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ASSOCIATION OF NEONATAL SEIZURES WITH SPECIAL REFERENCE TO BIOCHEMICAL PARAMETERS

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ABSTRACT **AIM:** To identify co relation between biological changes and neonatal seizures and the relation between neonatal seizures and infection. **MATERIAL AND METHOD:** It is a descriptive observational study in hospital setting. The study is to be conducted at SNCU of SSKM HOSPITAL, WEST BENGAL over one year; from 1st March 2018 to 1st March 2019. Children aged 0 days to 28 days admitted in Pediatric SNCU with signs and symptoms suggestive of seizure during the period of study was constitute the population under study. **RESULT:** Association of hypoglycemia vs. outcome was statistically significant (p=0.0017) and Association of hypocalcemia vs. outcome was statistically significant (p=0.0084). **CONCLUSION:** We found that hypoglycaemia was more common in 1 day of age which was statistically significant.

KEYWORDS : Neonatal, hypoglycemia, hypocalcemia, Biochemical.

INTRODUCTION

Seizures are a common occurrence in both term and pre term neonates. Despite their frequency and clinical significance, currently there are no clearly defined evidence – based guidelines to address major questions about their management and prevention. [1]

Neonatal seizures are fits occurring from birth to the end of the neonatal period. The neonatal period is the most vulnerable of all periods of life for developing seizures, particularly in the first 1–2 days to the first week from birth. They may be short-lived events lasting for a few days only. They often signify serious malfunction of or damage to the immature brain and constitute a neurological emergency demanding urgent diagnosis and management [2]

Preterm babies, especially those at lower gestational age and birth weights, have a higher incidence of neonatal seizures due to the associated morbidity of cerebral insults such as intraventricular haemorrhage and periventricular leucomalacia. [3]

Generally:

- Term babies: 1.5–5/1000 live births
- Birth weight: 1500–2500: 4.4/1000 live births
  Less than 1500 grams: 55–130/1000 live births
  Less than 1000 grams: up to 64/1000 live births

Generalised tonic clonic seizures (GTCS) are exceptional.most widely used scheme is by Volpe[4] of five main types of neonatal seizure.

- **Subtle seizures (50%)**
- **Tonic seizures (5%)**
- **Clonic seizures (25%)**
- **Myoclonic seizures (20%)**
- **Non-paroxysmal repetitive behaviours**

Neonatal seizures are usually focal and may be difficult to recognize. Common manifestations include migratory clonic jerks of extremities, alternating hemiseizures, and primitive subcortical seizures (which cause respiratory arrest, chewing movements, persistent eye deviations or nystagmoid movements, and episodic changes in muscle tone). Generalized tonic-clonic seizures are uncommon.

Clinically silent electrical seizure activity is often present after a hypoxic-ischemic insult (including perinatal asphyxia or stroke) and in neonates with CNS infections, especially after initial anticonvulsant treatment, which is more likely to stop clinical manifestations than electrical seizure activity[5].

There is a need to evaluate the metabolic factors related to neonatal seizures. So that the children at risk have a higher chance of prevention from seizure which in turn can lead to lesser cases of brain injury and a better quality of life for child.

1.To identify co relation between biological changes and neonatal seizures

- Calcium (Hypocalcemia)
- Glucose (Hypoglycemia)
- Sodium (Hyponatremia/Hypernatremia)
- Potassium (Hypokalemia)

2.To identify relation between neonatal seizures and infection

- Sepsis screen (Markers used-ANC,I/T ratio,CRP,Micro ESR)

3. To find out proportion of death among outcome of neonatal seizure

MATERIAL AND METHOD:

1. **TYPE OF STUDY:** It is a descriptive observational study in hospital setting. The study is to be conducted at of SSKM HOSPITAL, WEST BENGAL.
2. **DURATION OF STUDY:** The study was conducted over one year; from 1st March 2018 to 1st March 2019.
3. **POPULATION UNDER STUDY:** Children aged 0 days to 28 days admitted in Pediatric SNCU with signs and symptoms suggestive of seizure during the period of study was constitute the population under study.

INCLUSION CRITERIA:

1. All babies with seizure like presentation from birth till 28 days
2. Male and female babies up to the age of 28 days
3. Babies with seizure like presentation where mother has given the consent.

