a larger prospective cohort with standardised definitions, explicit adjustment for gestational age and other confounders, and assessment of predictive performance in an independent sample.

In summary, the study demonstrates significant differences in cord blood glucose and electrolyte concentrations between asphyxiated neonates and controls, alongside significant associations with HIE severity. These findings support early biochemical testing as an adjunct to clinical assessment, while further validation is required before using any individual parameter or cut-off for decision-making.

Conclusion

In this hospital-based study of 96 late-preterm and term neonates, birth asphyxia was associated with significantly lower cord blood glucose, sodium and calcium and higher potassium concentrations. Glucose and calcium decreased and potassium increased with worsening HIE stage, while sodium also showed a significant inverse association. Cord blood biochemical assessment may provide useful early supportive information when interpreted alongside clinical examination and established HIE staging. Larger multicentre studies with standardised criteria and longer follow-up are needed to establish generalisability and prognostic utility.

Strengths and limitations

Strengths include immediate cord blood sampling, inclusion of a control group, and evaluation of four routinely measurable biochemical parameters against HIE stage. Limitations include a single-centre sample, modest sample size, potential variability in defining birth asphyxia, and no long-term neurodevelopmental assessment. The study design demonstrates association rather than causation.

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