European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 09, Issue 04, 2022

Original Research Article

MAGNITUDE, RISK FACTORS, CLINICAL TYPES AND OUTCOME OF PATIENTS ADMITTED WITH NEONATAL SEIZURES IN NEONATAL INTENSIVE CARE UNIT OF A TERTIARY CARE CENTRE IN GUJARAT, INDIA

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Abstract

Background: This study was undertaken to estimate the incidence, etiological factor, time of onset & clinical types of neonatal seizures in our setup and to study the biochemical abnormalities among the different types of neonatal seizures in our setup.

Methods: This is a hospital based prospective observational study conducted in neonatal ICU, department of paediatrics, BMCRI during period of January 2020 to March 2022.

Results: Total number of patients which developed neonatal seizures were 82 in our study. The proportion of neonatal seizures among NICU admission of inborn patients were 10.8%. Out of 82 babies of neonatal seizures, 45 (54.8%) were males and 37(45.12%) were females in the ratio of 1.2:1, with male preponderance. Out of 82 babies who developed neonatal seizures, it was found that 50(60.9%) were pre-term babies, 28(34.14%) were term babies and 4(4.87%) were post-term babies. In this study out of 82 babies, 45 neonates (54.8%) were LBW babies and 37 (45.12%) were of >=2.5kg birthweight. Out of 82 neonates, in 35 (42.6%) neonates seizure occurred between 24-72hrs whereas in 28 (34.14%) neonates seizure occurred in <24hrs and in 19 (23.17%) babies seizure occurred in >72hrs which shows that most of seizures were observed between 24-72hrs of life. In this study, out of 82 cases, neonates with subtle seizures were 40(48.78%), neonates with tonic seizures were 32(39.02%), neonates with focal clonic were 8(9.75%) and the multifocal clonic seizures were 2(2.43%). This shows that subtle seizures were most common followed by tonic seizures. It was found that out of 82 cases of neonatal seizures in this study, maximum cases

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35(42.6%) were of birth asphyxia, followed by 15 cases of isolated hypoglycemia, (18.29%), 10(12.19%) cases were of neonatal meningitis/septicemia, 9(10.9%) cases were of isolated hypocalcemia, 10(12.19%) cases were of ICH (intracranial haemorrhage). There were 3(3.65%) cases of unknown causes of neonatal seizures. 2Out of 82 cases, 24 (29.26%) babies expired in spite of taking all efforts, and 58 (70.7%) babies were discharged successfully.

Conclusion: Neonatal seizures were more common in preterm, LBW. Birth asphyxia was the most common cause of all neonatal seizures followed by hypoglycemia. Subtle seizures were the commonest type of seizure observed followed by tonic. Subtle seizures were more common in 24-72 hours of life. Most common biochemical abnormality found in neonatal seizures is hypoglycemia followed by hypocalcemia.

