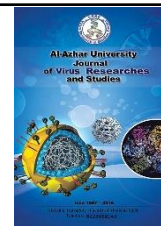




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### Serum Electrolytes and Glucose Levels in Neonates with Perinatal Asphyxia

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#### Abstract

Hypoxia, hypercarbia, and acidosis during perinatal period is called perinatal asphyxia which cause hypoxic-ischemic damage of tissues and electrolytes disturbances which may be the cause of perinatal morbidity and mortality. The aim of this study was to determine the serum electrolytes (Na, K, Ca, Mg) and plasma glucose levels in neonates with perinatal asphyxia and to determine their correlation with birth asphyxia severity. 100 neonates were divided into two groups (50 cases and 50 controls) based on the Apgar score after baby delivery. The cord blood serum sodium, potassium, calcium, and glucose levels were estimated in both two groups by independent t-test and Mann–Whitney U test using R software version 3.6.0. The serum electrolyte levels were correlated with hypoxic-ischemic encephalopathy stages. Using Spearman correlation. A statistically significant difference was found between the two groups in serum sodium, calcium, potassium and glucose levels ( $P < 0.05$ ). A significant negative linear correlation was found between serum sodium, calcium, and glucose levels and hypoxic-ischemic encephalopathy stages. A significant positive linear correlation was found between serum potassium level and hypoxic-ischemic encephalopathy stages. Hyponatremia, hypocalcemia, and hypoglycemia were detected in asphyxiated neonates and were correlated with severity of asphyxia. So, cord blood serum electrolytes and glucose estimation at high-risk neonates would be used for perinatal asphyxia early diagnosis and severity assessment.

**Keywords:** Asphyxia, respiratory distress, Apgar score, hypoxic-ischemic encephalopathy.

#### 1. Introduction

Perinatal asphyxia is the most common cause of early neonatal mortality. Perinatal asphyxia is the “failure to initiate and sustain breathing” according to the World Health Organization. Each year birth asphyxia is diagnosed in four to nine million neonates [1]. The factors which define birth asphyxia outcome are time taken for the first breath, heart rate at 90 s, duration of resuscitation, and Apgar score at 5 min of life [2]. Either neonatal death or

hypoxic-ischemic encephalopathy (HIE) are the early outcome of birth asphyxia. The severity of birth asphyxia is reflected by the degree of HIE. The asphyxia severity assessment is aided by HIE staging (by Sarnat and Sarnat) [3]. Adequate oxygen supply is essential for metabolism at cellular level. Cerebral oxidative metabolism may be impaired by hypoxia causing acid-base disturbances “metabolic acidosis” [4-6]. Decreased cardiac output,

cerebral blood flow, and hypoxic ischemic insult caused by prolonged hypoxia. Most of these insults happened during the periods of antepartum and intrapartum in term babies. Asphyxia cause dilutional hyponatremia due to antidiuretic hormone hypersecretion which increase water retention [7]. Hyponatremia in hypoxic neonates also caused by decreased capacity of sodium reabsorption [8] and partial aldosterone resistance [9]. hyperkalemia in early neonatal period is due to shift of potassium from the intracellular to extracellular space and more premature babies are more likely to have hyperkalemia. Asphyxia causes acute renal failure which may lead to hyperkalemia by decreasing potassium excretion [10]. Cord plasma total calcium concentration is directly proportional to gestational age normally [11]. At the time of delivery, there is increased serum parathyroid hormone (PTH) increased secretion of serum parathyroid hormone (PTH) due to sudden termination of calcium transport across the placenta. Birth asphyxia decreased PTH secretion due to postnatal fall in plasma calcium levels leading to hypocalcemia [12]. Low glucose levels may cause encephalopathy which leads to long-term neurological illness. In birth asphyxia, there is hypoglycemia due to severe glycogen depletion secondary to catecholamine release and idiopathic hyperinsulinemia [13]. Hypoxia and hypoglycemia caused profound brain damage and the early diagnosis is a challenging issue in neonates. The degree of electrolyte imbalance is defined by the severity of birth asphyxia [14]. Physiological association between electrolyte imbalance and hypoxic tissue damage are reported by several studies at 24 h of life or later [13]. Cord blood (immediately after birth) electrolytes and glucose are reported in few studies [15]. There are lacking of Case-control studies to correlate electrolyte and glucose levels with birth asphyxia severity. So, we do this case-control study to correlate cord blood electrolyte and glucose levels with

asphyxia severity. Aims of the work is to study electrolyte (sodium, potassium, calcium) and glucose disturbances in asphyxiated newborns and to correlate sodium, potassium, calcium and glucose levels with perinatal asphyxia in different severity.

