Prevalence of Biochemical Abnormalities in Neonatal Seizures in Term and Preterm Neonates

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Authors’ contributions

This work was carried out in collaboration among all authors. Author KMV designed the study, wrote the protocol and wrote the first draft of the manuscript. Author GSP performed the statistical analysis and the literature searches. Author SSP managed the analyses of the study. All authors read and approved the final manuscript.

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ABSTRACT

Background: The most vulnerable period of life to develop seizures is the neonatal period. These events very often signify serious damage or malfunction of the immature developing central nervous system. Neonatal seizures may arise as a result of diverse etiologies and can have varied presentations. Biochemical abnormalities are commonly observed in neonates who are admitted in neonatal intensive care unit with seizures. Early recognition and treatment of biochemical disturbances is essential for optimal management and satisfactory long-term outcome.

Objective: To assess clinical types and importance of biochemical abnormalities in neonatal seizures and to evaluate clinical type & time of onset of seizures in term and preterm neonates.

Methods: A prospective observational study, where 100 neonates presenting with seizures admitted to neonatal intensive care unit of Jagadguru Jayadeva Murugarajendra Medical College, Davangere, from September 2015 to August 2017 were enrolled in the study. The detailed history along with clinical examination, baseline characteristics of convulsing neonate were recorded at admission. Clinical details of each seizure episode reported by the mother and subsequently observed by the resident doctors on duty were recorded. The relevant biochemical investigations

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were done immediately after baby had seizures and before instituting any specific treatment. The descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical variables. The association between gestational age and other categorical variables were analyzed using chi-square test of independence. The comparison of mean of various quantitative variables was analyzed using ANOVA test. Etiology of neonatal seizures and associated biochemical abnormalities were diagnosed.

**Results:** In the present study, out of 100 neonates studied, 64 were full term of which 49(76.5%) were appropriate for gestational age and 15(23.5%) were small gestational age, whereas 36 cases were preterm. Most neonatal seizures occur in first 3 days of life, i.e. 59%. Most of them occurred on first day of life (34%). Birth asphyxia was the cause of neonatal seizures in 82.35% neonates who developed seizures on day-1 of life. Birth asphyxia and septicemia are common cause of neonatal seizures in our study (38 cases each), followed by pure metabolic disturbances 19%. In pure metabolic seizures, hypoglycemia (47.8%) is most common in preterm babies (55%) followed by hypocalcemia. In cases of non- metabolic seizures, which showed associated biochemical abnormalities, hypoglycemia was most common abnormality 23 of 52 cases (44.2%). 12 cases (52.1%) are associated with birth asphyxia and 11 cases (47.9%) are associated with septicemia. Subtle seizures were most common type of seizures in our study, followed by focal clonic, multifocal clonic, generalized tonic, subtle with GTC and subtle with clonic.

**Conclusion:** Biochemical abnormalities are common in neonatal seizures and often go unorganized. These abnormalities may significantly contribute to seizure activity correction of these abnormalities work up is necessary for all cases of neonatal seizures.

**Keywords:** Neonatal seizures; hypoglycemia; hypocalcemia; birth asphyxia.

1. INTRODUCTION

Seizure is defined as paroxysmal involuntary disturbance of brain function. It may manifest as impairment or loss of consciousness, abnormal motor activity, behavioural abnormality, sensory disturbance or autonomic dysfunction [1]. Any abnormal, repetitive and stereotypic behavior in neonates should be evaluated as possible seizure.

Neonatal seizures by definition occur within the first 4 weeks of life in a full-term infant and up to 44 weeks from conception for premature infants [2] and are most frequent during the first 10 days of life. [3] Neonatal seizures is a common neurological problem with a frequency range from 0.95 to 3.5/1000 live births [4]. Seizure incidence is higher during this period than in any other period of life. Incidence is as high as 57.5 per 1000 in infants with birth weights lower than 1500 grams, but only 2.8 per 1000 for infants with birth weights of 2500 to 3999 grams have seizures [5-7].

