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Research Article

Study of biochemical abnormalities in neonatal seizures with special reference to hyponatremia

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ABSTRACT

Background: Biochemical abnormalities are commonly observed in neonates who are admitted in NICU with seizures. In these babies, biochemical abnormalities can be either primary or secondary. Secondary biochemical abnormalities are commonly observed in the presence of other obvious causes of seizures like HIE, meningitis etc. Hyponatremia, hypoglycemia and hypocalcemia are common metabolic disturbances found in neonates with seizures. The present study is intended to evaluate the incidence of various biochemical abnormalities especially hyponatremia.
Methods: It is an observational study done in a tertiary care centre, Gandhi hospital, Secunderabad, Telangana, India involving 120 babies admitted with seizures in NICU.
Results: Biochemical abnormalities were found in 52 babies with the most common primary abnormality being hypoglycemia mostly encountered in preterm babies and the most common secondary abnormality being hyponatremia seen mostly in term babies. Prompt identification of the biochemical abnormalities in neonatal seizures enables specific intervention by the treating doctor resulting in better neurological outcome.
Conclusions: Early detection and prompt management of hyponatremia would help in preventing occurrence of seizures and also help in avoiding over use of anticonvulsants in the management of seizures resulting in favourable neurological outcome with less long term morbidity.

Keywords: Neonatal seizures, Hyponatremia, Term, Preterm, Biochemical abnormalities

INTRODUCTION

In the practice of neonatology, many a time neonatal seizures pose a challenge to paediatrician as well as neonatologist in identifying the underlying cause of seizures. Neonatal seizures represent non-specific responses of the immature nervous system to varied insults and result in considerable mortality in neonatal period and long term morbidity.[1,2] Neonatal seizure by itself is not a diagnosis but is a manifestation of an underlying disease of central nervous system which may result due to systemic and biochemical disturbances. Neonatal seizures is a common problem with an incidence of 0.5-3 per1000 term infants to 1-13% in preterm infants with very low birth weight.[3] Aetiology of neonatal seizures is variable and can be primarily related to disorders of brain eg. HIE, CNS infections, CNS bleeds and structural anomalies of brain or secondary to metabolic problems e.g. hypoglycaemia, hyponatremia and other electrolyte disturbances or cryptogenic. Many times, biochemical disturbances are identified in neonatal seizures either as an underlying cause or as an associated abnormality. Early identification of biochemical disturbances and timely correction can be rewarding as the seizures can be controlled by treating the specific metabolic defect and this will prevent CNS sequlae. Hyponatremia is defined as serum sodium levels below 130 m.eq/l and can manifest with seizures. Hyponatremia

is often found in association with other causes of neonatal seizures. Hyponatremia, besides causing seizures, is also known to result in adverse neurological developmental outcomes like increased risk of cerebral palsy and increased risk of hearing loss.[4] The present study aims to explore the incidence of hyponatremia in neonatal seizures and to study the clinical profile of neonatal seizures with hyponatremia.

METHODS

The present study was conducted in the department of pediatrics, Gandhi Medical College, a tertiary level teaching hospital, Secunderabad, Telangana, India. It is an observational study involving 120 neonates with seizures admitted to NICU from January 2013 to August 2014 consisting of term (82), pre-term (36) and post term (2) babies. Neonates with doubtful seizures, jitteriness and out born babies treated with anticonvulsants were excluded from the study.

Detailed antenatal, natal and postnatal history was taken, age of onset of seizures, type, duration and number of seizures were ascertained. Anthropometry was recorded and gestational age was assessed according to new ballard scoring. Thorough physical examination was done and seizures were diagnosed by clinical observation by the residents and the authors. The neonatal seizures were classified according to volpe's classification into tonic, clonic, multifocal and myoclonic seizures.[5] Investigations included complete blood counts, sepsis screen, blood culture and neurosonogram. Random blood glucose was done using glucometer and values were confirmed by glucose oxidase method. Serum levels of sodium, potassium, calcium, phosphorus and magnesium were estimated.

