

ORIGINAL RESEARCH

Study to evaluate serum Sodium level in relation with neonatal seizures

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ABSTRACT

Background: A seizure is defined clinically as a paroxysmal alteration in neurologic function, i.e. motor, behavior and/or autonomic function. It is critical to recognize neonatal seizures to determine their etiology, sometimes requiring specific therapy. Present study was aimed to evaluate serum sodium level in relation with neonatal seizures. **Material and Methods:** Present study was single-center, prospective, observational study, conducted in neonates with neonatal seizures occurring in the first 4 weeks of life in a full-term baby OR Newborn with history of birth asphyxia, hypoglycemia, hypocalcaemia, CNS infection and sepsis. Serum electrolytes were done on emergency basis, serum calcium, sodium, potassium and chloride were done. **Results:** Out of 645 newborns delivered, 100 neonates were taken for study who were admitted in NICU for seizure during study period. Incidence of neonatal seizures was 15.50 %. In our study, 47 were males and 53 were female babies with male to female ratio of 1:1.12. In our study onset of seizures on first day of life was seen 40 neonates (40%), on second day of life 30 neonates developed seizures (30%), on third day of life 14 (14%) babies developed convulsions. The first three days of life together constituted 87% of neonatal seizures. 44 neonates had subtle seizures, 29 neonates had generalized tonic seizures, 11 had multifocal clonic seizures and 8 had focal clonic seizures. Birth asphyxia was the commonest cause of neonatal seizures in our study (74%) followed by neonatal meningitis (8%), dehydration (17%) and hypocalcemia (1%). 70 had serum sodium level <130 meq/l (i.e. hyponatraemia), 2 of them had serum sodium >150meq/l (i.e. hypernatraemia) and 28 of them had serum sodium level within normal range (130-150 meq/l). **Conclusion:** 70 % had hyponatraemia & 2 % had hypernatraemia. Thus, hyponatraemia was significantly seen in cases of neonatal seizures.

Keywords: Birth asphyxia, neonatal seizures, hypocalcemia hyponatraemia, hypernatraemia.

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INTRODUCTION

A seizure is defined clinically as a paroxysmal alteration in neurologic function, i.e. motor, behavior and/or autonomic function. Seizures represent the most distinctive signal of neurological disease in the newborn period.^{1,2} The convulsive phenomenon are the most frequent of the overt manifestation of neonatal neurological disorders. Neonatal seizures are common and may be the first manifestations of neurological dysfunction after a variety of insults. Neonatal seizures are clinically significant because very few are idiopathic. It is critical to recognize neonatal seizures to determine their etiology, sometimes requiring specific therapy. Neonatal seizures may interfere with important supportive measures, such as alimentation and assisted respiration for associated disorders. Neonatal seizures present with varying manifestations like generalized tonic, multifocal clonic and subtle activity.^{3,4}

Therefore, it is important to recognize the seizures and treat it, as delay in recognition and treatment may lead to brain damage. The time of onset of seizure has relationship with the etiology and prognosis. For example, birth asphyxia usually presents in the first three days of life whereas meningitis presents after first week.^{5,6} If baby convulse within hours of delivery, it signifies poor prognosis and brain damage. Thus, study of etiology, onset and clinical manifestations of neonatal seizures has a significant role. Present study was aimed to evaluate serum sodium level in relation with neonatal seizures.

MATERIAL AND METHODS

Present study was single-center, prospective, observational study, conducted in NICU of C.U. Shah Medical College and Hospital, Surendranagar, India. Study duration was of 21 months (July 2015 to March

2017). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- Neonatal seizures occurring in the first 4 weeks of life in a full-term baby OR Newborn with history of birth asphyxia, hypoglycemia, hypocalcaemia, CNS infection and sepsis.
- Parents willing to participate in present study.

Exclusion criteria

- Newborn with hypomagnesaemia and prematurity.
- Newborn with intracranial haemorrhage.
- Newborn with Inborn Errors of Metabolism or family history of same.

