

Clinico-Etiological Profile Of Neonatal Seizures

Lobna A. Mansour¹, Reem N. Said¹, Marian Y. Fahmy¹, Hadeel M. Seif El Din¹, Zenab A.A. Abdel-Raheman¹

¹. Departments of Pediatrics and Radiology, Faculty of Medicine, Cairo University

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Abstract

Background Neonatal seizures are a paroxysmal alteration in neurologic functions (i.e. behavioral, motor or autonomic functions). The incidence of seizures is higher in the neonatal period than in any other age group. There are multiple causes of seizures presenting with many patterns and necessitating choice of anticonvulsant drugs. Serial ultrasound examination is very important for diagnosis of brain injury. **Objectives** To focus on the etiology and clinical classification of neonatal "convulsions" thus proper assessment for appropriate diagnosis and proper management. **Patients and methods** This prospective study was performed on 60 neonatal patients who developed neonatal seizures either prior or after admission to the NICU of Abul-Reesh and Kasr EL Aini Hospital below the age of 28 days. **Results** Birth weight was not a risk factor for increased morbidity or mortality among babies suffering from seizures. Majority of neonates with seizures were full-term (60%), while (28.3%) babies were preterm and (11.7%) babies were post-term. Our results found a relation between gender and the occurrence of seizures. The incidence of mortality was 25 cases (41.7%). There was statistically significant correlation between the presence of jaundice and the presence of abnormalities on cranial ultrasound. Burst suppression pattern was more common in (grade III) HIE, while multifocal spike pattern, positive sharp Rolandic waves and periodic low voltage activity patterns were more common in (grade II) HIE. **Conclusion** GA, birth weight, gender, route of delivery did not distinguish which infant with neonatal seizures would have a poor prognosis. Hypoxic ischemic encephalopathy was the major cause of neonatal seizures.

Key Words: Clinical profile, brain excitation, neonatal seizure

INTRODUCTION

Neonatal Seizures (NS) are the most frequent and distinctive clinical manifestation of neurological dysfunction in the newborn. Infants with neonatal seizures are at a high risk of neonatal death or neurological impairment/epilepsy disorders in later life ⁽¹⁾.

Though mortality due to etiology of NS has decreased from 40% to about 20% over the years, the prevalence of long-term neurodevelopment sequelae has largely remained unchanged at around 30%. Improper and inadequate management of seizures could be one of the major reasons behind this phenomenon ⁽²⁾.

The National Neonatal Perinatal Database (NNDP; 2002-03), which collected data from 18 tertiary care units across the country, has reported an incidence of 10.3 per 1000 live-births. 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) ⁽²⁾.

The decreased seizure threshold in the newborn is due to transient overdevelopment of excitatory systems compared to inhibitory systems ⁽²⁾.

Broadly speaking, neonatal seizures diagnosis can be categorized into: Etiological, Clinical, and Electroencephalographic (EEG) diagnosis. The etiologies of neonatal seizures ordered according to their incidence are [Cerebral hypoxia-ischemia (55%), Intracranial hemorrhage (15%), Metabolic diseases (6%), Central nervous system infection (5%), Cerebral dysgenesis (5%), Neonatal epileptic syndromes (1%), Neonatal abstinence syndrome (1%), and Unknown cause (10%)] ⁽²⁾.

The clinical neonatal seizures types can be classified into four groups: Subtle seizures, clonic seizures, Tonic seizures, and Myoclonic seizures ⁽³⁾.

By definition, an electrographic seizure is a repetitive series of electrical discharges that evolves in frequency, amplitude, and topographic field ⁽⁴⁾.

Cranial ultra-sonography (CUS) is frequently used for the diagnosis of major cerebral lesions (MCL) during the early neonatal period ⁽⁵⁾. Although (CUS) is a useful and minimally invasive, a study on 42 preterm neonates

suffering from neonatal seizures was performed at Essen University Hospitals showed that (MCL) appeared in 28.5% of cases <7 days of life & in 71.5% of cases >7days of life, so several days or few weeks are required for the brain insult to become evident on (CUS) (6).

