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Study of Clinical and Biochemical Profile in Neonatal Seizure in a tertiary care centre of Jharkhand

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Abstract
Background: *Neonatal seizures are one of the most common and distinctive clinical manifestations of dysfunction of neurological system. Neonatal seizures represent responses of the immature nervous system to varied insults resulting in considerable neonatal mortality and morbidity including motor and cognitive disabilities in the childhood. Neonatal seizures are more common in preterm compared to term neonates and metabolic abnormalities are common cause of neonatal seizure.*
Objectives: *Current study aims at to study: 1. the incidence of biochemical abnormalities associated with neonatal seizure & 2. The clinical presentation, time of onset and its relation to the neonatal seizures.*
Methods: *A prospective hospital based study was conducted for a period of 6 months from May 2017 to November 2017, a total of 80 newborns with seizure were enrolled in the study after taking complete history and appropriate physical examination. Blood sample was collected for detecting metabolic abnormalities before instituting specific therapy.*
Results: *In my study, neonatal seizure occurred more commonly in term babies especially in appropriate for gestational age babies compared to preterm neonates. There was a male predominance. Most seizures are due to intramural deliveries and occurred within 72 hours of life. Seizures are more common in babies with birth weight ≥2.5 kg and subtle seizure is the most common type. The most common biochemical abnormality noted was hypoglycemia (40%) and hypocalcemia (32%). There were cases reported with combination of hypoglycemia / hypocalcemia and hypocalcemia/hypomagnesemia particularly in preterm but their incidence is low.*
Conclusion: *The transient metabolic abnormalities are easily treatable when identified early and are associated with good prognosis. Hence biochemical work up should be done in all neonates with seizure and should be included as the first line of investigation in all cases, thereby preventing the further occurrence of seizure and overuse of anticonvulsants. It also improve the prognosis and outcome of the neonate and prevent the long term neurological sequelae associated with it.*
Keywords: *Neonatal seizure, hypoglycemia, hypocalcemia.*

Introduction

Neonatal seizures are one of the most common and distinctive clinical manifestations of dysfunction of neurological system. Neonatal seizures represent non specific responses of the immature nervous system to varied insults and results in considerable neonatal mortality and long term morbidity including motor and cognitive disabilities in the childhood[1,2]. Neonatal seizures are often under-recognized, and difficult to treat. Hence it is critical to recognize seizures early and initiate immediate therapy.

Recognition of etiology is often helpful in prognosis and treatment. Studies suggest that neonatal seizures and their etiology have a significant impact on developing brain; however, in clinical practice at neonatal intensive care unit (NICU), in developing countries where synchronized video-EEG monitoring is practically non-existent, clinical observation becomes the key to the diagnosis [3].

Hence we undertook this study in our centre where continuous video-EEG monitoring is not possible to identify neonatal seizures, thereby applying clinical criteria and also to find out the biochemical abnormalities associated with these clinical seizures.

Methods

This study was a hospital based prospective observational study conducted over a period of 6 months from May 2017 to November 2017 in the department of Paediatrics and neonatology, Rajendra institute of medical Sciences, Ranchi. A total of 80 neonates (birth to 28 days of life), all term and preterm, presenting with seizures admitted to the neonatal unit of Department of Paediatrics in Rajendra institute of medical sciences were included. Detailed antenatal history and baseline characteristics of all the babies noted which includes name, age, sex, address, weight, length, head circumference, gestational age. Thorough physical examination was done and seizures were diagnosed by clinical observation. Clinical details of each seizure episode were recorded like age at onset of seizures, duration of seizure, number and type of seizure. Seizure were classified into subtle, focal clonic, multifocal clonic, tonic and myoclonic as per criteria by Volpe.

Exclusion Criteria

1. Baby already on anticonvulsant therapy.
2. Mothers or caregivers not giving consent for the study.

Following investigations was done before initiating treatment:

1. Blood glucose.
2. Total serum calcium level.
3. Serum sodium level.
4. Serum magnesium level.
5. Serum potassium level.

Criteria for diagnosing various biochemical abnormalities:

1. Hyponatremia: <135 mEq/l
2. Hypernatremia: >145mEq/l
3. Hypoglycaemia: <40 mEq/dl (capillary blood)
   <45 mEq/dl (venous blood)
4. Hypocalcemia: <7 mg/dl for preterm neonates
   <8 mg/dl for term neonates
5. Hypomagnesemia: < 1.5 mg/dl
6. Hypermagnesemia: >2.5 mg/dl
7. Hypokalemia: <3.5 mg/dl
8. Hyperkalemia: >5.5 mg/dl.

