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Original Research Article

Serum calcium and glucose level in asphyxiated neonates: a prospective study

Darla Sri Sai Lahari*, Nazeer Ahmad Jeergal, A. N. Thobbi

Department of Paediatrics, Al -Ameen Medical College and Hospital, Vijayapura, Karnataka, India

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***Correspondence:**
Dr. Darla Sri Sai Lahari,
E-mail: darla@gmail.com

ABSTRACT

Background: Birth asphyxia is the primary cause of both mortality and death in newborns. Neonates that experience birth asphyxia are more likely to develop hypocalcemia and hypoglycemia. The primary objective of this study was to assess the calcium and glucose in newborns who had asphyxia and compare with the hypoxic-ischemic encephalopathy (HIE) severity.
Methods: This prospective observational study conducted on 75 asphyxiated neonates admitted to NICU. The serum calcium, ionized calcium and glucose level were measured using standard biochemical methods. The severity of HIE was assessed using the Sarnat and Sarnat staging system. The calcium and glucose level were compared across different stages of HIE using one-way ANOVA.
Results: The mean total calcium level was 7.87±1.87 mg/dl, mean ionized calcium level was 3.27±0.76 mg/dl and mean serum glucose level was 44.43±6.5 mg/dl respectively. Out of 75 neonates, majority 32 (42.7%) were in were in HIE stage II moderate risk. There was a significant decline in calcium level among the neonate in HIE stage III severe risk when compared to HIE stage II (3.65±0.97 vs 4.05±1.06) and HIE stage I (3.65±0.97 vs 5.76±1.32). The mean serum glucose level was significantly (p=0.001) lower in HIE stage III severe risk when compared to HIE stage II (38.12±4.65 vs 44.76±5.45) and HIE stage I (38.12±4.65 vs 50.43±6.28).
Conclusions: The ionic calcium and glucose levels were decreased in asphyxiated neonates and early intervention is required to reduce the neonatal mortality.

Keywords: Birth asphyxia, Electrolytes, Ionized calcium, Glucose, HIE

INTRODUCTION

Birth asphyxia in neonates, also known as perinatal asphyxia, is a clinical event characterized by the inadequate delivery of oxygen to a newborn during the birthing process. This can lead to a range of complications, including HIE, multiorgan dysfunction, and even death. Birth asphyxia is responsible for 900,000 newborn deaths worldwide and is a significant risk factor for early neonatal mortality.[1] Severe birth asphyxia is referred as if the 1 minute Apgar score is in the range 0-3. In the case of mild and moderate birth asphyxia, the 1 minute Apgar score is in the range 4-7.[1] The prevalence of birth asphyxia is higher in underdeveloped nations compared to developed countries due to the reduced availability of expert treatment during childbirth.[2] Various underlying causes contribute to the occurrence of birth asphyxia, but the primary cause is the decrease in cerebral blood flow. These include a range of disorders such as post-partum hemorrhage, preeclampsia, rupture of placenta and uterus, prolapse of umbilical cord and infection.[3] A recent investigation performed in India concluded that the prevalence of newborn asphyxia was 5.26% (92/1749) and fatality rate of 4.35% (4/92).[4] HIE is the term used to describe newborn encephalopathy caused by birth asphyxia. This condition leads to neurological impairments and cerebral palsy.[5] The Sarnat and Sarnat classification is used to categorize it into

various stages. In cases of severe HIE stage III, the newborn experiences a vegetative state, severe muscle weakness, protracted seizures, and is unable to breathe on their own.[6] The serum electrolytes is crucial in determining the outcome of infants with HIE. Any deviation in the levels of electrolytes (sodium, potassium, and calcium) can lead to seizures, shock, and other types of metabolic abnormalities.[7]

Glucose is a vital constituent for optimal brain functionality. A very low level can result in encephalopathy and possess the capacity to trigger chronic brain impairment. Birth asphyxia results in a significant reduction in glycogen due to the release of catecholamines and idiopathic hyperinsulinemia, leading to hypoglycaemia.[8] The severity of brain damage is significant in cases of hypoxia and hypoglycemia, and the prompt identification of the condition remains a difficult problem in neonatal healthcare. Moreover, the extent of birth asphyxia determines the level of electrolyte imbalance.[9] The objective of this study is to examine the levels of serum ionized calcium and glucose in term asphyxiated neonates at 24 hours after birth. In addition, the levels of serum ionized calcium and glucose were correlated with HIE severity.