Neonatal seizures represent the most distinctive signal of neurological disease in the newborn period. The convulsive phenomenon is clinically significant because very few are idiopathic. Neonatal seizures also differ considerably from seizures observed in older children, principally because the immature brain is less capable of propagating generalized or organized electrical discharges [8]. It is critical to recognize neonatal seizures to determine their etiology and to treat them for 3 major reasons as following

1. First, seizures are usually related to significant illness, sometimes requiring specific therapy.
2. Second, neonatal seizures may interfere with important supportive measures, such as alimentation and assisted respiration for associated disorders.
3. Third, experimental data give reason for concern that the seizures per se may be a cause of brain injury [9].

Seizures present with varying manifestations like generalized tonic, multifocal clonic and subtle activity. Therefore, it is important to recognize them and treat it, as delay in recognition and treatment may lead to brain damage [10].

The presence of seizure does not constitute a diagnosis but it is a symptom of an underlying central nervous system disorder due to systemic or biochemical disturbances. Among various etiologies birth asphyxia, neonatal meningitis and Biochemical abnormalities are the common etiologies of neonatal seizures. Biochemical abnormalities occur either as an underlying
cause or as an associated abnormality. Early recognition and treatment of these biochemical disturbances is essential for the optimal management and satisfactory outcome. So biochemical abnormalities should be excluded in every case of neonatal seizure in spite of presence of other causes such as meningitis or asphyxia and structural abnormalities. Therefore, this study clinical types importance of biochemical abnormalities in seizures in term and preterm neonates.

2. METHODS

With a level IV evidence, a prospective observational study was performed from 2015 to 2017 in the Department of Pediatrics, Neonatal intensive care unit of Bapuij Child Health & Research Institute and Chigateri General Hospital attached to JJM Medical College, Davangere, Karnataka, India. The cases for this study were recruited by convenient sampling technique. The consecutive 100 with seizures getting admitted to NICU were enrolled for the study.

Neonates with age less than 28 days of life and neonates with seizures irrespective of gestational age & birth weight with at least one of the following clinical type of seizures namely subtle seizures, multifocal clonic seizures, focal clonic seizures, myoclonic seizures and generalized tonic seizures were included in the study. Neonates with doubtful seizures, jitteriness & tetanic spasms and neonates with major congenital malformations.

All neonates admitted with history of seizures were evaluated at the time of admission with appropriate history, epidemiological data, sex of the victim, age of onset, type, duration and number of seizures, consciousness duration and between the seizures were taken. The detailed clinical examination of neonates was done. The detailed antenatal, natal and postnatal history were probed from the mother and documented. The relevant investigations such as complete blood count, sepsis screening (TLC, ANC, immature to total neutrophil ratio, CRP), blood glucose, serum electrolytes (sodium, potassium, calcium, phosphorus & magnesium), metabolic screening (serum ammonia, serum lactate, urine ketones and urine for reducing substance), CSE analysis, neurosonogram, EEG and CT & MRI of brain were done as per the need for the individual cases. A pre structured proforma will be used to record the relevant information from individual case selected for the study.

All cases were taken into consideration for statistical analysis (IBM SPSS Statistics for Windows, Version 20.0, IBM Corp, Chicago, IL). The descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical variables were determined. The association between gestational age and other categorical variables were analyzed using chi-square test of independence. The comparison of mean of various quantitative variables was analyzed using ANOVA test.

3. RESULTS

A total of 100 neonates with neonatal seizures admitted to NICU of 3 hospitals from September 2015 to August 2017 were analyzed according to different characteristics.

In the present study, about 64 neonates were full term of which 49 were AGA [28 (57%) were male and 21(43%) were female] and 15 were SGA [7(47%) cases were male and 8 (53%) cases were females], whereas 36 were preterm [21(58%) cases were male and 15 (42%) cases were females]. In our study, out of 100 babies, 56(56%) were males and 44(44%) were female babies with a male to female ratio of 1.28:1 (as shown in Table 1).

Out of 100 cases, 12 were born at home and 88 were born in hospital. Of the 49 Term AGA, 4 (8%) were home born and 45(92%) were hospital born. Of 15 Term SGA, 3 (20%) cases were home born and 12 (80%) cases were hospital born. Whereas 5(14%) of 36 preterm babies were home born and 31(86%) of 36 preterm babies were hospital born. The association between gestational age and place of delivery were highly insignificant with p value of 0.424.