Results

A total of 80 neonates were included in this study. Among them 37 were delivered by normal vaginal delivery, 37 neonates were delivered by caserean section and 6 by forceps delivery. Among the study population :

1. The number of babies born within institution was 65 and number referred from outside was 15.
2. The Preterm were 23 and term were 57 and there were no post-term.
3. The male were 45 and female were 35.
4. The babies with low birth weight (<2.5 kg) were 34 (42.5%) and Normal Birth weight (≥2.5kg) were 46 (57.5%).

5. the onset of seizures within 24 hours, day 1 to 3, day 4 to 7, and >7 days were 23 (28.75%), 35 (43.75%), 16 (20.00%) and 6 (7.5%) respectively. Convulsions in the first 3 days contributes to 72.5%.

Table-1: Descriptive analysis of type of seizures in study population

Type of Seizure	Number	Percentages
Subtle	49	61.25%
Tonic	20	25.00%
Clonic	11	13.75%

Table-2: Descriptive analysis of Hypoglycemia in study population

Hypoglycemia	Number	Percentages
Present	20	25%
Absent	60	75%

Table-3: Descriptive analysis of Hypocalcemia in study population

Hypocalcemia	Number	Percentages
Present	16	20%
Absent	64	80%

Table-4: Descriptive analysis of Hyponatremia in study population

Hyponatremia	Number	Percentages
Present	07	8.75%
Absent	73	91.25%

Table-5: Descriptive analysis of Hypomagnesemia in study population

Hypomagnesemia	Number	Percentages
Present	04	5.00%
Absent	76	95.00%

Table-6: Descriptive analysis of Hypernatremia in study population

Hypernatremia	Number	Percentages
Present	03	3.75%
Absent	77	96.25%

Table-7: Descriptive analysis of combination in study population.

Combination of	Number	Percentages
Hypoglycemia & Hypocalcemia	03	3.75%
Hypocalcemia & Hypomagnesemia	01	1.25%

Table-8: Association of TERM/ PRETERM with Variables of study population

Variables		Numbers	
		Pre-Term (N=23)	Term (N=57)
Hypoglycemia		8 (34.78%)	12 (21.05%)
Hypocalcemia		7 (30.43%)	9 (15.79%)
Hyponatremia		2 (8.7%)	4 (7.0%)
Hypomagnesemia		2 (8.7%)	1 (1.75%)
Hypernatremia		0 (0%)	3 (5.26%)
Hypoglycemia & Hypocalcemia		2 (8.7%)	0 (0%)
Hypocalcemia & Hypomagnesemia		1 (4.35%)	0 (0%)
Types of Seizures	Subtle	12 (52.17%)	31 (54.38%)
	Tonic	4 (17.39%)	14 (24.56%)
	Clonic	3 (13.04%)	6 (10.52%)