## 2. Patients and Methods

This prospective study was conducted for one year ranging from December 2019 to December 2020 in NICU El Galaa Teaching Hospital, Egypt, in asphyxiated newborns born at this institute and a total of 100 cases were enrolled in the study. Case (group A) and control (group B) groups asphyxiated, and non-asphyxiated neonates were included each with 50 neonates based on inclusion and exclusion criteria.

### 2.1 Inclusion criteria:

Term newborns born and admitted at El-Galaa Teaching Hospital NICU with Birth asphyxia as WHO definition- "failure to initiate and sustain breathing at birth" and an Apgar score of < 7 at 5 min of life even after receiving resuscitation according to Neonatal Resuscitation Program (NRP) guidelines.

### 2.2 Exclusion criteria:

Preterm, suspected metabolic diseases, cases receiving medications except vitamin K prior to collection of blood samples, intrauterine growth retardation, congenital malformations, mothers on antiepileptic, those born to mothers with diabetes mellitus, mothers with suspected or confirmed electrolyte abnormalities, those born to mothers treated with diuretics, general anesthesia, phenobarbitone, pethidine, magnesium sulphate, antihypertensive and parents not giving consent were also excluded from the study.

### 2.3 Collection and blood sample:

The umbilical cord blood samples after birth were collected in both groups, and clinically and neurologically all neonates were evaluated. At NICU, the asphyxiated neonates in early neonatal period were monitored for HIE by Sarnat and Sarnat staging which assess the severity of neonatal encephalopathy into mild, moderate, and severe.<sup>3</sup> Other systemic effects of asphyxia were monitored in the asphyxiated neonates. The cord blood samples were sent for serum electrolytes (sodium, potassium, and total calcium), glucose, complete blood count, septic screen total leukocyte count, absolute neutrophil count, band cell ratio, C-reactive protein, and creatinine. Serum glucose and electrolytes were analyzed by A25 autoanalyzer and electronic Na-K analyzer (by Abbott Healthcare Pvt. Ltd., Mumbai), respectively.

### 2.4 Statistical analysis:

Statistical analysis was done using R version 3.6.0 software (Revolution Analytics, Mountain View, CA, United States). Normality of the data was determined using the Shapiro–Wilk test. The continuous and categorical variables are presented in mean  $\pm$  standard deviation and frequency tables, respectively. A comparison between cases and controls was done using independent t-test and Mann–Whitney U-test. The correlation between ordinal and continuous data was determined using Spearman correlation.  $P < 0.05$  was considered statistically significant at 95% confidence interval.

### 2.5 Ethical consideration:

We have obtained all appropriate written informed consent forms from all parents. In the form, the parents have given their consent for their children's clinical information to be reported in the journal. The patients understand that their children's names and initials will not be

published, and due efforts will be made to conceal their identity.

### 3. Results

Table (1) shows the population characteristics of the two groups of babies: those born hypoxic ischemic encephalopathy (group A) and normal babies (Group B). There is highly statistically significant increase in RR in group A ( $57.8 \pm 10.9$ ) than group B ( $40 \pm 6$ ). Comparing Apgar score at 1, 5, and 10 minutes of the cases and control groups shows highly statistically significant decrease in group A than group B for each Apgar score. Table (2) shows highly statistically significant decrease in Na, Ca and glucose and increase K levels in group A than group B. Table (3) shows highly statistically significant difference in serum Na and Ca, K and glucose between subgroup A (A1, A2 & A3) but there is no statistically significant difference in serum Mg. Table (4) shows very high significant difference between subgroups regarding the incidence of death.

### 4. Discussion

Perinatal asphyxia leads to tissue damage, especially brain tissue and also causes electrolyte imbalance. Abnormal biochemical parameters with perinatal asphyxiated neonates can worsen their morbidity or increase their mortality [13]. The serum electrolyte and glucose levels determine severity of perinatal asphyxia [13]. This study showed that males were more prone to perinatal asphyxia, and these results were similar to Yadav et al. study (72% vs. 54.4%) [14]. In our study perinatal asphyxia incidence was higher in normal delivered neonates (70%) than cesarean section (30%) and these results were similar to findings observed in a study by Onyiriuka (71% vs. 29%) [15]. In our study, comparing Apgar score at 1, 5, and 10 minutes of the cases and control groups shows highly statistically significant ( $P <$

0.001) decrease in group A than group B for each Apgar score and these results were similar to study by Meena et al. Apgar

score is essential diagnostic tool for birth asphyxia [16].

