




Estimation of Sodium, Potassium, and Calcium Serum in Patients with Asphyxiated Neonates

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Abstract

Background: Birth asphyxia is a critical neonatal condition characterized by the failure to initiate and sustain breathing at birth, often due to impaired cerebral blood flow. Electrolyte imbalances may contribute significantly to its morbidity and mortality.

Objectives: To assess the serum sodium, potassium, and calcium levels in neonates with birth asphyxia of varying severities and healthy controls.

Patients and Methods: A hospital-based cross-sectional study was conducted at Al-Batool Teaching Hospital in Diyala, Iraq, from June to September 2023. A total of 200 term neonates were enrolled, 80 with birth asphyxia (defined by an Apgar score <7 at 5 minutes) and 120 healthy neonates as controls. Blood samples were collected within the first 24 hours of life, and serum levels of sodium, potassium, and calcium were measured using standard photometric methods.

Results: Hyponatremia (<130 mmol/L) was observed in 51.3% of asphyxiated neonates. Hyperkalemia (>5.2 mmol/L) was found in 50% and hypocalcemia (<2.2 mmol/L) in 55% of cases. Compared to controls, asphyxiated neonates had significantly higher potassium levels ($p < 0.05$) and lower calcium levels ($p < 0.05$); however, differences in sodium levels were not statistically significant ($p > 0.05$). Electrolyte abnormalities were more pronounced in neonates with altered tone, sucking, respiration, and heart rate.

Conclusion: Hyponatremia, hyperkalemia, and hypocalcemia are prevalent in neonates with birth asphyxia and correlate with clinical severity. Early identification and management of these disturbances are vital to improving outcomes and reducing neonatal morbidity and mortality.

Keywords: Birth asphyxia, Neonate, Hyponatremia, Hyperkalemia, Hypocalcemia.

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Introduction

Asphyxia in a neonate is defined as failure to regulate breathing at birth. Many conditions can affect an asphyxiated baby's birth, but the underlying etiology is decreased blood flow to the brain (1). Birth asphyxia (BA) can cause a series of reactions resulting in changes in brain function known as hypoxic-ischemic encephalopathy. The likelihood of outcomes for surviving birth asphyxia varies widely, from normal outcomes to death, with a variety of disabilities in between, including long-term neurodevelopmental disabilities, cerebral palsy, neuromotor delays, and developmental delays. Treatment of hypoxic-ischemic encephalopathy centres on dampening or blocking biochemical pathways that cause nerve cell death (2,3). The brain has limited sources of stored energy and relies on adequate blood flow to extract the needed energy supplies for neuronal cells. With reduced blood flow, neuronal cells cannot extract enough glucose to convert to energy-storing adenosine triphosphate (ATP). This decrease in ATP stimulates a cascade of biochemical reactions that lead to

early neuronal cell death via ischemia and necrosis (primary energy failure) or cell death via apoptosis (secondary energy failure). These reactions involve the destruction of cell membrane potentials as ATP levels decrease. Consequently, the control of ion movement across the cell membrane is impaired (4). Accumulations of intracellular calcium, sodium, chloride, and water reach toxic levels, and the level of the excitatory neurotransmitters is elevated at the synaptic junction. In a biological system, sodium, potassium, and calcium are the most important electrolytes, and any significant fluctuations in the blood concentrations can lead to metabolic derangements, causing convulsions and shock (5). Tight regulation and maintenance of normal blood concentrations of these electrolytes are essential for optimal functioning of the body. Assessment and management of electrolyte status in the newborn is a very crucial and challenging task. Water and electrolyte levels in the body can vary widely during the transition from fetal to newborn life. Before birth, the fetus receives the nutrients, including fluid and electrolytes, from the maternal blood, and their levels are predominantly controlled by the maternal regulatory system (4,5). The three main electrolytes in the human body are sodium, potassium, and calcium. Any change in these minerals' typical blood levels can result in convulsions, shock, and other metabolic disorders. Calcium is a crucial second messenger in the body that also aids in muscular contraction and serves as a cofactor for a number of enzyme processes (6). In addition, transitory alterations in the fluid and electrolyte levels can be expected, and even a minor change in the absolute concentrations of these electrolytes can suggest proportionately substantial variation for the newborn considering its relatively small size (7). Therefore, this study aimed to determine the serum sodium, potassium, and calcium levels in neonates with birth asphyxia.