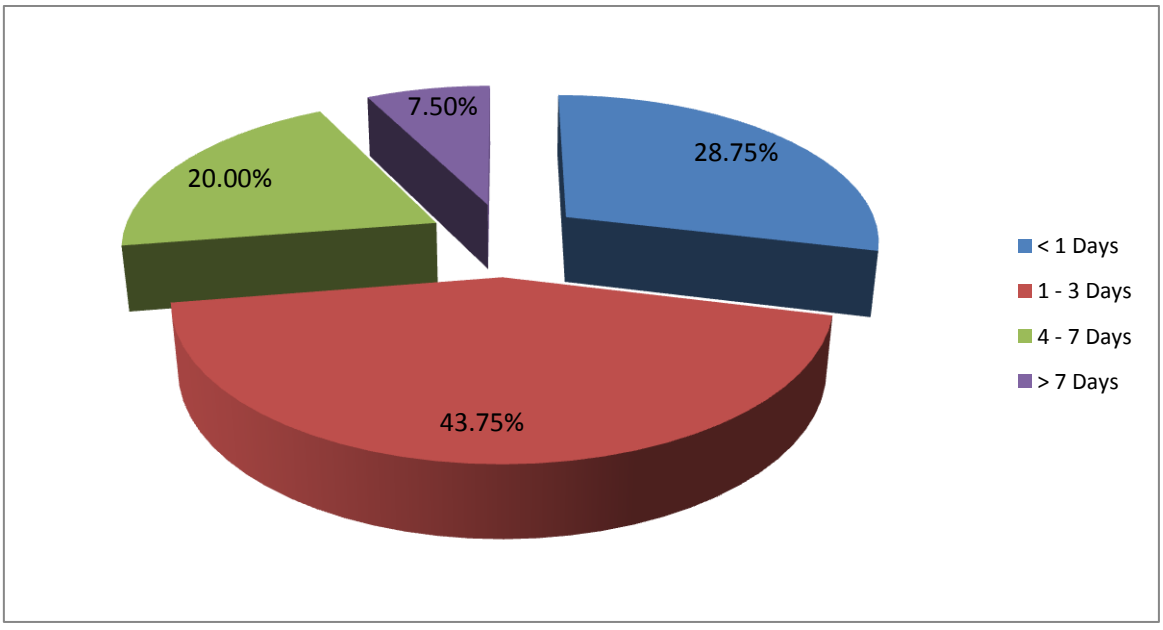

Fig-1: Percentages of Days of Onset of Seizures

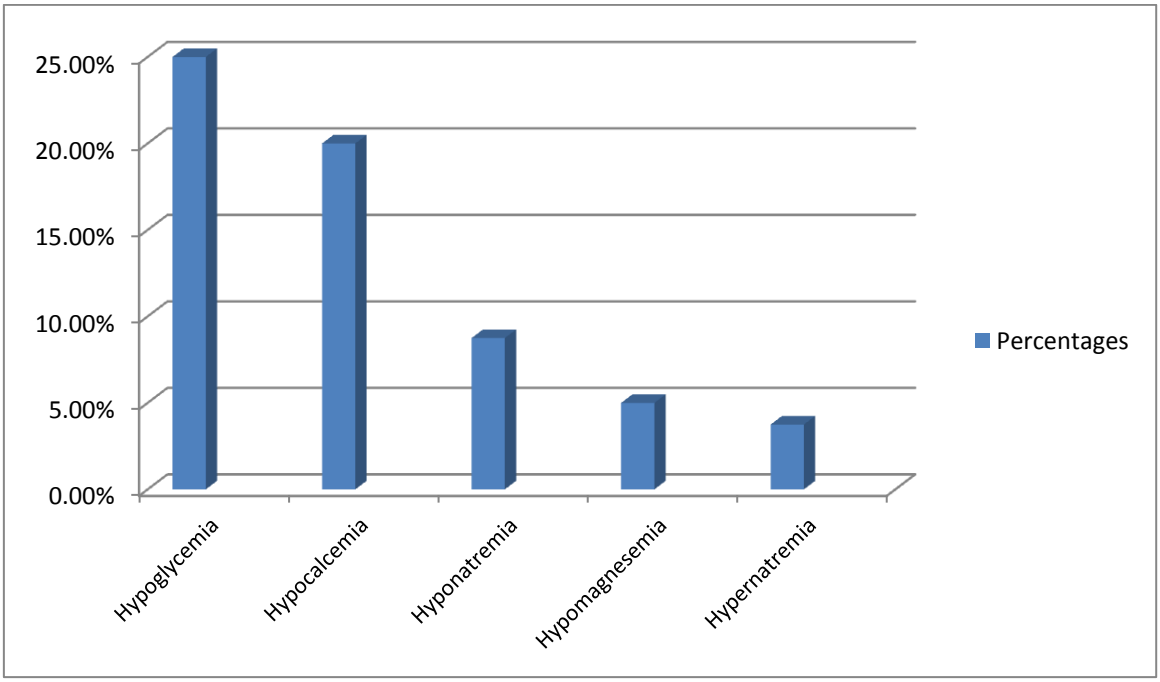

Fig-2: Summary of various biochemical abnormalities in study population.

Discussion

Seizures are most common neurological disorders in newborn which are more prevalent in preterm neonates compared to term neonates. Out of 80 neonates, full term neonates were 57 and preterm constitutes 23 in number. Majority of neonates with seizures in my study were full term neonates. Similar observation were seen in study by Aziz et al[4] where term babies constitutes 65% and preterm 35%. In studies by Park Weon et al[5] and Dinesh Das et al[6],they also reported a much higher incidence in term babies compared to preterm neonates.