The criteria for diagnosing various biochemical disturbances were as follows;

Hyponatremia: Na <130 m.eq/l

Hypernatremia: Na >150 m.eq/l

Hypoglycemia: Blood sugar <40 mg/dl,

Hypocalcemia: Calcium <7.0 mg/dl,

Hypomagnesemia: Magnesium <1.5 mg/dl,

Hypermagnesemia: Magnesium >2.5 mg/dl

Other investigations like CSF analysis, CT scan brain, MRI brain, EEG were done as per requirement on a case to case basis. The results were analysed by chi square test using openepimenu.com.

RESULTS

Out of total 120 neonates with seizures, 52 (43.3%) had biochemical abnormalities. Out of the 52 babies, 30 (57.69%) were term, 21 (40.38%) were preterm and one was post term baby.

In 23 (44.23%) of these 52 babies, only biochemical abnormalities were identified. In these babies with 'primary metabolic abnormalities' no other associated morbid condition that causes seizures could be made out. Twenty nine (55.76%) babies had other pathologies like HIE, meningitis/sepsis etc. along with biochemical abnormalities.

The overall biochemical profile of the study group showed that hyponatremia was found in 19 (36.53%) of the babies (Table 1). Serum levels of sodium in these cases ranged from 116 to 128 meq/L with a mean of 123 meq/L (Figure 1). Out of 19 cases of hyponatremia, term babies were 14 (74%) and preterm babies were 5 (26%). Hyponatremia (54%) was the most common biochemical abnormality noticed in term neonates and hypoglycemia (52%) was the most common biochemical abnormality in preterm neonates. Chi square value 7.23, p-value 0.03 (significant).

Table 1: Over all biochemical abnormalities in term and pre-term babies with seizures.

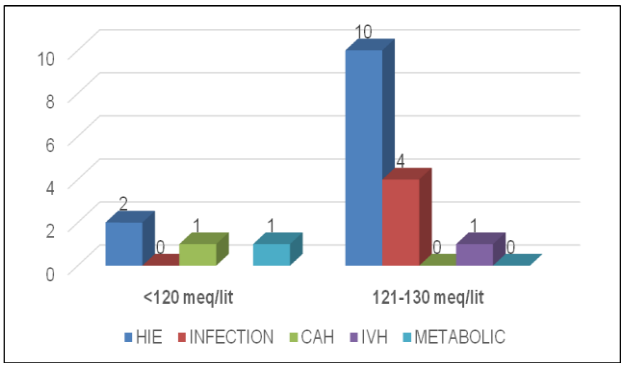
Type	Hyponatremia	Hypernatremia	Hypoglycemia	Hypocalcemia	Hypo Ca+Mg	Hypo-magnesemia	Total
Term	14	02	06	06	01	01	30
Preterm	05	01	11	04	00	00	21
Post-term	00	00	00	01	00	00	01
Total	19	03	17	11	01	01	52

In term neonates hyponatremia is the most common biochemical abnormality.In preterm neonates hypoglycemia is the most common biochemical abnormality.

11 (78.5%) of the 14 term babies with hyponatremia had seizures between 1-3 days and 3 babies had seizures between 4-7 days of life. Out of 5 preterm babies with hyponatremia, 2 babies had seizures between 1-3 days and 2 had seizures after seven days (Figure 2). This suggests that the most common period for occurrence of seizures with hyponatremia was between 1- 3 days of life and seizures that occurred after 7 days were exclusively seen in pre-term babies. This is statistically significant (chi-square value-6.26, p value-0.04(significant)).