Patients and Methods

Study design and sample collection: This was a hospital-based cross-sectional study conducted from the first of June to the 30th of September 2023, in the department of Pediatrics at Al-batool Teaching Hospital (neonatal Care unite and operating room) serum sodium (Na) and potassium (K) were measured in 80 term asphyxiated newborn (low Apgar score at 5 minute) and 120 healthy Newborn babies immediately after birth. A detailed antenatal and postnatal history was taken, and the findings were recorded using a well-prepared questionnaire. Electrolyte estimation (serum sodium, potassium, and calcium) was analyzed using a selective electrode by an automated machine. The cases were collected according to early signs of birth asphyxia (Tone, LOC, Moro Reflex, Sucking Reflex, HR, and RR) and applying inclusion and exclusion criteria.

Inclusion criteria: (neonate born admitted with appropriate gestational age and birth weight of 2.5-4 kg) who has birth asphyxia according to WHO, defined as failure to initiate and sustain breathing at birth, and also based on an APGAR score of less than 7 at 5 minutes of life, even after resuscitation according to NRP guidelines.

Exclusion criteria: Individuals with intrauterine growth restriction (IUGR) and those with gross congenital malformations were excluded from the study.

Determination of sodium: Sodium is estimated by the colorimetric method based on the modified Maruna and Trinder method. Sodium and proteins are precipitated together by magnesium uranyl acetate as uranyl magnesium sodium acetate salt. The intensity of the colour is measured photometrically at 530 nm (500-546 nm). Precipitation shake vigorously and incubate at room temperature for 5 min, then centrifuge at 2000-3000 rpm for 2 min to obtain a clear supernatant, and then transfer the supernatant immediately after centrifugation for standard and test. Sodium

RI which is consist of precipitating REA standard (1 ml) and test (1 ml) while from the sodium standard, it used 10 ml of standard and 10 ml from the serum of the test. Sodium estimation was done by sodium RI precipitating in blank (1 ml) and in standard (1 ml) and test (1 ml), sodium standard in blank and standard (20 ml) and in test (20 ml) and in serum (20 ml), then they mixed well and allow to stand at room temperature for 5 min, then it was measured the absorbance of standard and sample against reagent blank calculation; sodium concentration (mmol)= Abs of test – Abs of blank/ Abs of standard – Abs of blank*standard concentration (8).

Determination of potassium: Potassium is estimated using the turbidimetric method (9). The extent of turbidity is proportional to the potassium concentration. It is measured photometrically at 578 nm (570-620 nm). Potassium RI (precipitate Rea) standard (1000 ml) and test (1000 ml) and standard (10 ml) and in sample and 25 ml in test, mixed well and allow it to stand at room temperature for 5 min and measure the absorbance of standard and sample against distal water within 10 min, calculation; potassium concentration (mmol) =Abs of sample \Abs of standard *5.

Determination of calcium: Calcium OCPC procedure is based on the reaction of calcium ions (Ca+) with O-cresolphthalein complex in an alkaline solution to form an intense viol coloured

complex which shows maximum absorbance at 578 nm. Reagent in blank (1000 µL), standard (1000 µL), and in test (1000 µL), and ca standard in blank and 10 mL in standard and test and sample in blank and in standard and 10 mL in test. The calculation for Calcium concentration (mmol) = Abs of sample/ Abs of standard *10 (10).

Statistical analysis

The statistical analysis was performed using XLSTAT version 2019. Student's t-test determined the normality of distribution.

Results

Percentage of electrolyte concentrations in asphyxiated neonates: Patients divided into subgroups according to: gender, Tone, LOC, Moro Reflex, Sucking, Respiration and Heart Rate.

The baseline characteristics of the cases showed that: 51.3% had sodium concentration <130mmol, 31.3% had sodium concentration 130_146, and 17.4% had > 146, 7.5%had potassium concentration <3.5mmol, 41.3% had potassium concentration 3.3-5.5mmol, 50% had potassium concentration > 5.2, 55% had a calcium concentration <2.2 mmol, and 45% had a calcium concentration of 2.2-2.7 (Table 1).

Table 1. Percentage of electrolyte concentrations in asphyxiated newborns.

Parameter	Conc.	n	%
Sodium mmol/L	<130	41	51.3
	130-146	25	31.3
	> 146	14	17.4
Potassium mmol/L	<3.3	7	7.5
	3.3-5.2	33	41.3
	>5.2	40	50.0
Calcium mmol/L	<2.2	44	55.0
	2.2-2.7	36	45.0

Total electrolyte concentrations in the studied groups: The mean (\pm SD) of total electrolyte concentrations in the serum of the control group (healthy individuals) and the patients is illustrated in Table 2.