It is critical to recognize neonatal seizures, to determine their etiology, and to treat them for three major reasons. First, the seizures are usually related to significant illness, sometimes requiring specific therapy. Second, neonatal seizures may interfere with important supportive measures, such as alimention and assisted respiration for other associated disorders frequently present in neonates. Third, experimental data give reason for concern that the seizures per se may be a cause of brain injury and mental retardation and/or cognitive delay (7).

The aim of this work is to: To focus on the etiology and clinical classification of neonatal seizures .

Patients and Methods

This prospective study was performed on 60 neonatal patients who developed neonatal seizures either prior or after admission to the NICU of Abul-Reesh and Kasr EL Aini Hospital below the age of 28 days after an informed written consent from parents in the period between May 2014 and May 2015.

Inclusion criteria

Any full-term > 37 weeks or pre-term neonates manifested by more than one attack of seizure.

Exclusion criteria

1. Any baby above 28 days of age.
2. Conditions that mimic neonatal seizures such as jitteriness and benign neonatal sleep myoclonus.

Methods

All babies were subjected to

1. Full maternal history

Age, acute or chronic medical problems as diabetes mellitus, hypertension, thyroid disease, renal disease, urinary tract diseases, heart and lung disease, and blood disease), and medications.

2. Neonatal history

Gestational age, sex, birth weight, mode of delivery, full anthropometric measurement, prenatal risk factors, assessment of seizure type, duration, age of onset and frequency, neonatal illness, oxygen supply, nutrition, and medications.

3. Family history

Asking about consanguinity, other sibling with neonatal seizure and similar condition, history of abortion or previous death.

4. General examination

- a. Apgar score.
- b. Vital signs (heart rate, respiratory rate, temperature and capillary perfusion time).
- c. Gestational age assessment by Ballard scoring system.

5. Local examination

Head and neck, limbs, skin, back, genitalia, birth injuries.

6. Systemic examination

- a. **Cardiac examination** Central cyanosis, murmur, tachycardia or bradycardia.
- b. **Chest examination** Chest movement, cyanosis, air entry, and auscultatory finding.
- c. **Abdominal examination** distension, liver and spleen enlargement.
- d. **Neurological examination** Standardized neurologic examination was performed for all neonates within 24h after birth. Serial neurological examinations were done later during their period of stay using Sarnat and Sarnat staging for diagnosing hypoxic ischemic encephalopathy including; level of consciousness, muscle tone, neonatal reflexes and presence of seizures (type and duration).

7. Laboratory investigations

First line investigations were done in all neonates included blood glucose, serum electrolytes (calcium, sodium, magnesium, potassium and phosphorus), complete blood count, c-reactive protein, arterial blood gases and CSF for any evidence of infection.

Second line investigations e.g. blood culture, serum urea/creatinine, liver function tests, ammonia, lactate, organic acid profile, ketones in urine and tandem mass spectrometry were done in selected neonates as guided by history, physical examination and essential investigations suspected to have metabolic disorder.

8. Cranial ultrasound (CUS)

At least one imaging examination during the neonatal period was performed using a standardized protocol for screening of major cranial U.S lesions was performed through the anterior fontanel to obtain

standard coronal, sagittal, para-sagittal images using a portable sectorial ultrasound apparatus (Siemens/Adara Somoline) with a transducer of (5 and 7.5) MHZ.

9. Electroencephalogram (EEG)

It was done by using a (Nihon Kohden 910A) digital EEG machine with recording duration of (5-10) min. Cerebral electrodes were placed according to the modified international 10/20 system. Various montages were used with unipolar and bipolar recording channels covering 11 cerebral anatomic regions (Lt and Rt frontopolar, temporal, parietal and occipital midline electrodes) as well as (frontal, central and occipital midline electrodes). The EEG was analyzed by an experienced electro-encephalographer.

Statistical analysis

Statistical analyses in this study were described in terms of: frequencies (number of cases), percentage, mean and standard deviation.

Comparison of quantitative variables between the study groups was done using

1. Chi-square test for comparing categorical data.
2. Statistical significance is achieved when the probability value (p-value) is less than or equal (\leq) 0.001).