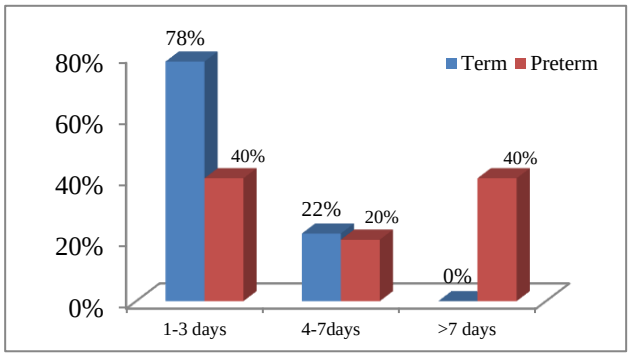
Hyponatremia was most commonly found in association with HIE in term babies and in preterm babies hyponatremia occurred in association with sepsis (Figure 3) (chi-square value-6.53, p-value-0.04 (significant)).

Subtle seizures were the commonest type in term neonates, where as in preterm babies clonic type was common. Clonic type of seizure was not observed in term neonates with hyponatremia (Figure 4). (Chi-square value-11.63, p-value-0.008 (significant)).



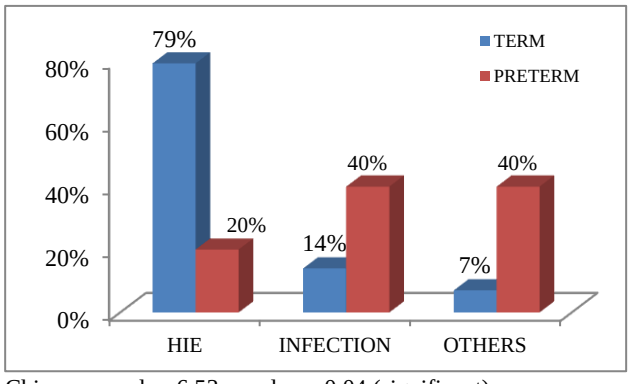
<120 meq/l : 4 cases Metabolic-1, HIE-2, CAH-1
120-130 meq/l : 15 cases HIE -10, Infection -1, IVH-1

Figure 1: Levels of serum sodium in hyponatremic seizures in HIE, infection, IVH, metabolic conditions.



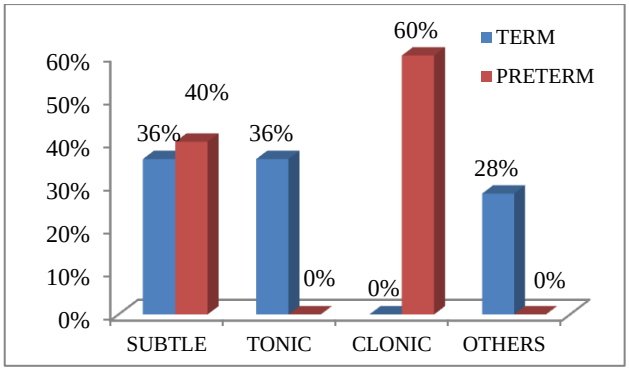
Chi-square value-6.26, p value-0.04(significant).

Figure 2: Timing of hyponatremic seizures in term vs preterm.



Chi-square value-6.53, p value – 0.04 (significant)

Figure 3: Secondary hyponatremia term vs preterm.



Chi-square value- 11.63, p value – 0.008(significant) Subtle seizures were commonest in term neonates, where as in preterm babies clonic type were common. Clonic type of seizure was not observed in term neonates with hyponatremic seizures.

Figure 4: Types of hyponatremic seizures in term vs preterm.

DISCUSSION

Sodium is the principal electrolyte in the extra cellular fluid. Sodium homeostasis is maintained by different physiological mechanisms. An imbalance in the homeostasis of sodium can affect CNS functions resulting in seizures. Hyponatremia is frequently observed in the neonatal seizures either as an underlying cause or as an associated abnormality. Sometimes, additional biochemical abnormalities like hypocalcemia, hypoglycemia and hypomagnesemia may be associated with neonatal seizures. In the presence of any of these biochemical abnormalities, it is difficult to control seizures and there is an increased risk of further brain damage.