Table 2. Total electrolytes concentrations in studied groups, which demonstrated as mean \pm SD.

Groups	Sodium mmol/L	Potassium mmol/L	Calcium mmol/L
Total Patients n=80	131.26 \pm 11.12	3.24 \pm 0.38	8.19 \pm 0.80
Total Control n=120	132.2 \pm 10.18	2.70 \pm 0.40	8.75 \pm 0.75
P value	>0.05	<0.05	<0.05

Effect of gender on electrolytes concentrations: The mean (\pm SD) of electrolytes concentrations in the serum of patients and control groups according to gender are illustrated in Table 3.

Table 3. Mean \pm SD of electrolyte concentrations according to sex.

According to Sex					
Groups		%	Sodium mmol/L	Potassium mmol/L	Calcium mmol/L
Patients n=80	Male n=50	(62.5%)	11.79 \pm 8.9	2.77 \pm 0.36	8.41 \pm 0.74
	Female n=30	(37.5%)	128.3 \pm 10.9	2.68 \pm 0.41	8.96 \pm 0.64
control n=120	Male n=78	(65%)	130.0 \pm 11.2	3.60 \pm 0.39	8.19 \pm 0.73
	Female n=42	(35%)	133.9 \pm 9.89	2.80 \pm 0.37	0.803 \pm 0.79
P value					
Parameters	Male/Female Control	Male/Female Patients	Male Control / MalePatients	Female Control / FemalePatients	
Sodium	>0.05	>0.05	>0.05	>0.05	
Potassium	>0.05	<0.05	>0.05	>0.05	
Calcium	>0.05	>0.05	>0.05	>0.05	

Electrolytes concentrations according to Tone and LOC: The study included mean (\pm SD) of electrolytes concentrations in serum of patients groups according to early clinical sign. The mean (\pm SD) of electrolytes concentrations in serum of patients groups according to Tone and LOC signs are illustrated in Table (4).

Table 4. Mean \pm SD of electrolytes concentrations according to Tone and LOC signs.

Study	Groups	Sodium mmol/L	Potassium mmol/L	Calcium mmol/L
Tone n=80	Flaccid (n=20) (25%)	129.7 \pm 10.73	3.17 \pm 0.46	8.07 \pm 0.65
	Hypotonic (n=60) (75%)	133.2 \pm 14.25	3.30 \pm 0.31	8.12 \pm 0.84

P value		>0.05	>0.05	>0.05
LOC n=80	Alert or irritable n=15 (18.75%)	134.52±10.7	3.31±0.33	7.90±0.82
	Comatose (n=20) (25%)	131.33±7.51	3.23±0.32	8.12±0.66
	Lethargy (n=45) (56.25%)	132.81±13.5	3.30±0.31	8.38±0.89
P value	Parameters	Alert or irritable/Letha rgy	Comatose/ Lethargy	Alert or irritable/Coma tose
	Sodium	>0.05	>0.05	>0.05
	Potassium	>0.05	>0.05	>0.05
	Calcium	<0.05	>0.05	>0.05

Electrolytes concentrations according to Moro reflex and sucking signs: The study included mean (±SD) of electrolytes

concentrations in serum of patients groups according to Moro reflex and sucking signs are illustrated in Table 5.

Table 5. Mean ±SD of electrolytes concentrations according to Moro reflex and sucking signs.

Study	Groups	Sodium mmol/L	Potassium mmol/L	Calcium mmol/L
Moro Reflex n=80	Absent (n=15) (18.75%)	133.5±7.70	3.19±0.31	8.12±0.75
	Weak (n=65) (81.25%)	131.65±11.32	3.23±0.35	0.90
	P value	>0.05	>0.05	>0.05
Sucking n=80	Absent (n=21) (26.25%)	128.5±11.18	5.8±0.33	8.10±0.78
	Unable to suck (n=30) (27.5%)	131.0±6.19	3.11±0.39	8.14±0.72
	Weak (n=29) (36.25%)	138.5±13.18	3.31±0.38	8.21±0.73
	Parameters	Absent/ Unable to suck	Absent/ Weak	Unable to suck/ weak
P value	Sodium	>0.05	>0.05	>0.05
	Potassium	>0.05	<0.05	>0.05
	Calcium	>0.05	>0.05	>0.05

Electrolyte concentrations according to respiration and heart rate: The study included the

mean (±SD) of electrolyte concentrations in the serum of patient groups according to respiration and heart rate signs, which were illustrated in Table 6.