Out of 100 cases, 47 cases were inborn, and 53 cases were outborn referred to our hospital. Of the 49 Term AGA, 19(39%) were inborn and 30(62%) were outborn. Of 15 Term SGA, 6 (20%) cases were inborn and 9(60%) cases were outborn. Whereas 22(61%) of 36 preterm babies were inborn and 14(39%) of 36 preterm babies were outborn. Of the 53 outborn referred to our hospital, 12 cases were delivered in home and 41 cases were delivered in hospital. The association between gestational age and inborn/outborn were highly insignificant with p value of 0.105. The association between gestational age and mode of delivery were highly
significant with p value of 0.001 (as mentioned in Graph 1).

In the present study, 73 out of 100 cases were spontaneous vaginal deliveries, 22 and 5 cases out of 100 were caesarean section and assisted forceps deliveries respectively. Indication for forceps delivery was prolonged second stage of labor. A total of 22 babies were born to mother with meconium stained amniotic fluid, 16 babies were born to mother with GDM, 3 mothers had fever during third trimester. In the present study, 19 out of 100 were <1.5 kgs, 17 were between 1.5-1.99, 16 were between 2.0-2.49, 41 were between 2.5-2.99 and 7 were between 3.0-3.49 (as mentioned in Table 2).

In the present study, on first day 34 cases developed seizures, 18 cases developed on second day, 7 cases developed on third day, 19 cases developed seizures from 4th-7th day, late on seizures i.e. after 8 days of life constitute 30% (12 of 41 cases). The most common type of seizures were subtle (42 cases), followed by focal clonic (19 cases), multifocal clonic (18 cases), generalized tonic (14 cases), subtle with GTC (4 cases) and subtle with clonic (3 cases). Most common type of seizures in term is subtle (24 of 64 cases) followed by multifocal clonic seizures (12 of 64 cases). Whereas in preterm most common type is subtle (18 of 36 cases) followed by focal clonic seizures (7 of 36 cases). The association between gestational age and type of seizures were highly insignificant with p value of 0.081.

Birth asphyxia and septicemia were the most common causes of neonatal seizures in our study (38 cases each), followed by pure metabolic disturbances were seen in 19 cases, intracranial bleed in 3 cases and unknown etiology in 2 cases. Most common causes of neonatal seizures in term was birth asphyxia (34 of 64 cases) followed by septicemia (20 of 64 cases). Whereas in preterm most common cause was septicemia (18 of 36 cases) followed by pure metabolic disturbance (12 of 36 cases).

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Table 2. Association between gestational age and birth weight

| Birth weight (kg) | Group | Total |
|------------------|-------|-------|
|                  | Preterm (n=36), n (%) | Term AGA (n=49), n (%) | Term SGA (n=15), n (%) |
| <1.5             | 19 (52.8) 0 (0.0) 0 (0.0) | 19                     |
| 1.5-1.99         | 16 (44.4) 0 (0.0) 1 (6.7) | 17                     |
| 2.0-2.49         | 1 (2.8) 1 (2.0) 14 (93.3) | 16                     |
| 2.5-2.99         | 0 (0.0) 41 (83.7) 0 (0.0) | 41                     |
| 3.00-3.49        | 0 (0.0) 7 (14.3) 0 (0.0) 7 |                     |

Chi-Square Test, P Value = <0.001, Significant

On 1st day, 34 cases developed seizures of which 28 were due to birth asphyxia and 4 were due to hypoglycemia, on the 2nd day 18 cases developed seizures of which 8 were due to birth asphyxia and 5 were due to hypoglycemia, 7 cases developed seizures on third day of which hypocalcemia (3 cases) were common. The overall biochemical abnormalities between metabolic and non-metabolic seizures were given in Table 3. A total of 32 neonates of preterm, 29 neonates of term AGA and 14 neonates of term SGA with seizures had biochemical abnormalities in our study.

Of the 52 cases of non-metabolic seizures, which are associated with biochemical abnormalities, hypoglycemia was most common abnormality 23 cases (44.2%). 12 cases (52.1%) were associated with birth asphyxia and 11 cases (47.9%) were associated with septicemia (as shown in Table 4).