All statistical calculations were done using computer programs Microsoft Excel 2003 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for Social Science; SPSS Inc. Chicago, IL, USA) version 15 for Microsoft windows.

Results

In tables (1) and (2), neonatal seizures were more common in males [32 (53.3%)] than females [28 (46.7%)]; their mean birth weight was 2748 grams; among this group of study, 50% were delivered vaginally. In addition, thirty five neonates (58.3%) were alive, and 25 (41.7%) died. 50% of patients of the study were complaining of perinatal asphyxia evidenced by history of prolonged or instrumental labor, and 28 babies (46.7%) with sepsis.

In the present study, out of 60 babies, 36(60%) were full term, 17(28.3%) babies were preterm and 7(11.7%) babies were post-term.

Concerning weight; 36 babies were above 2500gm comprising (60%), and 24 babies (40%) were below 2500gm

Regarding history of previous neonatal deaths, 9 (15%) mothers gave history of losing other babies in their neonatal period, 6 (10%) mothers gave history of previous abortion. There was one (1.7%) neonate with positive family history of neonatal seizures. there were 13 (21.6%) babies of consanguineous marriage among these 60 cases.

In table (3), regarding Level of consciousness in the studied group, the majority of babies were lethargic constituting (48.3%) of the cases, 13 babies deteriorated and 2 babies entered in coma.

For primitive neonatal reflexes; Moro and grasping reflexes were weak in 11 babies (18.3%), and absent in 19 babies (31.6%). Poor suckling was observed in 32 cases (53.3%).

In relation to deep reflexes; 43 babies (71.7%) presented with hyporeflexia, and 9 babies (15%) presented with hyperreflexia.

Concerning Tone; most of the babies in our study presented with hypotonia 34 cases (56.7%), and 21 (35%) babies were hypertonic.

The most common type of seizures observed were myoclonic 22(36.7%), followed by mixed type 17(28.3%), subtle 10(16.7%), clonic and tonic with a percent (8.3%) each. Only one baby had multifocal clonic type of seizure.

Duration of seizures in the neonates ranges between <3 minutes in 43 (71.7%) and \geq 3 minutes in 17 (28.3%) neonates.

Frequency of seizures in the neonates in this study ranges between <5 times/day in 35 babies (58.3%) and \geq 5 times/day in 25 babies (41.7%).

In table (4), myoclonic seizures were the most common type seen in the first day of life in 14 neonates (63.3%), and in 8 neonates (36.4%) in the period between day 2 to one week followed by mixed type in 8 neonates(47.1%)in the first day and 9 cases (52.9%) between day 2 to one week. Subtle seizures were present in 4 cases(40%) in the first day of life, clonic and tonic types presented in equal ratios (60%) whereas subtle type was seen later after one week in one case. There is no significant difference between type of seizure and time of onset.

The age of onset of seizures ranged from day 1 to 8 days, 53% of them began within the first 24 hrs of life. The incidence related to age of onset is presented **in table (5)**, it shows that most of hypoxic-ischemic causes presented during the first day, and only 1 case with sepsis presented after the first week. There is no significant difference between seizure's etiology and time of onset.

The neonatal mortality related to the etiology shows that the highest mortality was between those with intraventricular hemorrhage, metabolic disorders and meningitis (100%) as shown **in table (6)**.

Table (7) shows that all cases diagnosed with hypocalcaemia & sepsis are completely normal on discharge while only 3 (25%) neonates with hypoxic ischemic encephalopathy after treatment are normal on discharge. On contrary, 7(58.3%) neonates with hypoxic ischemic encephalopathy, 2(66.7%) with intracranial hemorrhage and only one diagnosed with Kernicterus had global developmental delay. Furthermore, 5 neonates had cerebral palsy; 2 neonates with hypoxic ischemic encephalopathy, 2 with kernicterus and one with intracranial hemorrhage.

In table (8) normal EEG pattern was most seen in 9(90%) cases with sepsis, 6(75%) cases with hypocalcemia and in only(12.5%)of the hypoxic ischemic cases.