Study was explained to parents in local language & written consent was taken for participation & study. Detailed antenatal, natal and post-natal history were taken in all cases. Age & parity of mother were noted. History of whether regular antenatal checkups were done or not was enquired. History of medical illness like diabetes, fever during first trimester or third trimester were asked. History of obstetric complications like PIH, eclampsia, antepartum hemorrhage, oligo or polyhydramnios were taken. History of PROM, prolonged second stage of labour, meconium staining of liquor, place of delivery, type of delivery and indication for forceps and caesarean section, were enquired. After delivery whether baby cried immediately or not, was it meconium stained and any resuscitation done, were enquired. If Apgar score was done, it was noted. The neonate was diagnosed with birth asphyxia if baby did not cry for more than three minutes after birth or documented Apgar score was ≤ 3 at one minute and < 7 at 5 minutes of birth. History of lethargy, poor feeding, jaundice, excessive cry, fever, vomiting and seizures were taken. The day of onset of seizures, type of seizures, the duration of seizures, number of seizures and consciousness during and between seizures were taken. After appropriate history, detailed examination of neonate was done. The vitals of the baby (Heart Rate, Respiratory Rate, Peripheral pulses, Blood pressure, temperature, Capillary filling time) were recorded. General physical examination of neonate was done according to the proforma and any disparity in head size and shape, skin lesions were noted. Anthropometry of the neonate was recorded & gestational age was assessed according to New Ballard scoring. CNS examination was done as per the proforma and HIE was staged according to modified Sarnat's staging in to stage I, II and III. Other systems were also examined.

The following investigations were done for neonatal seizures:

- Serum electrolytes: Serum electrolytes were done on emergency basis, serum calcium, sodium, potassium and chloride were done by semi auto analyzer (by Colorimetric method).

Hypocalcemia was diagnosed if serum calcium level was less than 8.0 mg/dL. Hyponatremia was diagnosed if serum sodium level is less than 130 mEq/L and hypernatremia if serum sodium is >150 mEq/L. The criteria for diagnosing various biochemical disorders were as follows: hypocalcemia (Ca <7.0 mg/dl), hyponatremia (Na <130 mEq/L), hypernatremia (Na >150 mEq/L), hypokalemia (K <3.5 mEq/L), and hyperkalemia (K >5.5 mEq/L).

- Complete blood count (hemoglobin, total count, differential count, platelet count).
- Sepsis screening: Peripheral smear for band cells and toxic granules, CRP and blood culture if necessary.
- Blood glucose: Random blood sugar was done urgently with glucostick and then confirmed by glucose oxidase method. Hypoglycemia was diagnosed if RBS is less than 40 mg / dL.
- CSF analysis: If septicemia or meningitis was suspected, LP was done and CSF analyzed for color, turbidity, protein, sugar, total and differential cell count and culture. Neonatal meningitis was diagnosed if CSF culture showed growth of organisms.
- Other metabolic screening like serum ammonia was done if particular metabolic disease was suspected.
- Chest X-ray: Chest x-ray was done to rule out meconium aspiration syndrome and respiratory distress syndrome.
- Ultrasound of cranium: done in all babies with neonatal seizures to rule out intracranial hemorrhage, hydrocephalus, congenital anomalies of brain and infarction.
- CT Scan of Head: CT scan of head was done as & when necessary.

All the patients were treated according to the diagnosis. Statistical analysis was done using descriptive statistics.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

RESULTS

Out of 645 newborns delivered, 100 neonates were taken for study who were admitted in NICU for seizure during study period. Incidence of neonatal seizures was 15.50 %. In our study, 47 were males and 53 were female babies with male to female ratio of 1:1.12. Majority of the neonates in the present study were born by spontaneous vaginal delivery (79 %), followed by caesarean section (19%), the indications were prolonged second stage of labor with

MSAF in 10 cases PIH in 3 cases. Forceps delivery were done in 1 case and the indication was prolonged second stage of labour in it and vacuum delivery was done in 1 case.

Table 1: General characteristics

	No. of patients	Percentage
Gender		
Male	47	47
Female	53	53
Type of deliveries		
Spontaneous vaginal delivery	79	79
Caesarean section	19	19
Outlet Forceps delivery	1	1
Vacuum delivered	1	1
Male		
Female		

In the present study 9 babies were born to mothers with PROM, 8 babies were born to mothers with PIH, 2 babies were born to mothers with APH and one mother had fever during last trimester. In our study 72 mothers had prolonged 2nd stage of labor (>2 hours), out of which 66 (91.7%) had birth asphyxia. 29 mothers had meconium stained amniotic fluid, out of which 28 (96.5%) had birth asphyxia. In our study onset of seizures on first day of life was seen 40 neonates (40%), on second day of life 30 neonates developed seizures (30%), on third day of life 14 (14%) babies developed convulsions. The first three days of life together constituted 87% of neonatal seizures.

