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Comparison of Serum Calcium Level Among Patients with Different Stages of Hypoxic Ischaemic Encephalopathy Due to Perinatal Asphyxia

Mst. Rukshana Begum Chowdhury,[1] Sifat Binte Karim,[2] Md. Mostafa Zaman,[3] Shanjeeda Shormin,[4] Md. Sariful Islam,[5] Nusrat Nuren[6]

1. Associate Professor
   Department of Pediatrics
   Rangpur Medical College
2. Assistant Professor (In situ)
   Upozila Health Complex
   Gangachara, Rangpur.
3. Associate Professor
   Department of Pediatrics
   Rangpur Medical College
4. Associate Professor
   Department of Pediatrics
   Rangpur Medical College
5. Assistant Professor (In situ)
   Department of Pediatrics
   Rangpur Medical College Hospital
   Rangpur
6. Assistant Professor (In situ)
   Department of Clinical Parthology
   Rangpur Medical College Hospital
   Rangpur

Correspondence to:
Mst. Rukshana Begum Chowdhury
Associate Professor
Department of Paediatrics
Rangpur Medical College, Rangpur
Email: rukshanabegum078@gmail.com

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Abstract

Background:
Perinatal asphyxia is a leading cause of neonatal hospital admission, particularly in low- and middle-income countries. It causes diminished oxygen supply to brain resulting hypoxic ischaemic encephalopathy with three distinct stages. Higher HIE grades have been associated with reduced calcium levels. This emergency condition can lead to multi-organ dysfunction and can affect the neonatal calcium profile causing mainly hypocalcemia.

Objective:
To compare the serum calcium level among different stages of Hypoxic ischaemic encephalopathy (HIE) in perinatal asphyxia

Methods:
This cross-sectional observational study was conducted in department of Paediatrics, Rangpur medical college hospital on 212 neonates with perinatal asphyxia with different stages of HIE.

Results:
Among 212 neonates birth asphyxia was predominant in male (56.5%). Birth asphyxia was predominant in vaginal delivery (64%). Majority of the neonates were in HIE stage II (58.5%) followed by stage III (21.7%) and stage I (19.8%). Serum calcium level was significantly lower in stage III to stage-II HIE (5.1±1.66 vs 6.1±1.1.54, p-value=0.0003) and stage II to stage-I (6.1±1.1.54 vs 7.2±1.35, p-value=.0003).

Conclusion:
Serum calcium level tends to decrease in asphyxiated neonate which is most subjacent in HIE stage III.

Keywords: Perinatal Asphyxia, Hypoxic Ischaemic Encephalopathy, Stages, Serum Calcium Level

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Introduction:

Perinatal asphyxia is a leading cause of neonatal hospital admission, particularly in low- and middle-income countries. It results from a lack of oxygen and/or inadequate blood flow (ischemia) to the foetus or newborn during the perinatal period. This emergency condition can lead to multi-organ dysfunction and can affect the neonatal calcium profile.[1] Neonatal hypocalcemia is a common biochemical abnormality occurred in asphyxiated neonates. It can occur early (within the first 72 hours) or late (after 72 hours) and often present without typical clinical symptoms, thus routine monitoring is often difficult.[2] Birth asphyxia generates a series of metabolic derangements, including hypoxia-induced acidosis and qualitative and quantitative alternance of parathyroid hormone. Furthermore, impaired calcium mobilization from bones and reduced intestinal calcium absorption also causes an increase in phosphate levels that further lowers calcium concentrations. The stress response to asphyxia, accompanied by elevated catecholamines and glucocorticoids, further aids to altered calcium metabolism.[3] Hypocalcemia in birth asphyxia may lead to seizure activity and cardiac dysfunction. Therefore, quantifying calcium offers a more comprehensive picture of

the neonate's calcium status and can serve as a useful prognostic indicator.[4] Sarnat and Sarnat classification aids in classifying the severity of asphyxia and can correlate with biochemical abnormalities. Higher HIE grades have been associated with lower calcium levels.[5] The pathophysiological mechanisms underlying neonatal hypocalcemia in asphyxiated infants are multifactorial. They include immature parathyroid hormone responses, increased phosphate levels due to cellular injury, magnesium deficiency, and renal losses of calcium.[6] Clinical studies conducted in different settings have registered a consistent association between birth asphyxia and decreased calcium concentrations, thereby reassuring the importance of biochemical screening in those neonates.[7]

Method:

A cross-sectional observational study was conducted in department of Paediatrics, Rangpur medical college hospital, Rangpur during March 2018 to October 2018 on 212 neonates with perinatal asphyxia with different stages of HIE. Preterm neonates (<37 weeks gestation), neonates with major congenital anomalies, sepsis or metabolic disorders, neonates born to mothers with known calcium metabolism disorders or whose mothers received magnesium sulfate before delivery were excluded. With aseptic precautions, 2 ml blood was drawn from peripheral vein. After removal of the needle from syringe blood sample was collected in a dry clean glass test tube. Within one hour of collection, blood was centrifuged and serum was separated. Serum calcium concentration was measured by auto analyzer machine (Dimension xpand plus) at the Department of Biochemistry & Department of Pathology, Rangpur Medical College, Rangpur, on the same day. Continuous variables were expressed as mean and standard deviation, while categorical variables were expressed as numbers and percentages. Unpaired t test was done as a test of significance, p-value <0.05 was considered statistically significant. The SPSS 22.0 for Windows was used for statistical computations.

Results:

Majority of the neonates were male accounting 56.5% and only 20% were low birth weight baby. NVD was the predominant mode of delivery at approximately 64% (Table-I).