METHODS

This prospective observational study conducted on 75 asphyxiated neonates admitted to NICU of department of paediatrics, Al-Ameen medical college and hospital, Vijayapura, Karnataka, India. The study was conducted for a period of one year from March 2023 to March 2024.

Inclusion criteria

Neonates with Apgar score <6 at 5 minutes, a base deficit greater than 12 mmol/L, a pH level below 7.1, presence of encephalopathy with clinical symptoms such as changes in consciousness, convulsions, decreased muscle tone, or inability to suck were included.

Exclusion criteria

Preterm and post term babies, neonates born with congenital abnormalities, inborn errors of metabolism and with septic shock were excluded from the study. Mothers who had experienced febrile illness within two weeks before delivery and had abnormal levels of serum electrolytes were also excluded from the study.

Study procedure

The data of newborns who had perinatal asphyxia were assessed using a preformatted questionnaire. The categorization of mild (HIE I), moderate (HIE II), and severe (HIE III) stages was determined using the modified Sarnat staging system for newborn encephalopathy.[6] Comprehensive information was recorded regarding the specific type and location of birth, the type of resuscitation needed, any complications that occurred before or during delivery, the timing and length of the seizure, and the results of the clinical examination, with particular emphasis on the central nervous system. The clinical assessment included neurological symptoms such as atypical movements, difficulties with feeding, both subtle and obvious convulsions, and any neurological impairment.

The serum ionized calcium levels were estimated using Ion selective Electrode method and neonates with <4 mg/dL were considered as hypocalcaemia. The serum glucose level was estimated by glucose oxidase peroxidase method and neonates with <45 mg/dL were considered as hypoglycemia. Further the serum levels of ionized calcium and glucose were correlated with HIE severity.

Statistical analysis

The data were represented as mean±SD. One way ANOVA was used to compare the variables across different stages of HIE. Chi square analysis was used for the correlation between serum levels of ionized calcium and glucose and HIE severity. A $p<0.05$ was considered as significant. The statistical package for social sciences version 24 (SPSS, IBM Company, Chicago, IL, USA) was used for the analysis.

RESULTS

The demographics and clinical characteristics of the asphyxiated neonates were shown in Table 1. Male preponderance was observed which constitute 45 (60%) and 24 (40%) were females neonates. Majority of the neonates, 90.7% had clear amniotic fluid and most of neonates were delivered for multigravida mothers, encompassing 53.3%. Majority of the neonates, 48 (64%) were delivered through vaginal delivery and caesarean delivery was observed in 36% of the cases. The mean total calcium level was 7.87±1.87 mg/dl, mean ionized calcium level was 3.27±0.76 mg/dl and mean serum glucose level was 44.43±6.5 mg/dl respectively.

The classification of asphyxiated neonates according to the HIE stages was shown in Table 1. Out of 75 neonates, 25 (33.3%) were in HIE stage I mild risk, 32 (42.7%) were in stage II moderate risk and 18 (24%) were in HIE stage III severe risk.

In this study out of 75 neonates, 19 (25.3%) had hypocalcaemia and 56 (74.7%) had normal ionized calcium levels and the data were shown in Table 3. There was a significant ($p=0.001$) decline in calcium level among the neonate in HIE stage III severe risk when compared to HIE stage II (3.65±0.97 vs 4.05±1.06) and HIE stage I (3.65±0.97 vs 5.76±1.32).