Table 2: Day of onset of Neonatal Seizures:

Day of onset of Neonatal seizures	No. of cases	Percent
First	40	40
Second	30	30
Third	14	14
Fourth	3	3
Fifth	0	0
Sixth	2	2
Seventh	3	3
8-28 days	8	8

In our study out of 100 neonatal seizures, 92 neonates had one of the classically described neonatal seizures. Among these 44 neonates had subtle seizures, 29 neonates had generalized tonic seizures, 11 had multifocal clonic seizures and 8 had focal clonic seizures. 8 neonates had mixed type of seizures, among these 5 had subtle with generalized tonic seizures and 3 had subtle with clonic seizures.

Table 3: Etiology of Neonatal Seizures

Type of Neonatal seizures	No. of cases	Percent
Subtle	44	44
Generalized tonic	29	29
Multifocal clonic	11	11
Focal clonic	8	8
Subtle with GTS	5	5
Subtle with clonic	3	3

Birth asphyxia was the commonest cause of neonatal seizures in our study (74%) followed by neonatal meningitis (8%), dehydration (17%) and hypocalcemia (1%).

Table 4: Etiology

Etiology	No. of cases	Percent
Birth Asphyxia	74	74
Dehydration	17	17
Neonatal meningitis	8	8
Hypocalcaemia	1	1

Out of 100 patients having seizures, 70 of them had serum sodium level <130 meq/l (i.e. hyponatraemia), 2 of them had serum sodium >150meq/l (i.e. hypernatraemia) and 28 of them had serum sodium level within normal range (130-150 meq/l).

Table 5: Serum Sodium Levels in Neonatal Seizures

Serum Sodium level (in meq/l)	No. of patients
< 130	70
130-150	28
> 150	2

Out of 100 patients having seizures, 26 of them had serum potassium level < 3.5 meq/l (i.e. hypokalemia) was observed, 1 of them had serum potassium level >5.5meq/l (i.e. hyperkalemia). All neonates had serum chloride level within normal range (97 - 107 meq/l).

DISCUSSION

The National Neonatal Perinatal Database (NNPD; 2002-03), which collected data from 18 tertiary care units across the country, has reported an incidence of 10.3 per 1000 live-births.² The incidence was found to increase with decreasing gestation and birth weight - for example, preterm infants had almost twice the incidence when compared to term neonates (20.8 vs. 8.4 per 1000 live-births) while very low birth weight infants had more than 4-fold higher incidence (36.1 per 1000 live-births). Neonatal seizures have no sex predilection. However, in our study, 47 were males and 53 were female babies with male to female ratio of 1:1.12., similar with the study of neonatal seizures by Lakra Mahaveer *et al.*,⁷ where male to female ratio was 2:1. In our study majority of neonates with seizures were born by normal vaginal delivery (79%) followed by LSCS (19%) followed by vacuum delivery (1%) and outlet forceps delivery (1%). In a study of neonatal seizures by Lakhra Mahaveer *et al.*,⁸ 68.7% were born by normal vaginal delivery, 28.1% by LSCS and 3.1% by forceps delivery. In our study 84 out of 100 neonates with seizures had onset within first three days of life, among these 73% had onset of seizures within first 2 days life and 43% had onset of seizures within first day of life. 16 neonates (16%) had onset of seizures after 3 days of life, among these, 8 neonates had onset of seizures on between 8th and 28th day of life.

In a study of neonatal seizures by Ronen Gabriel *et al.*,⁹ onset of seizures on first day of life was 36%, 64% had onset of seizures within first 48 hours, and 83% within first week of life, which is similar to our study. Onset of seizures within first 3 days constitute the majority of cases, more so within first 48 hours of life. After 3 days there is a small second peak at the end of first week and early second week. In the present study 44 (44%) babies had subtle seizures either in the form of orobuccal movements, eye blinking, cycling movements of limbs or apnea associated with tachycardia (i.e., HR > 160/min) or hypertension. Generalized tonic seizures was observed in 29% i.e., 29 cases followed by multifocal clonic in 11 cases (11%), focal clonic seizures in 8 babies (8%) and 8 babies had mixed type of seizures. In a study of neonatal seizures by Brunquell Philip J *et al.*,¹⁰ subtle seizures were the commonest occurring in 51% (27 of 53), followed by focal clonic (42%), multifocal clonic (30%) and GTS (23%). Lakra Mahaveer *et al.*,⁷ also reported that subtle seizures were the commonest. But in a study of neonatal seizures by Soni Arun *et al.*,¹¹