**Table (1):** Clinical characteristics of studied neonate group A (case group) & B (control group).

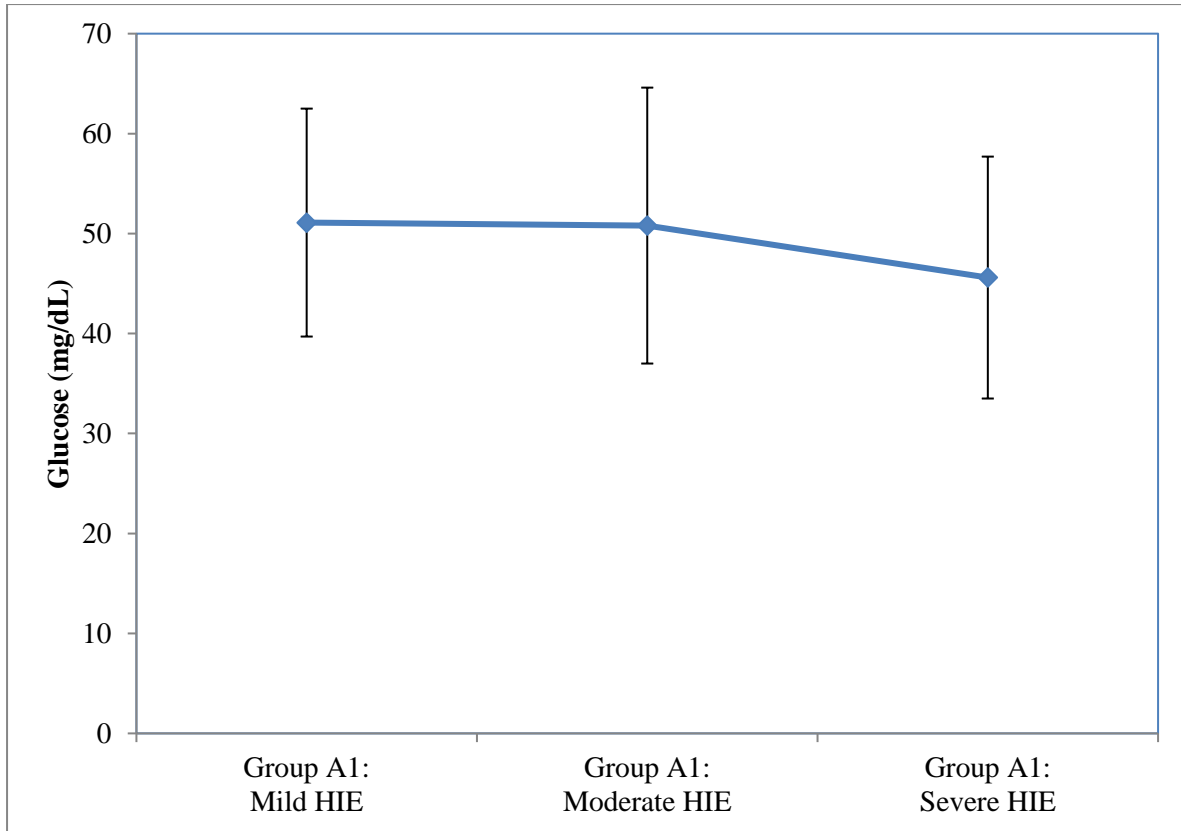
Clinical characteristics	Group A No = 50 (Mean ± SD)	Group B No=50 (Mean ± SD)	P-value
Gestational age (wks)	39 ± 3.2	38.7± 2.9	t = 0.35 P > 0.05
Sex (Male %) (Female%)	35(70%) 15 (30%)	35 (70%) 15 (30%)	NA
HR (min)	129.8 ± 12.9	134.9 ± 6.6	t=1.8 P>0.05
RR (min)	57.8 ± 10.9	40 ± 6	< 0.05*
Temp. °C	35.9±0.7	36.7±0.4	t=0.47 P>0.05
Apgar 1min.	3.6±2.3	6.4±1.9	< 0.05*
Apgar5min.	5.3±1.8	8.2±0.8	< 0.05*
Apgar10min.	6.4±1.6	9.2±0.5	< 0.05*
NVD	13 (26.0%)	12 (24%)	> 0.05
CS	17 (34%)	18 (36%)	
Forceps	3 (6.0%)	3(6%)	
Ventose	17 (34%)	17 (34%)	