In this study out of 75 neonates, 15 (20%) had hypoglycemia and 60 (74.7%) had normal glucose levels.

The comparison of mean glucose level across various stages of HIE was shown in Table 4. The mean serum glucose level was significantly (p=0.001) lower in HIE stage III severe risk when compared to HIE stage II (38.12±4.65 vs 44.76±5.45) and HIE stage I (38.12±4.65 vs 50.43±6.28).

Table 1: Demographics and clinical characteristics of the asphyxiated neonates.

Variables	Asphyxiated neonates, (n=75) (%)
Gender (N, %)	
Male	45 (60)
Female	25 (40)
Birth weight (gm), mean±SD	2676±420
Gestational period (weeks), mean±SD	39.21±4.34
APGAR scores (mean±SD)	
1 min	3.54 ±0.98
5 mins	5.12±1.05
10 mins	7.28±1.45
Amniotic fluid	
Clear	68 (90.7)
Stained	7 (9.3)
Parity	
Primigravida	35 (46.7)
Multigravida	40 (53.3)
Mode of delivery	
Vaginal	48 (64)
Caesarean	27 (36)
Serum total calcium (mg/dl), mean±SD	7.87±1.87
Serum ionized calcium (mg/dl), mean±SD	4.49±0.76
Serum glucose (mg/dl), mean±SD	44.43±6.5

Table 2: Distribution of neonates based on HIE stages.

HIE stages	Asphyxiated neonates, (n=75) (%)
I	25 (33.3)
II	32 (42.7)
III	18 (24)
Total	75 (100)

Table 3: Comparison of serum ionized calcium levels among the neonates in different HIE stages.

HIE stages	N	Serum ionized calcium, mg/dl (mean±SD)	P value
I	25	5.76±1.32	0.001*
II	32	4.05±1.06	
III	18	3.65±0.97	

*Indicates significant p<0.05 (One-way ANOVA).

Table 3: Comparison of glucose levels among the neonates in different HIE stages.

HIE stages	N	Serum glucose level (mean±SD)	P value
I	25	50.43±6.28	0.001*
II	32	44.76±5.45	
III	18	38.12±4.65	

*Indicates significant p<0.05 (One-way ANOVA)

DISCUSSION

Birth asphyxia and neonatal encephalopathy are widely recognized factors that contribute to illness and death in newborns globally. The main causative factor for the occurrence of HIE is the hypoxic-ischemic environment during the peripartum period. Although there have been significant advancements in the availability of effective diagnostic and therapeutic tools for gynaecologists and paediatricians in recent decades, neurological and intellectual disabilities continue to be a significant burden for families and societies. This is particularly true for approximately 25% of the children with mild Sarnat grade of HIE.[10] HIE is mainly due to sudden or chronic lack of oxygen supply to the body and diminished blood flow to the brain. Hypoxic-ischemic alterations in the full-term newborn elicit many molecular and cellular changes that might lead to cell death and local/systemic inflammation.[10]

Perinatal asphyxia also caused imbalances in the body's electrolytes. The degree of tissue damage (and severity of hypoxia) depends on the serum electrolyte levels and glucose levels. The current study observed and correlated the serum calcium and glucose levels in asphyxiated neonates.

In our study the incidence rate of birth asphyxia was predominant in male neonates constituting 60%. Likewise, in a study done by Bahatkar and Aundhakar, 74% were males and in another study done by Patidar et al.[11,12] 70% were males. The male predominance in this case is attributed to transitory cerebral anoxia and decline in neurons related to respiratory control located in brainstem. These factors can reduce the emergency or auto resuscitation in male babies. In addition, females exhibit greater resistance to hypoxia compared to males, which can be attributed to the existence of an extra X chromosome.[13]