Early recognition and treatment of biochemical disturbances is essential for optimal management and satisfactory long term outcome. The common metabolic causes for neonatal seizures include hyponatremia, hypoglycemia, hypocalcemia and hypomagnesemia.[6]

In the present study over all bio chemical abnormalities were observed in 52 (43.33%) cases. Of these, Hyponatremia was observed in 19 cases (36.53%), hypoglycemia in 17 (32.69%) cases, hypocalcemia in 11 (21.11%) cases, hypernatremia in 3 (6%) cases and hypomagnesemia in 1 case (2%). While 1 case was found to have combined hypocalcemia and hypomagnesemia (Table 2).

Kumar et al, in their study on 35 neonates with seizures found biochemical abnormalities in 22 (62.8 %) cases.[6] These subjects had one or more biochemical abnormalities with an incidence of hyponatremia 45.5%, hypoglycemia 50%, hypocalcemia 31.8% and hypomagnesemia 13.63% of cases. Hypermagnesemia and hyperphosphatemia were seen in 4.54 % and 13.63 % of cases respectively.

Table 2: Biochemical abnormalities in neonates with seizures.

Aetiology	Neonates with metabolic abnormalities	Hypo-natremia	Hypo-glycemia	Hypo-calcemia	Hypo-magnesemia	Hyper-natremia	Hypomagnesemi +hypocalcemia
HIE* (n=59)	18	13	1	6	-	-	-
Septicemia/ meningitis (n=31)	7	3	4	-	-	-	-
IVH** (4)	1	1	-	-	-	-	-
Kernicterus (n=1)	-	-	-	-	-	-	-
Structural (n=1)	-	-	-	-	-	-	-
CAH$ (n=1)	1	1					-
Primary metabolic (n=23)	23	1	12	5	1	3	1

HIE*Hypoxic ischemic encephalopathy, IVH**intra ventricular hemorrhage, CAH$ Congenital adrenal hyperplasia

In a similar study of 59 neonates for biochemical abnormalities by Sood A et al overall biochemical abnormalities were observed in 29 cases (49.15%).[7] Hyponatremia was found in 17.25 %, hypoglycemia in 12 (41.37%), hypocalcemia in (51.72%), hypomagnesemia in 4 (13.79%) while hypermagnesemia and hyperphosphatemia were found in 3.44%, 3.44% respectively (Table 3).[7]

Table 3: Comparison of biochemical abnormalities in neonatal seizures as reported by various authors.

Biochemical	Kumar	Arvind Sood	Present study (120)
Parameter	1995	1997	
	(n=35)	(n=59)	
Hyponatremia	10	5	19
Hypoglycemia	11	14	17
Hypocalcemia	7	14	11
Hypomagnesemia	3	5	1*
Hypo Ca+hypo Mg	0	0	1
Hypernatremia	0	0	3
Hypermagnesemia	1	0	0
Hyperphosphatemia	3	0	0

Of the 52 subjects with metabolic abnormalities in the present study, 23 (44.23%) neonates showed primary metabolic abnormalities. Hypoglycemia 12(52.17%) was the commonest abnormality, mostly seen in preterm (9) babies. Hypocalcemia was seen in 5 (21.73%) babies presenting with primary metabolic seizures while hyponatremia and Hypomagnesemia were found in 1 case (4.3%) each. Hypernatremia was found in 3 cases (13.04%). one case had combined hypocalcemia and hypomagnesemia (Table 4, 5).

In the study done by Kumar in 35 neonates, primary metabolic abnormalities were seen in 9 cases accounting for 25.7% of the cases of neonatal seizures. The common abnormalities were hypoglycemia, combinations of hypoglycaemia with hypocalcemia and hypocalcemia with hyperphosphatemia. Hyponatremia was seen in 11.1% of cases.[6]

Table 4: Comparison of primary and secondary metabolic seizures as reported by various authors.