EXCLUSION CRITERIA:

1. Babies of age more than 28 days
2. Stillborn babies
3. Babies where mother has not given consent
4. Babies with gross congenital malformation.

STATISTICAL METHODS:

Sample size was calculated with help of Epi Info (TM) 3.5.3. EPI INFO which is a trademark of the Centres for Disease Control and Prevention (CDC). The SPSS 20.0.1 software was used for statistical analysis of data of this study. Chi-squared test wasused to test the association of different study variables. t-testwas used to compare the means. Significance level will set at ≤ 0.05.

RESULT AND DISCUSSION

100 Children aged 0 days to 28 days admitted in Pediatric SNCU with signs and symptoms suggestive of seizure during the period of study was constitute the population under study.

Mishra S et al [6] (2018) found that hypoglycemia, as a cause was found in only 4% of cases. HIE was the commonest cause (51.8%) followed by metabolic abnormalities (23.2%). Most common cause of neonatal seizure is HIE and in maximum cases it is seen in first 72 hours of life.

MarpiSuryaprasada Rao et al [7] (2017) found etiology in majority of the cases of neonatal seizures was hypoxic ischemic encephalopathy

(45%) followed in frequency by intracranial haemorrhage (14%), meningitis (12%), hypoglycaemia (11%), hypocalcaemia (4%) and others (14%). Most common biochemical abnormalities noted were hypoglycemia, hypocalcaemia and hyponatremia. Biochemical abnormalities may significantly contribute to seizure activity and possibly correction of these abnormalities may play a significant role in seizure control.

We found that 35(35.0%) children were 1 day of age, 29(29.0%) children were 2 days of age, 17(17.0%) children were 3 days of age and 19(19.0%) children were ≥4 days of age. The mean age (mean± s.d.) of children was 3.2700 ± 3.8055 days.

We found that 24(24.0%) children had hypoglycaemia, 4(4.0%) children had hypocalcaemia. 1(1.0%) child had hypernatremia, 1(1.0%) child had hypo natremia and 98(98.0%) children had normal natremia and 1(1.0%) child had hypokalemia.

It was found that12(12.0%) children had ANC low, 19(19.0%) children had sepsis.We also found that 97(97.0%) children were alive and 3(3.0%) children were dead. 47(47.0%) children had HIE.

Tekgul H et al [8](2006) found that Global cerebral hypoxia-ischemia, the most common Etiology.

Das D et al [9](2016) found that birth asphyxia was the most common cause of neonatal seizures in our study (64, 56%), followed by neonatal meningitis (24, 21%) and metabolic disorders (13, 11%). The most common biochemical abnormality detected in neonatal seizures in our study was hyponatremia (26, 65%), of which 21 (72.4%) were due to hypoxic ischemic encephalopathy (HIE). In metabolic seizures, hypoglycemia (66.7%) was common. Incidence of hypomagnesemia with hypocalcemia occurred in two (1.73%) cases. The most common etiology of neonatal seizures is HIE and onset is during first 3 days of life. Hyponatremia is the most common biochemical abnormality associated with non-metabolic seizures, mainly HIE. Hypoglycemia is a more common metabolic disorder, more so in low birth weight. Incidence of hypomagnesemia with hypocalcemia is low but recognition of such abnormality has important therapeutic implications.

We found that the mean serum glucose (mean± s.d.) of children was 73.7100 ± 31.8964, The mean serum calcium (mean± s.d.) of children was 9.8120 ± 1.1983, The mean serum sodium (mean± s.d.) of children was 139.1200 ± 3.7017, The mean serum potassium (mean± s.d.) of children was 4.2432 ± .5058, The mean HB (mean± s.d.) of children was 13.9900 ± 1.8745, The mean ANC (mean± s.d.) of children was 5243.1000 ± 3279.9965, The mean micro ESR (mean± s.d.) of children was 6.9500 ± 7.0916, The mean I:T neutrophil (mean± s.d.) of children was .1295 ± .0710 and the mean CRP (mean± s.d.) of children was 7.2344 ± 16.4679.

Madhusudhan K et al [10] (2016) found that 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. 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.