Positive sharp Rolandic waves pattern was common in (20.8%) cases with hypoxic ischemic encephalopathy, (37.5%) withintraventricular hemorrhage and (50%) with intracranial hemorrhage.

Burst suppression pattern was seen in (25%) neonates with hypoxic encephalopathy, in (50%) withintraventricular hemorrhage& metabolic disorders each, and in (10%) with sepsis

Multiple polyspike pattern was seen in most seizure etiologies in this study in ratios; (25%) in hypoxic ischemic encephalopathy, (33.3%) in Kernicterus, (100%) in meningitis, (50%) metabolic disorders, (25%) in intracranial hemorrhage and (12.5%) in hypocalcaemia

High voltage delta activity pattern was seen only in one neonate diagnosed with Kernicterus with (66.7%) ratio

Persistent marked voltage suppression was seen in ratios (4.16%) & (25%) in hypoxic ischemic encephalopathy and intracranial hemorrhage respectively. Also, isoelectric background pattern was seen in one neonate with intraventricular hemorrhage with (12.5%) ratio.

Table (9) showed that burst suppression pattern was more common in (grade III) HIE, while multifocal spike pattern, positive sharp Rolandic waves and periodic low voltage activity patterns were more common in (grade II) HIE.

In table (10) there is a statistical significant difference between seizure types, level of consciousness and the fate of included patients

Concerning seizure types; myoclonic seizure was the most common type of seizure seen in cases who died while mixed type was the most in discharged patients.

Regarding level of consciousness, most cases who died in this study presented with disturbed conscious level, while most neonates who were discharged were lethargic.

There is a statistical significant difference between metabolic acidosis and the poor outcome (**table 11**).

In table (12) there was statistically significant correlation between the presence of jaundice and poor tone on clinical examination and the presence of abnormalities on cranial ultrasound.

Table (1) Demographic characteristics of neonates with seizures in this study

| Variables | | Count | Column N % |
|---------------|--------------|-------|------------|
| Sex | F | 28 | 46.7% |
| | M | 32 | 53.3% |
| Weight | <= 2500 g | 24 | 40.0% |
| | >2500g | 36 | 60.0% |
| GA | FT (37-40w) | 36 | 60.0% |
| | POST (>40w) | 7 | 11.7% |
| | PT (<or=35w) | 17 | 28.3% |
| Consanguinity | No | 47 | 78.3% |
| | Yes | 13 | 21.7% |

MOD=mode of delivery NVD=normal vaginal delivery CS=cesarean section F=female M=male
GA=gestational ageFT=full termPT=pre term POST=post term

Table (2) Risk Factors of all neonates included in the study

| Variables | No | % |
|-------------------------------------|----|-------|
| Sex | | |
| Males | 32 | 53.3% |
| Females | 28 | 46.7% |
| Mode of delivery | | |
| NVD | 30 | 50% |
| CS | 30 | 50% |
| Perinatal asphyxia | 24 | 40% |
| Sepsis | 28 | 46.7% |
| Consanguinity | 13 | 21.7% |
| Family history of Neonatal seizures | 1 | 1.7% |

NVD: normal vaginal delivery CS: cesarean section

Table (3) Neurological examination of all patients included in the study

| Variables | | No | % |
|------------------------|---------------------------|----|-------|
| Seizure type | focal clonic | 5 | 8.3% |
| | Multifocal clonic | 1 | 1.7% |
| | mixed | 17 | 28.3% |
| | myoclonic | 22 | 36.7% |
| | subtle | 10 | 16.7% |
| | tonic | 5 | 8.3% |
| Seizure duration | <3 minutes | 43 | 71.7% |
| | >=3 minutes | 17 | 28.3% |
| Seizure Frequency | <5 times/day | 35 | 58.3% |
| | >= 5 times/day | 25 | 41.7% |
| Neonatal Reflexes | weak | 11 | 18.3% |
| | absent | 19 | 31.6% |
| Deep Reflexes | hyperreflexia | 9 | 15% |
| | hyporeflexia | 43 | 71.7% |
| | normal | 8 | 13.3% |
| Muscle Tone | hypertonia | 21 | 35.0% |
| | hypotonia | 34 | 56.7% |
| | normotonia | 5 | 8.3% |
| Level of consciousness | Coma | 2 | 3.3% |
| | Conscious | 16 | 26.7% |
| | Disturbed conscious level | 13 | 21.7% |
| | Lethargy | 29 | 48.3% |