The association between etiology and type of seizures were tabulated in Table 5.

In the present study, 18 of 38 cases (16 were term and 2 were preterm) of birth asphyxia are associated with biochemical abnormalities of which 11 cases are associated with hypoglycemia, followed by 5 cases associated with hypocalcemia and 2 cases associated with hyponatremia.

Of 38 cases of sepsis, 22 cases (12 were term and 10 were preterm) are associated with biochemical abnormalities of which 11 cases are associated with hypoglycemia 6 cases are associated hyponatremia and 5 cases were associated with hypocalcemia.

Of the 22 cases of metabolic abnormalities, 11 cases had seizures due to hypoglycemia (6 were preterm and 5 were term) followed by 5 cases due to hypocalcemia (3 were preterm and 2 were term), 2 cases due to hypocalcemia with hypomagnesemia (2 preterm) and 1 case is due to hypomagnesemia (preterm). Of 3 cases of IC Bleed, 1 case is associated with hypocalcemia (33.3%). The association between gestational age and etiology were tabulated in Table 6.

4. DISCUSSION

In the present study, out of 100 neonates with seizures, 64% (64 cases) were full term of which 49 cases (76.5%) were appropriate of gestational age and 15 cases (23.5%) were small for gestational age, whereas 36% (36 cases) were preterm which was similar to the study done by Yadav R K et al. [11]. There is no sex predilection for neonatal seizures. In our study, the male to female ratio of 1.28:1 were observed which was similar to G. Sahana et al. [12] (1.09:1) and Moayedi AR et al. [13] (1.3:1).

In the present study, 19 out of 100 were <1.5 kgs, 17 were between 1.5-1.99, 16 were between 2.0-2.49, 41 were between 2.5-2.99 and 7 were between 3.0-3.49. Jasim M. Marzoki et al. [14] reported that 93.1% were weighting >2500 g, 2.3% were very low birth weight <1500 g and the remaining 2.3% were low birth weight. Lakhra Mahaveer et al. [15] reported similar results on mode of delivery as per our study on neonatal seizures with 73 out of 100 cases are spontaneous vaginal deliveries, 22 and 5 cases out of 100 are caesarean section and assisted forceps deliveries respectively.

In the present study, 59% of cases developed seizures in first three days, 70% of the remaining 41% had seizures in 4th-7th day, late on seizures i.e. after 8 days of life constitute 30%. Azif Aziz et al. [16] reported that 83 neonates (83%) presented with seizures within the first 72 hours of life. Rose et al. [17] also found early onset seizures in 75 (50.33%) babies whereas Coen RW et al. [18] found that 81% of babies had early onset seizures which were similar to our study.
### Table 3. Biochemical abnormalities between metabolic and non-metabolic seizures

| Etiology          | Biochemical abnormalities | Total |
|-------------------|---------------------------|-------|
|                   | Hyponatraemia | Hypernatraemia | Hypoglycaemia | Hypophosphatemia | Hypomagnesaemia | Hypocalcaemia |
| Metabolic         | 0 (0.0)       | 0 (0.0)        | 11 (47.8)     | 4 (17.4)         | 3 (13.0)        | 5 (21.7)      | 23 (100)     |
| Non-Metabolic     | 2 (3.8)       | 6 (11.5)       | 23 (44.2)     | 8 (15.4)         | 1 (1.9)         | 12 (23.1)     | 52 (100)     |
| Total             | 2 (2.7)       | 6 (8.0)        | 34 (45.3)     | 12 (16)          | 4 (5.3)         | 17 (22.7)     | 75 (100)     |
| P Value           | 0.340         | 0.089          | 0.773         | 0.827            | 0.048           | 0.898         |              |

### Table 4. Distribution of non-metabolic seizures with respect to biochemical abnormalities

| Etiology   | Biochemical abnormalities | Total |
|------------|---------------------------|-------|
|            | Hyponatraemia | Hypernatraemia | Hypoglycaemia | Hypophosphatemia | Hypomagnesaemia | Hypocalcaemia |
| Birth Asphyxia (n=38) | 2 (5.3)     | 0 (0.0)        | 12 (31.6)     | 2 (5.3)          | 1 (2.6)         | 4 (10.5)      | 21           |
| IC Bleed (n=3)     | 0 (0.0)       | 0 (0.0)        | 0 (0.0)       | 0 (0.0)          | 0 (0.0)         | 1 (33.3)       | 1            |
| Septicemia (n=38)  | 0 (0.0)       | 6 (15.8)       | 11 (28.9)     | 6 (15.8)         | 0 (0.0)         | 7 (18.4)       | 30           |