We have also observed predominance of birth asphyxia in babies born to multigravida mothers, 53.3% and vaginal delivery, encompassing 64% respectively. Likewise, in a study done by Onyiriuka, 71% of the asphyxiated neonates had vaginal delivery.[14] In another study done by Singh et al, 54% of the neonates had vaginal delivery which is consistent with our reports.[15]

Ionized calcium plays a vital role in various biochemical mechanism in infants, such as blood clotting, neuronal

excitability, maintaining the cell membrane integrity and function, as well as cellular enzymatic and secretory activities. Hypocalcemia in perinatal asphyxia can be attributed to renal failure, metabolic acidosis, and reduced secretion of parathyroid hormone.[16] In our study, the mean serum total calcium level and ionized calcium level was 7.87±1.87 mg/dl and 4.49±0.76 mg/dl respectively. Similarly, in Singh et al study the serum total calcium level was 8.04±0.89 mg/dl and Ionic calcium level was 3.62±0.46 mg/dl, which is comparatively lower when compared to normal threshold value for newborns.[15]

In the present study, majority of the neonates were in stage 2 moderate HIE encompassing 42.7% and stage 3 severe HIE in 24% of the neonates. Similarly, in a study conducted by Acharya et al 57.33% of infants are in the stage 2 moderate HIE.[17] Possible causes for this include risk factors such as meconium staining, respiratory depression, oligohydramnios, fetal birth abnormalities and macrosomic babies.

In this research, the serum ionized calcium was compared among the different stage of HIE. The neonates in HIE stage III severe risk had lower calcium level when compared to HIE stage II (3.65±0.97 vs 4.05±1.06) and HIE stage I (3.65±0.97 vs 5.76±1.32) and it was significant (p=0.001). Similarly, in Mahajan et al study the serum ionized calcium level was significantly lower in neonates in HIE stage III, 3.12±0.342 mg/dl as compared to stage II (3.54 mg/dl) and stage I (3.61 mg/dl) and it was significant (p<0.001).

Blood glucose abnormalities in neonates is mainly due to birth asphyxia, which occur in 29.6% of cases, making it the second most frequent complication.[18] Dysregulation in blood glucose level is mainly due to the changes in body metabolism mediated by hypoxia ischemia. Infants lack enough liver glycogen reserves, yet their energy needs are comparatively high. During the initial phase of neonatal birth hypoxia, there is a prevalence of anaerobic glycolysis, accompanied by an increased rate of metabolic activity and excessive oxygen and glucose utlilization.[19] Additionally, the blood of neonates who have been deprived of oxygen is redirected to prioritize vital organs like the brain and heart. This results in a decrease in blood and oxygen supply to the gastrointestinal tract, which in turn impacts the absorption of glucose.[20] Thus the reason for hypoglycemia in birth asphyxia can be caused by all of the aforementioned conditions.

In our study, there was a significant (p=0.001) decline in the serum glucose level in HIE stage III severe risk when compared to HIE stage II (38.12±4.65 vs 44.76±5.45) and HIE stage I (38.12±4.65 vs 50.43±6.28). Likewise, Rai et al study in severely asphyxiated babies there was a significant (p<0.05) decline in the blood glucose level, 46.8±4.58 mg/dl when compared to the mild (59.71±11.47 mg/dl) and moderately asphyxiated babies (53.69±6.97 mg/dl).[8] In addition, the glucose level was lower in moderately asphyxiated as that of the mild asphyxiated newborns and it was significant (p<0.05). This indicates that there is an inverse relationship between glucose levels and hypoxia severity at 24 hours of life.

CONCLUSION

Our study indicates that neonates who experience birth asphyxia develop hypocalcemia and hypoglycemia after delivery, with the severity of asphyxia directly correlating to the extent of these conditions. Timely identification and efficient treatment of hypocalcemia and hypoglycemia in a newborn experiencing hypoxia reduces the risk of death and eliminates negative effects on neurological development, thereby improving the long-term outlook for these infants. It is also advisable to routinely examine the serum calcium and glucose levels of all infants who have had asphyxiation after birth.

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