Table (4) Relation between seizure types of 60 NICU cases and time of onset

| | | | Age of onset | | | Total | |
|--------------|-------------------|-------|--------------|-------------|----------|---------|---------|
| | | | D1 | D2 – Week 1 | > Week 1 | | |
| Seizure Type | Myoclonic | Count | 14 | 8 | 0 | 22 | |
| | | % | 63.6% | 36.4% | 0.0% | 100.00% | |
| | Mixed | Count | 8 | 9 | 0 | 17 | |
| | | % | 47.1% | 52.9% | 0.0% | 100.00% | |
| | Subtle | Count | 4 | 5 | 1 | 10 | |
| | | % | 40.0% | 50.0% | 10.0% | 100.00% | |
| | Focal clonic | Count | 3 | 2 | 0 | 5 | |
| | | % | 60.0% | 40.0% | 0.0% | 100.00% | |
| | Tonic | Count | 3 | 2 | 0 | 5 | |
| | | % | 60.0% | 40.0% | 0.0% | 100.00% | |
| | Multifocal clonic | Count | 0 | 1 | 0 | 1 | |
| | | % | 0.0% | 100.0% | 0.0% | 100.00% | |
| | Total | | Count | 32 | 27 | 1 | 60 |
| | | | % | 53.30% | 45.00% | 1.67% | 100.00% |

Fisher's Exact P-value=0.649

Table (5) Seizure's etiology as regard to time of onset for 60 NICU cases

| Etiology | | Age of onset | | | Total |
|---------------|--------|--------------|---------------|---------|---------|
| | | Day1 | Day 2 - Week1 | > Week1 | |
| HIE | Number | 17 | 7 | 0 | 24 |
| | % | 70.8% | 29.2% | 0.0% | 100.00% |
| Hypocalcaemia | Number | 5 | 3 | 0 | 8 |
| | % | 62.5% | 37.5% | 0.0% | 100.00% |
| ICH | Number | 2 | 2 | 0 | 4 |
| | % | 50.0% | 50.0% | 0.0% | 100.00% |
| IVH | Number | 5 | 3 | 0 | 8 |
| | % | 62.5% | 37.5% | 0.0% | 100.00% |
| Kernicterus | Number | 0 | 3 | 0 | 3 |
| | % | 0.0% | 100.0% | 0.0% | 100.00% |
| Meningitis | Number | 0 | 1 | 0 | 1 |
| | % | 0.0% | 100.0% | 0.0% | 100.00% |
| Metabolic | Number | 0 | 2 | 0 | 2 |
| | % | 0.0% | 100.0% | 0.0% | 100.00% |
| Sepsis | Number | 3 | 6 | 1 | 10 |
| | % | 30.0% | 60.0% | 10.0% | 100.00% |
| | Number | 32 | 27 | 1 | 60 |
| | % | 53.30% | 45.00% | 1.67% | 100.00% |

Fisher's Exact P-value=0.094

Table (6) Seizure's Etiology as regard to fate

| Etiology | | Fate | | Total |
|---------------|-------|--------|-----------|--------|
| | | Death | Discharge | |
| HIE | Count | 12 | 12 | 24 |
| | % | 50.0% | 50.0% | 100.0% |
| Hypocalcaemia | Count | 0 | 8 | 8 |
| | % | 0.0% | 100.0% | 100.0% |
| ICH | Count | 1 | 3 | 4 |
| | % | 25.0% | 75.0% | 100.0% |
| IVH | Count | 8 | 0 | 8 |
| | % | 100.0% | 0.0% | 100.0% |
| Kernicterus | Count | 0 | 3 | 3 |
| | % | 0.0% | 100.0% | 100.0% |
| Meningitis | Count | 1 | 0 | 1 |
| | % | 100.0% | 0.0% | 100.0% |
| Metabolic | Count | 2 | 0 | 2 |
| | % | 100.0% | 0.0% | 100.0% |
| Sepsis | Count | 1 | 9 | 10 |
| | % | 10.0% | 90.0% | 100.0% |
| Total | Count | 25 | 35 | 60 |
| | % | 41.7% | 58.3% | 100.0% |