generalized tonic seizure was commonest type of seizure, followed by subtle seizures. In contrary to older children and adults, neonates present with subtle and generalized tonic seizures more commonly because of immaturity of central nervous system and more mature limbic system compared to other parts of CNS in neonates. Subtle seizures are difficult to recognize and also difficult to interpret, as they may be normal neonatal activity and one should be careful in assigning subtle movements as seizures in neonates. Birth asphyxia is the most common cause of neonatal seizures in our study (74 of 100 cases – 74%) followed by dehydration in 17 babies (17%), 1 baby had hypocalcemia. Neonatal meningitis was seen in 8 babies (8%). Birth asphyxia is the commonest cause of neonatal seizures in studies by soni Arun *et al.*,¹¹ seen in 76.9% of cases and Ronen Gabriel *et al.*,⁹ seen in 40% of cases. Birth asphyxia is the most common cause for neonatal seizures (74%) in our study and also in majority of other studies. It can be associated with other metabolic disorders like hypoglycemia and hypocalcemia (1 case), as it is a risk factor for those metabolic abnormalities. Finer MM *et al.*,¹² showed that 48% of infants having seizures within 24 hours were significantly handicapped compared to 24% whose seizures began after 24 hours. Birth asphyxia is staged according to Sarnat HB.,¹³ as HIE-I, II and III and convulsions are common in HIE-II neonates. In our study 89% of birth asphyxia had HIE-II. In our study 44 babies (44%) with birth asphyxia had subtle seizures followed by generalized tonic seizures seen in 29 neonates (29%), focal convulsions are less likely because of diffuse cerebral involvement. The risk factors for birth asphyxia are preventable if identified early and proper resuscitation of baby after delivery could reduce the incidence of birth asphyxia significantly. Hyponatremia may result from SIADH following CNS infection and birth asphyxia. Other inborn errors of metabolism also present with seizures in the neonatal period usually in the first week of life and should be suspected when all other etiologies are ruled out or if there is a family history.

In present study, 70 % had hyponatraemia & 2 % had hypernatraemia. Hyponatremia is a metabolic disturbance that may result from inappropriate secretion of antidiuretic hormone following severe brain trauma, infection or asphyxia but is an uncommon isolated cause of neonatal seizures. Hypernatraemia also is a rare cause of seizures usually associated with congenital adrenal abnormalities from the use of IV fluids with high concentrations of sodium. Neonatal meningitis is one

of the important causes of neonatal seizures. In our study 8 babies had meningitis (8%). 3 were early onset, which presented on or before 7th day remaining were late onset, which presented after 7th day of life. Early onset septicemia is usually acquired from the maternal genital tract or ascending infection through ruptured membranes (PROM). Common organisms in early onset sepsis are, group-B streptococcus, E. Coli and rarely listeria. Late onset is usually due to acquired infection e.g., Staph aureus, streptococcus pneumonia, Klebsiella, E. coli, Pseudomonas. The risk factors are unhygienic practices, handling the babies without hand washing in the NICU etc. Most common organisms grown in CSF culture in our study was Staphylococcus aureus followed by E. coli, one baby had hydrocephalus shown by ultrasound of cranium. Tushar Parikh B *et al.*,¹⁴ showed that late onset meningitis is more common than early onset meningitis. Mortality in our study was 17% (17 cases) and birth asphyxia was the commonest cause seen in 13 cases (76%). Mortality in studies by Sandhu Ravneet *et al.*,¹⁵ and Ronen Gabriel *et al.*,⁹ were 11.25% and 9% respectively and birth asphyxia was the commonest cause.

CONCLUSION

Birth asphyxia is the commonest cause of neonatal seizures, followed by dehydration, neonatal meningitis and hypocalcemia. Mortality in our study was 17% & birth asphyxia is the leading cause seen in 13 cases. In present study, 70 % had hyponatraemia & 2 % had hypernatraemia. Thus, hyponatraemia was significantly seen in cases of neonatal seizures.

Conflict of Interest: None to declare

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