Biochemical abnormality	Kumar 1995 (n=35)	Arvind Sood 1997 (n=54)	Present study
Primary	10	20	23
Secondary	12	9	29
No abnormality	13	30	68
Total	35	59	120

Table 5: Comparison of biochemical abnormalities in primary metabolic seizures as reported by various authors.

Biochemical	Kumar	Arvind Sood	Present study (23)
Parameter	1995	1997	
	(n=9)	(n=10)	
Hyponatremia	1	0	1
Hypoglycemia	5	4	12
Hypocalcemia	5	7	5
Hypomagnesemia	1	3	1
HypoCa+hypo Mg	0	0	1
Hypernatremia	0	0	3
Hyperphosphatemia	2	1	0
Hypermagnesemia	0	0	0

A similar study done by Sood et al reported primary metabolic abnormalities in 10 (16.94%) cases out of 59 neonatal seizures, the most common being hypocalcemia

7 (70%) followed by hypoglycemia 4 (40%).[7] Rose et al from Boston observed hypocalcemia in 28 (20.4%) cases, followed by hypoglycemia in 7 (5.1%) cases.[8] Calciolari et al reported 8 cases of neonatal seizures with primary metabolic abnormalities, out of which 38 % had hypoglycemia, 50 % had hypocalcemia and 12.5 % had hyponatremia.[9]

In this study, 29 (55.76%) of 52 babies presenting with seizures having electrolyte abnormalities were associated with HIE, IVH and meningitis/sepsis. Hyponatremia 18 (62.06%) is the most common electrolyte disturbance found in these cases of secondary biochemical abnormalities. Of these 12 cases were associated with HIE, 4 cases with meningitis/sepsis and 1 case each with CAH and IVH. A similar association of Secondary biochemical abnormalities with HIE, meningitis/septicemia and IVH was noticed by Kumar et al and Sood A et al. in their studies.[6,7] Kumar et al. showed hyponatremia as most common biochemical abnormality which is similar to this study.[6] In contrast to this study, Sood A et al. reported hypoglycemia as the commonest abnormality in HIE followed by hypocalcemia and hypomagnesemia and hyponatremia in that order.[7]

Secondary hyponatremia (dilutional) is mainly because of water retention resulting from renal compromise or due to inappropriate secretion of antidiuretic hormone as seen in HIE.[10] Hyponatremia in infants with meningitis, and intracranial haemorrhage can be explained on the basis of inappropriate secretion of antidiuretic hormone seen in these conditions. CNS infections in our study were associated with hyponatremia (3 cases) and 4 hypoglycemia (4 cases). Kumar et al also showed similar findings while Arvind et al, showed that intracranial infections were associated with hypocalcemia and hyponatremia in 2 cases each.

CONCLUSION

Biochemical abnormalities are found in 43.33% (52 cases) of neonates with seizures. Primary biochemical abnormalities without other co morbid conditions were seen in 23 cases (44.23%). Hypoglycemia (52.7%) and hypocalcemia (21.73%) were the common biochemical abnormalities found in this group. Secondary biochemical abnormalities were seen in 29 (55.77%) cases. Hyponatremia (62.06%) was the commonest biochemical abnormality in this group. Hyponatremic seizures were commonly seen in association with hypoxic ischaemic encephalopathy in term babies. In preterm babies infection was the commonest underlying aetiology associated with hyponatremia. These abnormalities may significantly contribute to seizure activity and possibly correction of these abnormalities may play a vital role in seizure control. A thorough biochemical work up is necessary in all cases of neonatal seizures. The type of seizure does not correlate with any specific etiology.

Serum sodium levels should be measured in every case of neonatal seizure especially term babies manifesting with seizures in first three days of life even in the presence of obvious causes like asphyxia, meningitis/sepsis. Early detection and prompt management of hyponatremia would help in preventing occurrence of seizures and also help in avoiding over use of anticonvulsants in the management of seizures resulting in favourable neurological outcome with less long term morbidity.

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