Table 6. Mean ±SD of electrolytes concentrations according to respiration and heart rate signs.

Study	Groups	Sodium mmol/L	Potassium mmol/L	Calcium mmol/L
Respiration n=80	Apneic (n=37) (46.25%)	128.9±12.0	5.4±0.76	8.10±0.89
	Periodic (n=43) (53.75%)	134.2±14.45	3.55±0.78	8.21±1.33
P value		>0.05	>0.05	>0.05

Heart Rate n=80	Bradycardia and Tachycardia n=28 (35%)	129.1±11.23	5.6±0.44	8.09±0.64
	Normal n=52(65%)	134.7±13.48	3.6±0.41	8.21±0.86
P value		>0.05	<0.05	>0.05

Correlations study: Correlation Coefficient (r) is measure the association between two variables to same sample. The values of r above 0.38 have stronger correlation (Table 7).

Table 7. Correlation Coefficient between parameters.

Correlation coefficient (r)			
Groups	Parameters	Sodium mmol/L	Potassium mmol/L
Patients	Potassium	0.20	-
	Calcium	0.313	0.485
Control	Potassium	0.023	-
	Calcium	0.234	0.342
Male Control	Potassium	-0.004	-
	Calcium	0.21	0.35
Female Control	Potassium	0.086	-
	Calcium	0.26	0.32
Male Patients	Potassium	0.17	-
	Calcium	0.34	0.48
Female Patients	Potassium	0.31	-
	Calcium	0.29	0.49

Discussion

There was no significant difference in the serum sodium levels between the control and patient groups. At the same time, there was a substantial increase in the serum levels of potassium, and a significant decrease in the serum levels of calcium in the patient groups when compared with the control group. These results are different from other study that found, hyponatremia in 34% of neonates, hypernatremia in 0% of asphyxiated neonates, hyperkalaemia in 0% and found hypocalcaemia observed in 4 (8%) asphyxiated neonates, compared to 2 (4%) cases in comparison group, which is statistically not significant, but proportionally, it is comparable to other studies in this issue in

newborns (11). It was shown that specific symptoms of electrolyte abnormalities commonly coexist with indicators of underlying hypoxic ischemic encephalopathy, or HIE, and the use of fluid and electrolytes in such cases increases morbidity and death. The results disagreed with those of Lackmann et al. (12), who measured potassium levels in 98 asphyxiated newborns, and none of them showed significant hyperkalaemia in the initial 144 h of life. Basu et al. (13) concluded that decreased calcium levels are associated with increased severity of birth asphyxia. In case-control study by Jajoo et al. (14), and Rai et al. (15) they established lower serum calcium level in asphyxiated newborns compared to their controls, and in disagreement with a case control study by Varma V et al. (16) among asphyxiated newborns, mean values of electrolytes

showed no significant difference among cases and controls. Hyperkalaemia can be explained by the fact that asphyxia is associated with acidosis, and in metabolic acidosis, more than half of the excess hydrogen ions are buffered in the cells. In this setting, electro-neutrality is maintained partially by the movement of intracellular potassium into the extracellular fluid. It can also be due to acute renal failure secondary to birth asphyxia, which leads to reduced excretion of potassium and hence hyperkalaemia (17). The modification of potassium from the intracellular to extracellular space in early neonatal period may lead to hyperkalaemia and depends on the degree of immaturity; further premature babies are more possibly to have hyperkalaemia. Acute renal failure secondary to asphyxia causes hyperkalaemia by declining the elimination of potassium (18). Normally, gestational age is directly proportional to cord plasma total calcium concentration. At the time of delivery, unexpected cessation of calcium transport through the placenta decreases the serum calcium levels, which in turn leads to augmented secretion of serum parathyroid hormone [PTH] (19).

In this study, it was shown that there were no significant differences in the serum level of sodium in age groups, except a significant decrease in the serum levels of potassium in female patients group compared with male patients group. In addition, in the current study it was illustrated that among enrolled patients, males predominated (65%) while female (35%). These results were agreement with the other studies by Ahmed N et al (20), who reported that the percentage of males was 64%, and Bahatkar and Aundhakar were found 72% of patients were males (21). Furthermore, many studies were agreed with our study that showed predominated male

(54.3%) (13, 22). The difference in the percentage between male and female could be due to differences in time, area of the study, and registration of neonatal data. In addition, other reason for male babies being more affected is due to the death of respiratory control neurons in brainstem which mediates the function of emergency resuscitation in male gender (20).