TanveerNawab et al [11] (2016) found that Out of the 110 neonates studied, birth asphyxia was the commonest cause of neonatal seizures in 66 (60%) cases, followed by neonatal sepsis and metabolic disorders. Primary metabolic abnormalities occurred in 13(11.8%) cases of neonatal seizures, most common being hypoglycemia 9 (69.3%) followed by hypocalcaemia. Associated biochemical abnormalities were seen in 33 (30%) cases with hyponatremia 13 (39.3%) being most common followed by hypoglycemia. These were most often seen with Hypoxic- ischaemic-encephalopathy.

It was found that in 1 day of age, 16(45.7%) children had hypoglycaemia. In 2 days of age, 3(10.3%) children had hypoglycaemia. In 3 days of age, 2(11.8%) children had hypoglycaemia. In ≥4 days of age, 3(15.8%) children had hypoglycaemia. Association of hypoglycemia vs. age in days group was statistically significant (p=0.0028).

We found that association of hypocalcemia vs. age in days group was not statistically significant (p=0.2724). Association of hypo or hyper natremia vs. age in days group was not statistically significant (p=0.7051). Association of hypokalemia vs. age in days group was not statistically significant (p=0.5986).Association of HIE vs. age in days group was not statistically significant (p=0.1172).

Mishra S et al [12] (2018) found that HIE was the commonest cause (51.8%) followed by metabolic abnormalities (23.2%).

In 1 day of age, 2(5.7%) children had ANC low. In 2 days of age, 3(10.3%) children had ANC low. In 3 days of age, 1(5.9%) child had ANC low. In ≥4 days of age, 6(31.6%) children had ANC low. Association of ANC low vs. age in days group was statistically significant (p=0.0309).

In 1 day of age, 35(100.0%) children were alive. In 2 days of age, 29(100.0%) children were alive. In 3 days of age, 17(100.0%) children were alive. In ≥4 days of age, 16(84.2%) children were alive and 3(15.8%) children were dead. Association of outcome vs. age in days group was statistically significant (p=0.0043).

Aziz A et al [13] (2015) found that Hypoxic ischemic encephalopathy was the commonest etiology of neonatal seizures.Majority of Hypoxic ischemic encephalopathy patients presented with seizures in the first 72 hrs.Hypocalcaemia was the commonest biochemical abnormality in primary metabolic seizures and was present in 70% neonates in this group. Hypoglycaemia was the next commonest abnormality and was present in 41% neonates within this group.

We found that in alive, 21(21.6%) children had hypoglycemia. In dead, 3(100.0%) children had hypoglycemia. Association of hypoglycemia vs. outcome was statistically significant (p=0.0017). In alive, 3(3.1%) children had hypocalcemia. In dead, 1(33.3%) child had hypocalcemia. Association of hypocalcemia vs. outcome was statistically significant (p=0.0084). Association of hypo or hyper natremia vs. outcome was not statistically significant (p=0.9689). Association of hypokalemia vs. outcome was not statistically significant (p=0.8597). Association of HIE vs. outcome was not statistically significant (p=0.6301).

Borkenhagen JF et al [14] (2013) found that Hypocalcemia is a common, treatable cause of neonatal seizures.

Bhaskar Reddy A et al [15] (2016) found that Etilogy in majority of cases of neonatal seizures was hypoxic ischemic encephalopathy (43%). Biochemical changes accounted for 17% of neonatal seizures. Meningitis accounted for 11% of neonatal seizures.

Hu SC et al [16] (2017) found that Perinatal asphyxia (59.1%) was the most common cause of neonatal seizures, followed by CNS infection (18.2%), malformation syndrome (9.1%) and intracranial hemorrhage (9.1%).

In alive, 9(9.3%) children had ANC low. In dead, 3(100.0%) children had ANC low. Association of ANC low vs. outcome was statistically significant (p<0.0001). In alive, 16(16.5%) children had sepsis. In dead, 3(100.0%) children had sepsis. Association of sepsis vs. outcome was statistically significant (p=0.0002). Distribution of mean age in days vs. sepsis was statistically significant (p=0.0001). Distribution of mean serum glucose vs. sepsis was not statistically significant (p=0.9653). Distribution of mean serum calcium vs. sepsis was not statistically significant (p=0.3170). Distribution of mean serum sodium vs. sepsis was not statistically significant (p=0.4818). Distribution of mean serum potassium vs. sepsis was not statistically significant (p=0.6709).