Table 5. Association between etiology and type of seizures (n = 100)

| Etiology                  | Focal clonic | Generalised clonic | Multifocal clonic | Subtle | Subtle + clonic | Subtle + generalised clonic | Total |
|---------------------------|--------------|--------------------|-------------------|--------|----------------|-----------------------------|-------|
| BA/ Hypocalcemia          | 3 (60.0)     | 0 (0.0)            | 0 (0.0)           | 2 (40.0)| 0 (0.0)        | 0 (0.0)                     | 5     |
| BA/ Hypoglycemia          | 2 (18.2)     | 1 (9.1)            | 1 (9.1)           | 7 (63.6)| 0 (0.0)        | 0 (0.0)                     | 11    |
| BA/ Hyponatremia          | 0 (0.0)      | 1 (50.0)           | 1 (50.0)          | 0 (0.0) | 0 (0.0)        | 0 (0.0)                     | 2     |
| Birth Asphyxia            | 2 (10.0)     | 2 (10.0)           | 3 (15.0)          | 8 (40.0)| 2 (10.0)       | 3 (15.0)                    | 20    |
| Hypocalcemia              | 0 (0.0)      | 1 (20.0)           | 3 (60.0)          | 1 (20.0)| 0 (0.0)        | 0 (0.0)                     | 5     |
| Hypocalcemia+             | 2 (100.0)    | 0 (0.0)            | 0 (0.0)           | 0 (0.0) | 0 (0.0)        | 0 (0.0)                     | 2     |
| Hypoglycemia              | 0 (0.0)      | 0 (0.0)            | 0 (0.0)           | 11 (100.0)| 0 (0.0)       | 0 (0.0)                     | 11    |
| Hypomagnesemia            | 1 (100.0)    | 0 (0.0)            | 0 (0.0)           | 0 (0.0) | 0 (0.0)        | 0 (0.0)                     | 1     |
| IC Bleed                  | 0 (0.0)      | 1 (33.3)           | 0 (0.0)           | 1 (33.3)| 1 (33.3)       | 0 (0.0)                     | 3     |
| Septicemia                | 6 (37.5)     | 0 (0.0)            | 5 (31.3)          | 4 (25.0)| 0 (0.0)        | 1 (6.3)                     | 16    |
| Septicemia/ Hypernatremia | 1 (16.7)     | 3 (50.0)           | 1 (16.7)          | 1 (16.7)| 0 (0.0)        | 0 (0.0)                     | 6     |
| Septicemia/ Hypocalcemia  | 1 (20.0)     | 1 (20.0)           | 1 (20.0)          | 2 (40.0)| 0 (0.0)        | 0 (0.0)                     | 5     |
| Septicemia/ Hypoglycemia  | 1 (9.1)      | 4 (36.4)           | 3 (27.3)          | 3 (27.3)| 0 (0.0)        | 0 (0.0)                     | 11    |
| Unknown                   | 0 (0.0)      | 0 (0.0)            | 0 (0.0)           | 2 (100.0)| 0 (0.0)       | 0 (0.0)                     | 2     |

Chi-Square Test, P Value = 0.082, Not Significant
Table 6. Association between gestational age and etiology