Keywords: Neonatal seizures, NICU

Introduction

The neonatal seizure is defined as paroxysmal electrical discharge from the brain which may manifest as motor, sensory, behavioural or autonomic dysfunctions [1]. Seizures in the neonatal period are the most common neurological emergency and are associated with high mortality and morbidity [2]. Infants with neonatal seizures are at a high risk of death during the neonatal period and neurological impairment/epilepsy disorders in later life. Though mortality due to neonatal seizures has decreased from 40% to about 20% over the years, the prevalence of long-term neuro-development sequelae has largely remained unchanged at around 30% [3]. The National Neonatal Perinatal Database (NNPD; 2002-03), has reported an incidence of 10.3 per 1000 live-births [4]. The incidence was found to increase with decreasing gestation and birth weight, preterm neonates (20.8 vs. 8.4 per 1000 live-births) while very low birth weight neonates had more than 4-fold higher incidence (36.1 per 1000 per 1000 live-births) [4]. The neonatal central nervous system is particularly susceptible to seizures due to a combination of enhanced excitability and low levels of the inhibitory neurotransmitter gamma-aminobutyric acid [5]. The occurrence of seizure may be the first indication of a neurological disorder and the time of onset of seizure has a relationship with the aetiology of seizures and prognosis [6]. Neonatal seizures can be divided into epileptic and nonepileptic seizures; neonatal seizures of epileptic origin are generated by hypersynchronous cortical neuronal discharges. There are age-dependent properties of the immature brain that enhance seizure initiation, maintenance of the seizure discharge, and propagation of the seizure discharge. Nonepileptic seizures occur in the absence of electrical seizure activity [7]. Volpe classified seizures into five clinical types, namely subtle, multifocal clonic, focal clonic, generalized tonic and myoclonic [8]. Seizures in neonates are different from those seen in older children. The differences are perhaps due to the neuroanatomic and neurophysiologic developmental status of the new-born infant. In the neonatal brain glial proliferation, neuronal migration, the establishment of axonal deposition, dendritic contacts and myelin deposition are incomplete. For these reasons, clinical presentation differs [9]. Hypoxia-ischemia is nonetheless traditionally considered the most common cause of neonatal seizures [10, 11]. Cerebral infarction and stroke are the second most common cause of neonatal seizures occurring in otherwise well term infants, without previous risk factors [12]. Hypoglycemia is a well-known cause of neonatal seizures. Infants with sepsis and meningitis frequently have hypoglycemia which can be attributed to inadequate intake, increased metabolic rate and

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impaired ability to metabolize glucose [13]. Hypocalcemia is total serum Ca levels <7mg/dl although the exact level at which seizure occurs is debatable. Late onset hypocalcemia due to use of high phosphate infant formula has been cited as common cause of seizures [14, 15]. However commonly hypocalcemia occurs in infants with trauma, hemolytic disease, asphyxia and IDM and usually coexist with hypoglycemia and hypomagnesemia and presents at 2-3 days of life. Hypomagnesemia with serum <1.5mg/dl can occasionally manifest with tetany and seizures at 2-4 weeks of age and has secondary hypocalcemia associated. Mg depletion is known to predispose to decreased PTH secretion. Hyperphosphatemia may be caused by ingestion of milk formulas containing high amounts of phosphorous, excessive parenteral administration of phosphorus, impaired renal function, and hypoparathyroidism. Hyponatremia because of fluid overload, renal compromise and SIADH (syndrome of inappropriate ADH secretion) can be a frequent complication of birth asphyxia. Outcome is predicted by the underlying aetiology [16]. Patients with hypoxic ischemic encephalopathy (HIE), intraventricular haemorrhage and structural brain malformation have the worst prognosis [16, 17]. while those with transient metabolic abnormalities and benign idiopathic or familial aetiologies have the best prognosis [18].

Material & Methods

This is a hospital based prospective observational study conducted in neonatal ICU, department of paediatrics, BMCRI during period of January 2020 to March 2022. Cases were selected by applying the inclusion and exclusion criteria irrespective of gestational age and gender of the neonates.

Inclusion criteria

All intramural babies admitted with clinically identified seizure before 28 days of life.

Exclusion criteria

- Uncertain clinical manifestations.
- 1st seizures >28 days of life.
- Seizure mimics (e.g., jitteriness).
- Extramural babies.

Informed written consent was obtained from the parents of neonates admitted in the NICU.

- Data collection was done by using a structured case recording form to enter the patient details, detailed clinical history including maternal antenatal history, intrapartum history, and baseline characteristics of convulsing neonates.
- Clinical details of each seizure episode observed by the mother and subsequently observed by the resident doctors was recorded. Venous blood was collected as soon as possible and blood glucose, total serum calcium, sodium, potassium, and phosphate level was done immediately after the baby had seizures and before instituting any treatment.
- Venous blood was collected & sent for investigation [blood glucose, *S. calcium* (Ionized calcium if needed), *S. electrolytes, S. magnesium*, (s. phosphate if needed); USG skull & neuroimaging was done when needed.
- All treatment protocols were as per standard guidelines.