Conclusions

According to the results of study was conducted that included hyponatremia, hypocalcaemia and hyperkalaemia occur in neonates with birth asphyxia which may cause increased morbidity and mortality, and its percentage in male more than in female. In addition, serum sodium levels in the asphyxiated newborns were in the hyponatremic range and in proportion to the severity of asphyxia. As serum sodium levels are low in birth asphyxia, fluids must be managed judiciously in asphyxiated newborns. The study findings revealed that birth asphyxia was more common in irregular or no neonatal care cases. It was recommended to follow up on optimal electrolyte disturbances, which are essential to improve outcomes and prevent life-threatening events.

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Ethical clearance: Ethical approval for this study was obtained from the Research Ethical Committee of the College of Medicine/ University of Diyala (No:2023DTA798)

Conflict of interest: None.

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تقدير مصل الصوديوم والبوتاسيوم والكالسيوم لدى حديثي الولادة المختنقين

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الملخص

الخلفية: يعرف الاختناق عند الأطفال حديثي الولادة بأنه الفشل في تنظيم التنفس عند الولادة. يمكن أن تؤثر العديد من الحالات على ولادة طفل مختنق، ولكن المسببات الأساسية هي انخفاض تدفق الدم إلى الدماغ. يمكن أن يسبب الاختناق الولادي (BA) سلسلة من التفاعلات تؤدي إلى تغيرات في وظائف المخ المعروفة باسم اعتلال الدماغ بنقص الاوكسجين.

الأهداف: قياس مستوى الصوديوم والبوتاسيوم والكالسيوم في الدم عند حديثي الولادة المختنقين بدرجات مختلفة في فترة مابعد الولادة مع مجموعة المولودين حديثين الولادة.

المرضى والطرق: هذه الدراسة مقطعية وتم إجراؤها في مستشفى البتول التعليمي في محافظة ديالى من ١ يونيو إلى ٣٠ سبتمبر ٢٠٢٣. تؤخذ عينات من الدم من ٢٠٠ طفل حديثي الولادة في وحدة رعاية الأطفال حديثي الولادة وغرفة العمليات لقياس مستوى المصل بالكهرباء. تم تضمين مجموعه ٨٠ من حديثي الولادة المختنقين و ١٢٠ عينة من الأطفال حديثي الولادة الاصحاء، وتم سحب دم من الأوردة ٥ مل. من المريض في أنبوب هلام لاختبار الكيمياء الحيوية تتمثل النتائج التي تم قياسها بتأثير مجموعة من العوامل حسب الجنس، الموضع، منعكس مورو. المص، التنفس، معدل ضربات القلب.

النتائج: ظهرت الدراسة للحالات ١,٣٪ من الأشخاص المصابين بالمرض كان تركيز الصوديوم أقل من ١٣٠ أقل من ٣١,٣٪. كان تركيز الصوديوم ١٣٠-١٤٦ و ١٧,٤٪ كان < ١٤٦ بينما ٥٠٪ من حالات حديثي الولادة كان تركيز البوتاسيوم أقل من ٣,٥ ملم، ٤١,٣٪. كان تركيز البوتاسيوم ٣,٣-٥,٥ ملم و ٧,٥٪ مل مول و ٦ ملم ٥٥٪. من الحالات المختنقة كان تركيز الكالسيوم أقل من ٢,٢ مل مول، ٤٥٪ منها كان تركيز الكالسيوم فيها ٢,٢, ٢,٧.

الاستنتاج: نقص صوديوم الدم، نقص كالسيوم الدم وفرط بوتاسيوم الدم يحدث عند حديثي الولادة المصابين بالاختناق عند الولادة مما قد يسبب زيادة في معدلات المرضى والوفيات. كانت مستويات الصوديوم في الدم عند الأطفال حديثي الولادة المختنقين في نطاق نقص صوديوم الدم ومتناسبة مع شدة الاختناق. بما أن مستويات الصوديوم في الدم تكون منخفضة في حالة الاختناق الولادي، فيجب إدارة السوائل بحكمة عند الأطفال حديثي الولادة المختنقين. وكشفت نتائج الدراسة أن حالات الاختناق الولادي كانت أكثر شيوعاً في حالات رعاية الأطفال حديثي الولادة غير المنتظمة أو التي لم توجد على الإطلاق.

الكلمات المفتاحية: اختناق الولادة، حديثي الولادة، نقص صوديوم الدم، فرط بوتاسيوم الدم، نقص كالسيوم الدم.

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