Fisher's Exact P-value <0.001

Table (7) Relation between outcome of discharged cases and etiology of seizures

| Etiology | Normal | Global developmental Delay | Cerebral palsy |
|---------------------------------|---------|----------------------------|----------------|
| Hypoxic ischemic Encephalopathy | 3(25%) | 7(58.3%) | 2(16.7%) |
| Sepsis | 9(100%) | 0 | 0 |
| Hypocalcaemia | 8(100%) | 0 | 0 |
| Intracranial Hemorrhage | 0 | 2(66.7%) | 1(33.3%) |
| Kernicterus | 0 | 1(33.3%) | 2(66.7%) |

Table (8) Relation between EEG pattern and etiology of seizures

| EEG pattern | HIE | Sepsis | Hypocalcemia | ICH | IVH | Metabolic disorder | Menigitis | Kernicterus |
|--|----------|--------|--------------|--------|----------|--------------------|-----------|-------------|
| Normal | 3(12.5%) | 9(90%) | 6(75 %) | 0 | 0 | 0 | 0 | 0 |
| Positive sharp waves | 5(20.8%) | 0 | 0 | 2(50%) | 3(37.5%) | 0 | 0 | 0 |
| Excessive sharp Waves activity | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Periodic low Voltage activity | 3(12.5%) | 0 | 1(12.5%) | 0 | 0 | 0 | 0 | 0 |
| Multiple poly sp Pattern | 6(25%) | 0 | 1(12.5%) | 1(25%) | 0 | 1(50%) | 1(100%) | 2(33.3 %) |
| Gross asynchrony/ High voltage de activity | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1(66.7%) |
| Persistent marked Voltage suppression | 1(4.16%) | 0 | 0 | 1(25%) | 0 | 0 | 0 | 0 |
| Burst suppression Pattern | 6(25%) | 1(10%) | 0 | 0 | 4(50%) | 1(50%) | 0 | 0 |
| Isoelectric Background pat | 0 | 0 | 0 | 0 | 1(12.5%) | 0 | 0 | 0 |

Table (9) Relation between EEG pattern and encephalopathy grading in 24 cases diagnosed with ischemic encephalopathy

| EEG pattern | GradeII | GradeIII |
|--|---------|----------|
| Normal | 3 | 0 |
| Positive sharp Rolandic waves | 4 | 1 |
| Excessive sharp waves activity | 0 | 0 |
| Periodic low voltage activity | 3 | 0 |
| Multifocal spike pattern | 6 | 0 |
| Gross asynchrony/High voltage Delta activity | 0 | 0 |
| Persistent marked voltage suppression | 0 | 1 |
| Burst suppression pattern | 0 | 6 |
| Isoelectric background pattern | 0 | 0 |

Encephalopathy grading according to Sarnat and Sarnat, 1976

Table (10) Comparison between clinical pictures of patients included in the study as regard to their outcome

| | | Fate | | | | Fisher's Exact P-value |
|------------------------|---------------------------|-------|-------|-----------|-------|------------------------|
| | | Death | | Discharge | | |
| | | Count | % | Count | % | |
| Seizure Type | Myoclonic | 13 | 59.1% | 9 | 40.9% | <0.001 |
| | Mixed | 5 | 29.4% | 12 | 70.6% | |
| | Subtle | 1 | 10% | 9 | 90.0% | |
| | Focal clonic | 0 | 0.0% | 5 | 100% | |
| | Tonic | 5 | 100% | 0 | 0.0% | |
| | Multifocal clonic | 1 | 100% | 0 | 0.0% | |
| Level Of Consciousness | Conscious | 1 | 6.3% | 15 | 93.8% | |
| | Disturbed Conscious level | 12 | 92.3% | 1 | 7.7% | |
| | Lethargy | 10 | 34.5% | 19 | 65.5% | |
| | Coma | 2 | 100% | 0 | 0.0% | |
| Tone | hypertonia | 5 | 23.8% | 16 | 76.2% | 0.099 |
| | hypotonia | 17 | 50.0% | 17 | 50.0% | |
| | normotonia | 3 | 60.0% | 2 | 40.0% | |
| Deep Reflexes | hyperreflexia | 2 | 45.0% | 8 | | 0.765 |
| | hyporeflexia | 20 | | 23 | | |
| | normoreflexia | 3 | 42.9% | 4 | 57.1% | |