We found that in sepsis, the mean HB (mean± s.d.) of children was 11.8053 ± 1.9501. Distribution of mean HB vs. sepsis was statistically significant (p<0.0001). In sepsis-yes, the mean ANC (mean± s.d.) of children was 1884.7368 ± 1027.3016. Distribution of mean ANC vs. sepsis was statistically significant (p<0.0001). In sepsis-yes, the mean micro ESR (mean± s.d.) of children was 18.9474 ± 7.3520. Distribution of mean micro ESR vs. sepsis was statistically significant (p<0.0001).

It was found that in sepsis-yes, the mean I:T neutrophil (mean± s.d.) of children was .2442 ± .0711. Distribution of mean I:T neutrophilvs. sepsis was statistically significant (p<0.0001).

LakheyAet al [17] (2017) found that CRP (77.8%) and immature: total neutrophils ratio (73%) showed highest sensitivity. CRP (66.7%), I/T ratio (61.5%) and micro ESR (60.2%) showed highest specificity. Positive predictive value was highest for CRP (68.2%) followed by I/T ratio (63.8%) and corrected total leukocyte count (56.2%). Serum CRP is the most sensitive marker of sepsis.

It was found that in sepsis-yes, the mean CRP (mean± s.d.) of children was 33.5789 ± 19.7886. Distribution of mean CRP vs. sepsis was statistically significant (p<0.0001).

CONCLUSION

We found that hypoglycaemia was more common in 1 day of age which was statistically significant.

Hypocalcemia, Hypo or Hyper natremia, Hypokalemia were higher in 1 day of age but which was not statistically significant.

ANC LOW was significantly higher in ≥4 days of age baby.

Sepsis was found to more common in higher age of baby which was statistically significant.

ANC low was significantly higher sepsis patients and poor outcome was observed in death patients.

Hypoxic ischaemic encephalopathy was significantly associated with sepsis patients.

Hypoglycaemia, hypocalcaemia, ANC low were significant associated poor outcome.

We found that high CRP, high I:T NEUTROPHIL, high MICRO ESR, low Hb and low ANC were significantly associated with sepsis patients.

Table: Association between Hypoglycemia, Hypocalcemia, Hypo or Hyper natremia and Hypokalemia: OUTCOME

		OUTCOME			Chi-square value	p-value
		ALIVE	DEAD	TOTAL		
Hypoglycemia	**NO**	76	0	76	9.7938	0.0017
	Row %	100.0	0.0	100.0		
	Col %	78.4	0.0	76.0		
	YES	21	3	24		
	Row %	87.5	12.5	100.0		
	Col %	21.6	100.0	24.0		
	TOTAL	97	3	100		
	Row %	97.0	3.0	100.0		
	Col %	100.0	100.0	100.0		
Hypocalcemia	**NO**	94	2	96	6.9301	0.0084
	Row %	97.9	2.1	100.0		
	Col %	96.9	66.7	96.0		
	YES	3	1	4		
	Row %	75.0	25.0	100.0		
	Col %	3.1	33.3	4.0		
	TOTAL	97	3	100		
	Row %	97.0	3.0	100.0		
	Col %	100.0	100.0	100.0		
Hypo or Hyper natremia	**HYPER**	1	0	1	.0631	0.9689
	Row %	100.0	0.0	100.0		
	Col %	1.0	0.0	1.0		
	HYPO	1	0	1		
	Row %	100.0	0.0	100.0		
	Col %	1.0	0.0	1.0		
	NORMAL	95	3	98		
	Row %	96.9	3.1	100.0		
	Col %	97.9	100.0	98.0		
	TOTAL	97	3	100		
	Row %	97.0	3.0	100.0		
	Col %	100.0	100.0	100.0		
Hypokalemia	**NO**	96	3	99	0.0312	0.8597
	Row %	97.0	3.0	100.0		
	Col %	99.0	100.0	99.0		
	YES	1	0	1		
	Row %	100.0	0.0	100.0		
	Col %	1.0	0.0	1.0		
	TOTAL	97	3	100		
	Row %	97.0	3.0	100.0		
	Col %	100.0	100.0	100.0		

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