**Table (2):** Electrolytes and glucose for studied group A & B.

Electrolytes	Group A No = 30 (Mean ± SD)	Group B No=20 (Mean ± SD)	P-value
K+ (mEq/dL)	5.3 ± 1.8	4.0±0.9	P< 0.05
Na+ (mEq/dL)	130.4 ± 8.7	142.2±4.4	P<0.001
Ca++ (mg/d)	8.4 ± 1.5	9.5± 1.6	P<0.001
Mg++ (mg/dL)	1.9 ± 0.2	1.9± 0.2	P > 0.05
Glucose (mg/dL)	44.8±11.9	56.9 ±13	P<0.001

**Table (3):** Electrolytes for subgroup A (A1, A2 &A3).

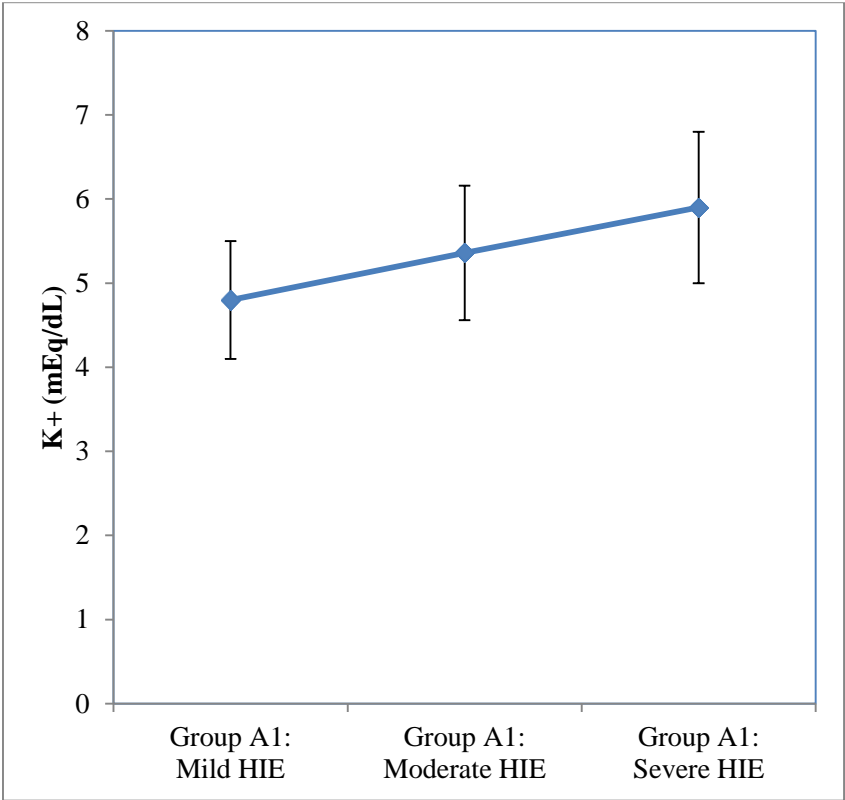
Electrolytes	Group A1 No = 15 Mean ± SD	Group A2 No=15 Mean ± SD	Group A3 No = 20 Mean ± SD	Correlation coefficient	P-value
K+ (mEq/dL)	4.8± 0.7	5.36± 0.8	5.9± 0.9	0.351r	P < 0.05
Na+ (mEq/dL)	132.2±3.4	129± 4.8	126.9±6.9	-0.582r	P < 0.001
Ca++ (mg/dL)	9 ±1.5	8.1± 1.1	8.0± 0.6	-0.557r	P < 0.001
Mg++ (mg/dL)	1.9± 0.2	2 ±0.2	1.8± 0.2	0.060r	P > 0.05
Glucose (mg/dL)	51.1 ± 11.4	50.8 ± 13.8	45.6± 12.1	-0.582r	P <0.01