| Etiology                      | Preterm (n=36), n (%) | Term AGA (n=49), n (%) | Term SGA (n=15), n (%) | Total |
|-------------------------------|-----------------------|------------------------|------------------------|-------|
| BA/Hypercalcemia              | 0 (0.0)               | 3 (6.1)                | 2 (13.3)               | 5     |
| BA/Hypoglycemia               | 2 (5.6)               | 8 (16.3)               | 1 (6.7)                | 11    |
| BA/Hyponatremia               | 0 (0.0)               | 2 (4.1)                | 0 (0.0)                | 2     |
| Birth Asphyxia                | 2 (5.6)               | 16 (32.7)              | 2 (13.3)               | 20    |
| Hypocalcemia                  | 3 (8.3)               | 1 (2.0)                | 1 (6.7)                | 5     |
| Hypocalcemia+                 | 2 (5.6)               | 0 (0.0)                | 0 (0.0)                | 2     |
| Hypomagnesemia                |                       |                        |                        |       |
| Hypoglycemia                  | 6 (16.7)              | 2 (4.1)                | 3 (20.0)               | 11    |
| Hypomagnesemia                | 1 (2.8)               | 0 (0.0)                | 0 (0.0)                | 1     |
| IC Bleed                      | 2 (5.6)               | 1 (2.0)                | 0 (0.0)                | 3     |
| Septicemia                    | 8 (22.2)              | 6 (12.2)               | 2 (13.3)               | 16    |
| Septicemia/ Hyponatremia      | 2 (5.6)               | 3 (6.1)                | 1 (6.7)                | 6     |
| Septicemia/ Hypocalcaemia     | 3 (8.3)               | 0 (0.0)                | 2 (13.3)               | 5     |
| Septicemia/ Hypoglycemia      | 5 (13.9)              | 5 (10.2)               | 1 (6.7)                | 11    |
| Unknown                       | 0 (0.0)               | 2 (4.1)                | 0 (0.0)                | 2     |

Chi-Square Test, P Value = 0.052, Not Significant
Subtle seizures (42 cases) were most common type of seizures in our study, followed by focal clonic (19 cases), multifocal clonic (18 cases), generalized tonic (14 cases), subtle with GTC (4 cases) and subtle with clonic (3 cases) in our study. A.R. Moayedi et al. [13], A.L. Bairwa et al. [19] and Martinez et al. [20] also reported that commonest neonatal seizure were subtle seizures. Among non-metabolic seizures, which are associated with biochemical abnormalities, hypoglycemia was most common abnormality observed. Arvind Sood et al. [21] and Ericksson Met et al. [22] showed that hypoglycemia was the most common biochemical abnormality associated with birth asphyxia followed by hypocalcemia, hypomagnesemia and hyponatremia [23-27].

Birth asphyxia and septicemia were the most common cause of neonatal seizures in our study, followed by pure metabolic disturbances in 19 cases, intracranial bleed in 3 cases and unknown etiology in 2 cases. The results were compared with studies of Jin et al, Malik et al and Park et al. Birth asphyxia was the commonest cause in all the studies which is similar to our study, followed by septicemia / meningitis, metabolic abnormalities. The pure metabolic seizures were seen in 23 cases. Most common cause of metabolic seizures is due to hypoglycemia followed by hypocalcemia, hypophosphatemia and hypomagnesemia which was comparable to the study done by Lilien Lawrence D et al. [30] and Singhal PK et al. [31]. Hypoglycemia is more common in preterm babies as there is depletion of glycogen storage and inadequate feeding during early postnatal days. Hypoglycemic seizures were most commonly seen in first 3 days. The diagnosis of hypoglycemia should not be delayed as it can lead to significant brain damage.

Hypocalcemia should be diagnosed early and treated with IV calcium. In a study by Cockburn F et al. [32] serum calcium was low in neonates who were top fed then the babies who were breastfed. Cockburn F et al. [32] showed hypomagnesemia with hypocalcemia was common in top fed baby with cow’s milk. However, our babies were exclusively breastfed. The deficiency of magnesium can lead to convulsive disorder with permanent neurologic impairment. In neonates, transient hypomagnesemia is known to occur in toxemic and diabetic mother or in IUGR babies or with transient hypoparathyroidism. Acute intravenous loading of calcium increases renal excretion of magnesium and thus aggravates the hypomagnesemia and maintains the convulsive state. On the other hand, an increased

In our study, on 1st day, 34 cases developed seizures of which 28 cases (82.35%) were due to birth asphyxia which were comparable to the studies done by Aziz A et al. [16], Rose et al. [17] and Coen RW et al. [18] Birth asphyxia usually presents with seizures within first three days of life. Hypoglycemia presents on second and third day. Hypocalcemia presents on first and second day or in late first week and second week. Neonatal meningitis usually presents in late first week and second week.