Table-I: Demographic characteristics of patients (N=212)

Demographic characteristics	no. (%)
Gender	
Male	122(56.5)
Female	90(43.5)
Birth weight	
≥2.5 Kg	170(80)
<2.5Kg	42(20)
Delivery	
NVD	135(64)
LUCS	77(36)

Most of the neonates were classified under HIE stage II (52.5%). Meanwhile HIE-I (19.8%) and, HIE-III (21.7%) were also documented.

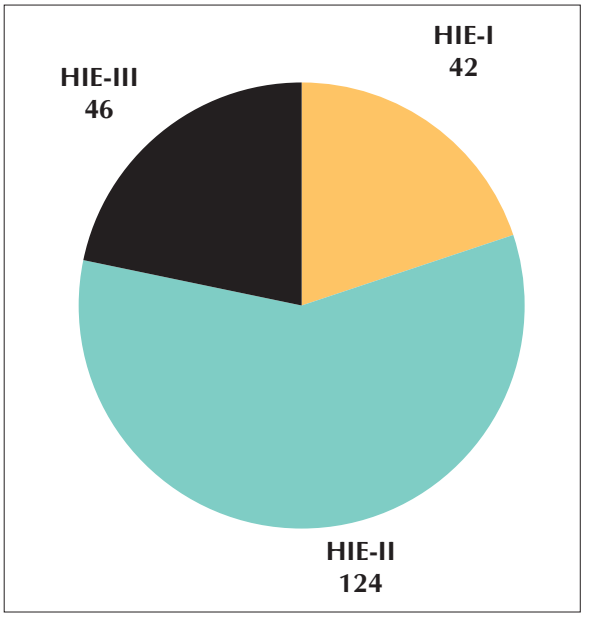

Figure-1: Neonates of different HIE stage

Mean serum calcium was lowest in HIE- III which was 5.1±1.66 mg/dl. Neonates with HIE-II had lower calcium level (6.1±1.54 mg/dl) than HIE-I (7.2±1.35 mg/dl) (Table-II).

Table-II: Level of serum calcium of different stages of HIE

Stages of HIE	Serum calcium (mg/dl) (Mean±SD)
HIE-I	7.2±1.35
HIE-II	6.1±1.54
HIE-III	5.1±1.66

Serum calcium level in HIE-II is significantly lower in comparison to HIE-I (p-value <0.01) (Table-III).

Table-III: Comparison of serum calcium level between HIE stage I (n=42) and stage II (n=124)

Serum calcium	HIE-I	HIE-II	p-value
Mean±SD (mg/dl)	7.2±1.35	6.1±1.54	<0.001

Serum calcium level in HIE-III is significantly lower in comparison to HIE-II (p-value=0.0003) (Table-III).

Table IV: Comparison of serum calcium level between HIE stage II (n=124) and stage III (n=46)

Serum calcium	HIE-III	HIE-II	p-value
Mean±SD (mg/dl)	6.1±1.54	5.1±1.66	0.0003

Discussion:

Perinatal asphyxia, is a clinical event characterized by the inadequate delivery of oxygen to a newborn during the intrauterine fetal period or birthing process which causes a wide range of complications, including HIE, multiorgan dysfunction, and finally death. HIE is primarily due to sudden or chronic insufficiency of oxygen to the body resulting in diminished blood flow to the brain. HIE is divided into three distinct stages according to the presentation of the affected neonate. HIE stage I is a mild form which exhibits only history of delayed crying with notably no significant bad prognostic sign. HIE stage II is a more complicated stage where convulsion is an inevitable feature. Stage III is more advanced stage with lethal involvement in nervous system and other various organs causing multifactorial effect.[8]

In our study the incidence rate of birth asphyxia was predominant in male neonates constituting 56.5% in comparison to female neonates which is similar but other studies registered more male predominance like 70%- 74%.[9,10] This may be due to transitory cerebral anoxia and decline in neurons related to respiratory control. This further reduces the emergency or auto resuscitation in male babies. Thus they become more prone to develop perinatal asphyxia and furthermore consequences of the fatal process. On contrary females exhibit greater resistance to hypoxia compared to males due to the existence of an extra X chromosome which allows them to tolerate more lower level of oxygen with less cerebral anoxia and qualitative functional derrangement in affected neuron.[11]

We have also observed predominance of birth asphyxia in vaginal delivery 64% in frequency which is similar to the findings of other studies notably 54% by Singh et al and a bit high like 71% by Onyiriuka. This probably due to the prolonged labour or obstructed labour terminating into NVD, less fetal monitoring during NVD, NVD done in home with low skilfull or traditional non medical person.[12,13]

In the present study, majority of the neonates were in HIE stage II (58.5%) compared to stage I (19.8%) and stage III (21.7%) which is identical to a study conducted by Acharya et al where 57.33% of infants were in the stage II. Most of the HIE I neonate is treated in home. When convulsion occurs along with other features of stage II they are admitted to SCANU. With proper support very few neonate advance to stage III. This is why Stage II is the predominant stage in our result.[14]

In this research, the serum calcium was compared among the different stage of HIE. The neonates in HIE stage III had significantly lower calcium level compared to HIE stage II (5.1±1.66 vs 6.1±1.1.54). Subsequently HIE stage II had lower calcium level than stage I(6.1±1.1.54 vs 7.2±1.35). Other studies have also documented similar comparison of serum calcium level in different stages of HIE. Those studies have listed few of their observation regarding this. Most of the HIE -III neonates suffer multiorgan dysfunction including parathyroid dysfunction, poor absorption of calcium from intestine as well as reabsorption from renal tubule.[15]

Conclusion:

Serum calcium level tends to decrease in asphyxiated neonate which is most subjacent in HIE stage III.

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