Table (11) Outcome of patients included in the study and the results of their investigations

| variables | | Discharged | | Died | | Fisher's exact P-value |
|-----------------------|---------------------|------------|------|------|------|------------------------|
| | | No | % | No | % | |
| Metabolic acidosis | uncompensated | 1 | 2.8 | 19 | 76 | 0.001 |
| | compensated | 20 | 57.1 | 4 | 16 | |
| | normal | 14 | 40 | 2 | 8 | |
| Calcium | low | 9 | 25.7 | 4 | 16 | 0.593 |
| | normal | 26 | 74.3 | 21 | 84 | |
| sodium | high | 11 | 31.4 | 5 | 20 | 0.436 |
| | low | 6 | 17.1 | 3 | 12 | |
| | normal | 18 | 51.4 | 17 | 48.6 | |
| creatinine | high | 10 | 28.6 | 9 | 36 | 0.936 |
| | low | 2 | 5.7 | 4 | 16 | |
| | normal | 23 | 65.7 | 12 | 48 | |
| CRP | negative | 14 | 40 | 18 | 72 | 0.054 |
| | positive | 20 | 5.7 | 8 | 32 | |
| Cranial US (40 cases) | IVH | 0 | 0 | 8 | 20 | 0.241 |
| | HIE | 12 | 30 | 12 | 30 | |
| | Metabolic disorders | 0 | 0 | 2 | 5 | |
| | ICH | 3 | 7.5 | 1 | 2.5 | |
| | Meningitis | 0 | 0 | 1 | 2.5 | |
| | Sepsis | 0 | 0 | 1 | 2.5 | |

CRP: C-reactive protein US: ultrasound IVH: intraventricular hemorrhage HIE: hypoxic ischemic encephalopathy ICH: intracranial hemorrhage Normal serum calcium level (7 to 12 mg/dl), Normal serum sodium level (134 to 145 mg/dl), Normal serum creatinine level (0.3 to 1 mg/dl), Normal serum CRP level (up to 6 mg/dl)

Table (12) Relation between CUS findings and clinical examination

| Clinical examination | Cranial ultrasound(no.60neonates) | | | | P-value |
|----------------------|-----------------------------------|----|----------|----|---------|
| | Normal | | Abnormal | | |
| Poor tone | 6 | 30 | 28 | 70 | 0.0 |
| Poor reflexes | 14 | 70 | 33 | 82 | 0.2 |
| Presence of cyanosis | 3 | 15 | 7 | 17 | 0.8 |
| Presence of jaundice | 10 | 50 | 6 | 10 | 0.0 |
| Poor perfusion | 6 | 30 | 15 | 37 | 0.5 |
| Tachypnea | 9 | 45 | 11 | 27 | 0.1 |
| Abnormal temperature | 14 | 70 | 19 | 47 | 0.0 |

Fisher's Exact P-value<0.05

Discussion

Seizures in the neonatal period are usually concomitants of serious neurological disease. The convulsive phenomena take certain distinctive and often subtle forms because of the status of the neuroanatomical and neurophysiologic development of the neonatal brain ⁽⁸⁾.

Neonatal seizures are easy to be detected, diagnosed, and managed. The golden standard method to recognize neonatal seizures is video-EEG. However, this equipment is not always available in many neonatal units around the world ⁽⁹⁾.

Management of seizures involves identifying and treating the underlying etiology of the seizure and appropriate use of pharmacologic interventions ⁽¹⁰⁾.

The aim of this study is to focus on the clinical classification of neonatal "convulsions" thus proper assessment for appropriate diagnosis and proper management.