In the present study, biochemical abnormalities were seen in 75 cases, of which 52 (69.3%) were non-metabolic and 23 (30.6%) were pure metabolic seizures. The most common biochemical abnormality in neonatal seizures was hypoglycemia (45.3%) followed by hypocalcemia (22.7%). Among pure metabolic abnormalities, most common abnormality was hypoglycemia followed by hypocalcemia, hypophosphatemia and hypomagnesemia. In the present study, biochemical abnormalities were seen in 75 cases, of which 52 (69.3%) were non-metabolic and 23 (30.6%) were pure metabolic seizures. The most common biochemical abnormality in neonatal seizures was hypoglycemia (45.3%) followed by hypocalcemia (22.7%). Among pure metabolic abnormalities, most common abnormality was hypoglycemia followed by hypocalcemia, hypophosphatemia and hypomagnesemia.

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Table 7. Comparison of biochemical abnormalities in neonatal seizures

| Biochemical parameters | Kumar et al. [28] (n=35) | Arvind Sood et al. [26] (n=59) | Madhusudhan et al. [29] (n=120) | Present study (n=100) |
|------------------------|--------------------------|-------------------------------|--------------------------------|----------------------|
| Hyponatremia           | 10                       | 5                             | 19                             | 2                    |
| Hypoglycaemia          | 11                       | 14                            | 17                             | 34                   |
| Hypocalcaemia          | 7                        | 14                            | 11                             | 17                   |
| Hypomagnesemia         | 3                        | 5                             | 1                              | 2                    |
| Hypocalcemia +         | 0                        | 0                             | 1                              | 2                    |
| Hyponatremia           | 0                        | 0                             | 3                              | 6                    |
| Hypophosphatemia       | 0                        | 0                             | 0                              | 12                   |
| Hypermagnesemia        | 1                        | 0                             | 0                              | 0                    |
| Hyperphosphatemia      | 3                        | 0                             | 0                              | 0                    |
Table 8. Comparison of biochemical abnormalities in primary metabolic seizures

| Biochemical abnormalities | Kumar et al. [28] (n=9) | Arvind Sood et al. [26] (n=10) | Madhusudhan et al. [29] (n=23) | Present study (n=23) |
|---------------------------|--------------------------|-------------------------------|-------------------------------|---------------------|
| Hyponatremia              | 1                        | 0                            | 1                            | 0                   |
| Hypoglycaemia             | 5                        | 4                            | 12                           | 11                  |
| Hypocalcaemia             | 5                        | 7                            | 5                            | 5                   |
| Hypermagnesemia           | 1                        | 3                            | 1                            | 1                   |
| Hypocalcemia +            | 0                        | 0                            | 1                            | 2                   |
| Hypermagnesemia           | 0                        | 0                            | 3                            | 0                   |
| Hyperphosphatemia         | 2                        | 1                            | 0                            | 0                   |
| Hypophosphatemia          | 0                        | 0                            | 0                            | 4                   |

Magnesium in patients with hypocalcemia and hypomagnesemia results in an increase in ionized calcium. Thus, administration of magnesium in infants with hypocalcemia and hypomagnesemia is likely to correct both conditions.

In our study, 3 babies had neonatal seizures and were diagnosed as IVH on neurosonogram of which 2 cases were preterm and one case was term baby. Preterm babies are prone for intraventricular hemorrhage because of fragile blood vessels and ineffective supporting structures for periventricular blood vessels.

5. CONCLUSION

In conclusion, identifying the etiology of neonatal seizures is often helpful with respect to treatment and for a better outcome.

- The most common etiology of neonatal seizures is birth asphyxia. Seizures during first 3 days of life has significant correlation with birth asphyxia.
- Subtle seizures are commonest type of clinical seizures, which is difficult to identify, therefore careful observation of at-risk neonates is necessary.
- Biochemical abnormalities are commonly observed as underlying cause or associated in neonatal seizures. Recognition of associated biochemical abnormalities is crucial in managing neonatal seizures. Early recognition and correction of these abnormalities play a significant role in seizures control and better outcome.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Ethical approval was taken from department of Forensic Medicine, JJM Medical College.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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