In my study, neonatal seizures were common in male babies contributing about 56.25% and female about 43.75%, similar to study done by Aziz et al[4] (male 60%, female 40%) and Dinesh Das et al[6] (male 62.6%, female37.4%) also reported male predominance.

In my studies, 37 babies (46.25%) born by normal vaginal delivery, 37 (46.25%) by caserean section and 6 (7.5%) babies by forceps delivery. Aziz et al[4] in his study reported neonates with seizures born by normal vaginal delivery 48%, by caserean 28% and operated vaginal 24%.

In my study, 46 neonates (57.5%) had birth weight ≥2.5 kg and 34 neonates (42.5%) had birth weight <2.5 kg similar observations were made by Dinesh Das et al[6] where neonates >2.5 kg were 65% and <2.5 kg were 35% respectively.

Out of 80 neonates in my studies 23 had seizures within 24 hours (28.75%), 35 neonates between 24-72 hours (43.75%),16 babies between day 4 to 7 (20.00%) and 6 babies above 7 days (7.5%). Thus most of the seizures occurred within 3 days of life contributing about 72.5% similar to observations made by Dinesh Das et al[6] and Nawab et al[7] where seizures within 3 days was 71.3% and 73.6% respectively.

The most common type of neonatal seizures in our study was subtle contributing about 61.25% in about 49 neonates, followed by tonic seizures in 25.00% (20) and clonic 13.75% (11), similar to findings of Sudia et al[8] and Dinesh Das et al[6] where subtle seizures occurred in 63.33% and 42.6% ,tonic seizures 19.33% and 33.9%, clonic in 10% and 15.7% respectively.

Out of 80 neonates, 50 babies with seizures had one or more biochemical abnormality contributing to about 62.5% in total. Sood et al[9] in his study overall biochemical abnormalities in 29 cases (49.15%) comparable to my study. Similar observation were made by Nawab et al[7] in his studies where out of 110 neonates, 46 babies had

biochemical abnormality contributing to 41.8%. Kumar et al[10] has found overall biochemical abnormalities in 62.8% of neonates against Madhusudan et al[11] 43.33%.

Comparison of most common biochemical abnormalities in neonatal seizures as reported by various authors:

Biochemical abnormalities (overall)	KUMAR 1995 N = 35	ARVIND SOOD 1997 N = 59	MADHUSUDAN 2016 N = 120	PRESENT STUDY N = 80
Present	22 (62.8%)	29 (49.15%)	52 (43.33%)	50 (62.5%)
Absent	13 (37.2%)	30 (50.85%)	68 (56.66%)	30 (37.5%)
Total	35 (100%)	59 (100%)	120 (100%)	80 (100%)

The most common biochemical abnormality in my study was hypoglycaemia followed by hypocalcemia particularly in preterm neonates. Among preterm babies the incidence of hypoglycaemia were 34.78% compared to 21.05% in term babies. Hypocalcemia was reported in 30.43% among preterm babies which was higher when compared with term babies about 15.79%. Suganthi et al[12] in her study has made similar observation where Metabolic abnormalities were present in 89 (59.3%) out of 150 cases. Of these hypoglycaemia and hypocalcemia were the most common with 39 (48.8%) and 28 (35.4%) cases respectively. Sameer kumar jain et al[13], Shah et al[14] and Iype maya Prasad et al[15] also found hypoglycaemia followed by hypocalcemia to be most common metabolic disturbances in their study further supporting my finding.

Conclusion

Neonatal seizures are one of the most common neurological problems in neonates. There are various causes for neonatal seizures which not only determines the course of the disease but also helps in determining its associated long term neurological outcome along with morbidity and mortality. Quick assessment, timely diagnosis and aggressive management according to the etiology are necessary to prevent these problems. Moreover biochemical abnormalities may either occur as a primary problem or may be associated with other etiologies.

These transient abnormalities are easily treatable when identified early and are associated with good prognosis. Hence biochemical work should be done in all neonates with seizures and should be included as the first line investigation in all cases. Early correction of these biochemical abnormalities help in preventing the further occurrence of seizures and also help in avoiding overuse of anticonvulsants which may be unnecessary in some cases. Further early correction of these metabolic abnormality improve the prognosis and outcome of the neonate and also prevent the long term neurological sequelae associated with it.

Wherever possible continuous video-EEG monitoring should be included in identifying the neonatal seizures to know the real magnitude of the problem and to treat these seizures promptly.

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