In the present study, birth weight was not a risk factor for increased morbidity or mortality among babies suffering from seizures. This finding is in concordance with **McIntire et al.**⁽¹¹⁾ who studied a total of 122,754 women and adolescents delivered singleton live infants without malformations between 24-43 weeks of gestation. There was no specific birth-weight percentile at which morbidity and mortality increased among preterm and full term babies.

In this study, majority of neonates with seizures were full-term (60%), while (28.3%) babies were preterm and (11.7%) babies were post-term, similar observation was seen in study by **Das and Debbarma** ⁽¹²⁾ where term babies were (91.3%), pre-term were (7.8%) and post-term were (0.9%)

Regarding influence of the gender, our results found a relation between gender and the occurrence of seizures; similarly, it was identified as a higher risk for male infants by **Das and Debbarma** ⁽¹²⁾. On contrary, **Talebian and Rabiee**⁽¹³⁾ found that gender was insignificant for neonatal seizures

Many types of seizures are represented in our study with different ratios; out of which 22 (36.7%) had myoclonic seizures, 17 (28%) had mixed, 10 (16.7%) babies had subtle, both clonic and tonic types were in the same ratio (5%), and only 1(1.7%) baby had multifocal clonic fit. In comparable to these results, in another study conducted by **Das and Debbarma** ⁽¹²⁾, 49(43%) cases had subtle seizures, followed by tonic in (34%), and clonic seizures were present in (16%).

The incidence of mortality was 25 cases (41.7%) out of 60 cases, of which 12 cases (50%) died of hypoxic ischemic encephalopathy, 8 cases (100%) died of intra-ventricular hemorrhage. These findings agree with the study done by **Tekgul et al.**⁽²⁾ who reported that mortality due to HIE was 7%, in contrary to other studies; our results was higher in comparable with mortality in a study reported by **Ravneet** ⁽¹⁴⁾; 11.25% and 9% respectively. This higher rate could be due to the etiology of the seizures.

Neonatal sepsis constituted an important etiology of neonatal seizures which is the second most common etiology in the current study accounting for (17%) of the cases, and this agreed with **Aziz et al.**⁽¹⁵⁾ and **Sadeghian et al.**⁽¹⁶⁾ with higher incidence (22%) & (19%) respectively.

On contrary, in a study conducted by **Das and Debbarma**⁽¹⁷⁾ 24 (21%) cases had meningitis and **Rabindran et al.**⁽¹⁵⁾ also reported meningitis as a cause of neonatal seizures in (17.2%)

Intra-cranial bleeding (including intracranial hemorrhage & intraventricular hemorrhage) was diagnosed as the etiology of neonatal seizures in 12 cases (20%) of our study. And this agreed with **Mizrahi and Milh** ⁽¹⁹⁾ who found intra-cranial hemorrhage as a frequent cause of neonatal seizures accounting for (15-

25%) of cases in his study. While **Aziz et al.**⁽¹⁵⁾, **Anandeveena and Nair**⁽²⁰⁾ and **Kumar et al.**⁽²¹⁾ noted that the incidence of ICH was (13%), (7.4%) and (2%) respectively which are lower incidence than in our study.

In this study, only (12.5%) of the hypoxic ischemic encephalopathy cases had normal EEG pattern and (87%) had abnormalities; similarly, **Rose and Lombroso**⁽²²⁾ reported abnormalities in HIE in 70% cases while **Mizrahi and Milh**⁽¹⁹⁾ reported it in (46.3%) cases.

Conclusion

In our prospective study on infants with neonatal seizures, we found that

1. GA, birth weight, gender, route of delivery did not distinguish which infant with neonatal seizures would have a poor prognosis.
2. Early control of neonatal seizures helps to improve the outcome, while prolonged time of cessation of seizures carry poor prognosis.
3. Hypoxic ischemic encephalopathy was the major cause of neonatal seizures.
4. The myoclonic seizures carry the worst prognosis. Also, it is the commonest seizure type in our study.
5. The EEG background is prognostically more important to determine the outcome of neonatal seizures.
6. Combination between neuro-imaging and neonatal EEG allows the detection of mild and moderate brain lesions

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