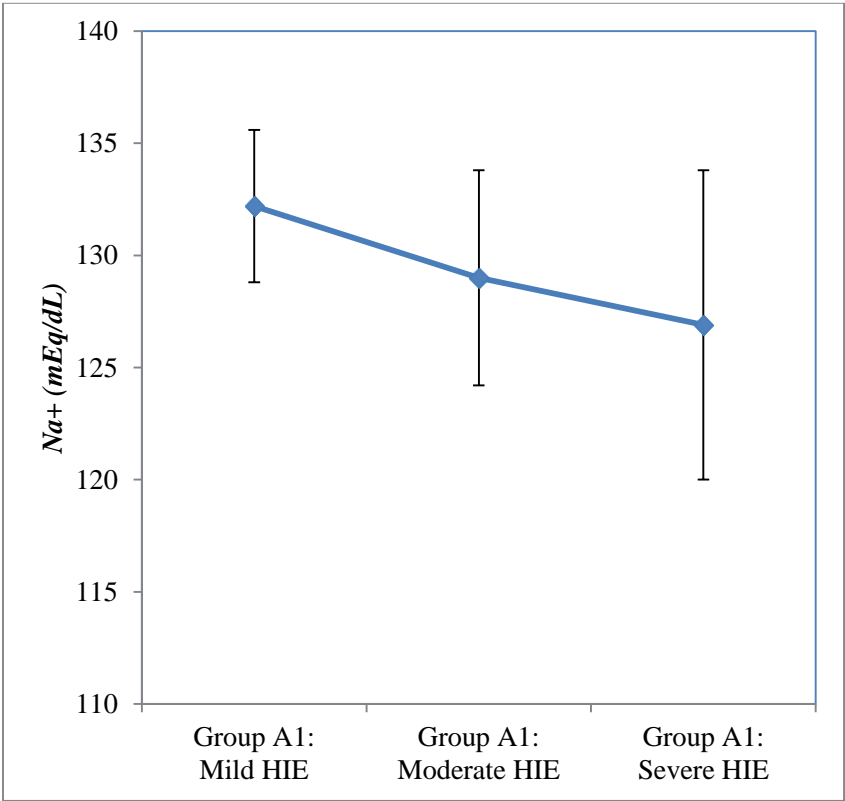
**Figure (1):** Comparison between the studied groups as regard TNM stage.

**Table (4):** Mortality in subgroups (A1 & A2& A3).

Mortality	Group A1 No = 15	Group A2 No=15	Group A3 No = 20	P-value
Survival	8 (80%)	7 (70%)	0	* P =0.001
Mortality	2 (20%)	3 (30%)	10 (100%)	



r=0.351



r=0.582

Increased or decreased blood electrolytes levels in asphyxiated neonates were present in our study with higher incidence in the asphyxiated neonates than the non – asphyxiated control group. Estimation of all serum electrolytes in asphyxiated neonates in comparison to the non-asphyxiated neonates in studies in Nigeria are rare [19]. Most of the previous studies [20], estimated only one to three electrolytes serum levels, so comparison of the multi-electrolyte based our study with the previous studies would be difficult. In our study, the mean sodium levels were significantly lower in cases compared to controls similar results as regards serum sodium level reported by Basu et al. and Vandana et al [21]. In the present study, the serum potassium level was significantly higher in cases compared to controls and there was a significant positive linear correlation with HIE grades. Similar results as regards serum potassium level reported by Kavya et al [22] who reported the serum potassium and serum creatinine levels were higher in asphyxiated neonates and were correlating with the severity of asphyxia. In this study, the mean Calcium level was significantly lower in cases compared to controls, similar results reported by Rai et al., [23] Schedewie et al., [24] and Jajoo et al. [25]. In our study, the decrease in serum sodium and calcium levels in cases showed significant negative correlation with degree of HIE severity and was similar to significant negative correlation observed by Basu et al [26] study. In the present study, plasma glucose levels in cases are lower than controls, which is similar to Lakra et al. study [27]. Our study showed a significant negative correlation between severity of HIE and hypoglycemia similar to Abdul Hakim et al.study [28]. In our study and in the literature, cord blood serum levels of sodium, potassium, calcium and glucose were the best indicators to assess (HIE) asphyxia severity [29].

## 5. Conclusion

Asphyxiated neonates showed Significant hyponatremia, hyperkalemia, hypocalcemia, and hypoglycemia. There were negative linear correlations between cord blood levels of Na, Ca, glucose and HIE grades. Also, there was positive linear correlations between cord blood levels of K and HIE grades. In our study and in the literature, cord blood serum levels of sodium, potassium, calcium and glucose were the best indicators to assess (HIE) asphyxia severity.

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