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Criteria for diagnosing various biochemical abnormalities

- Hypoglycemia: <40 mg/dl.
- Hypocalcemia: <7 mg/dl.
- Hypomagnesemia: <1.4 mg/dl.
- Hyponatremia: <135 meq/l.
- Hyponatremia: >145 meq/l.

Results

Total number of NICU admission during study period was 1617, among them 756 were intramural and 861 were extramural neonates. Extramural patients were excluded from the study. Total number of patients who developed neonatal seizures were 82. The proportion of neonatal seizures among NICU admission of inborn patients were 10.84%. Out of 82 babies of neonatal seizures, 45 (54.8%) were males and 37 (45.12%) were females in the ratio of 1.2:1, with male preponderance. Out of 82 babies who developed neonatal seizures, it was found that 50(60.9%) were pre-term babies (less than 37 weeks of gestation), 28(34.14%) were term babies (gestation age-37 to 42 weeks) and 4 (4.87%) were post-term babies (more than 42 weeks). Neonatal seizures was found to be more prevalent in pre-term babies. In this study out of 82 babies, 45 neonates (54.87%) were LBW babies (birth weight <2.5kg) and 37(45.12%) were of >=2.5kg birthweight. Out of 82 neonates, in 35 (42.6%) neonates seizure occurred between 24-72hrs whereas in 28 (34.14%) neonates seizure occurred in <24hrs and in 19(23.17%) babies seizure occurred in >72hrs which shows that most of seizures were observed between 24-72hrs of life. In this study, out of 82 cases, neonates with subtle seizures were 40(48.78%), neonates with tonic seizures were 32(39.02%), neonates with focal clonic were 8(9.75%) and the multifocal clonic seizures were 2(2.43%). This shows that subtle seizures were most common followed by tonic seizures and no case of myoclonic seizure was found in this study. It was found that out of 82 cases of neonatal seizures in this study, maximum cases 35(42.6%) were of birth asphyxia, followed by 15 cases of isolated hypoglycemia (18.29%), 10(12.19%) cases were of neonatal meningitis/septicemia, 9(10.9%) cases were of isolated hypocalcemia, 10(12.19%) cases were of ICH (intracranial haemorrhage). There were 3(3.65%) cases of unknown causes of neonatal seizures. Out of 82 cases, 24(29.26%) babies expired in spite of taking all efforts and 58(70.7%) babies were discharged successfully.

Discussion

Neonatal seizures adversely affect a wide range of phenomena in the developing brain, including cell division and migration, formation of receptors, sequential expression of receptors, synaptogenesis, and apoptosis. These changes appear to have long-term detrimental consequences with respect to seizure threshold, cognition, and learning. Therefore, all efforts should be made to recognise seizure early & treat accordingly. The proportion of neonatal seizures among NICU admission of inborn patients were 10.84% in our study. In studies conducted by Ajay Kumar *et al.* [19], Shah GS *et al.* [20], Amar *et al.* [21] incidence of neonatal seizures varied from 10.3 to 16.6 per 1000 live births (16.6/1000). However, the reported incidence of neonatal seizures varies widely across studies, a variability that is primarily the

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result of inconsistent diagnostic criteria, as well as the often-subtle clinical manifestations of neonatal seizures, and their potential confusion with non-epileptic neonatal behaviours. In our study seizures showed preponderance towards male babies of 54.8%, while females contributing with 45.12% with male to female ratio of 1.2:1. This is comparable to Shah GS *et al*. [20], Ajay *et al*. [19], Sanjeev Kumar Digra *et al*. [22] (Jammu, India) reported male: female ratio of 2.4:1. In our study out of 82 babies who developed neonatal seizures, maximum were pre-term & LBW babies. This is similar to findings found in previous studies done by Ajay *et al*. [19], Rennie JM *et al*. [23], Laroia *et al*. [24] who also reported increased incidence of seizures in pre-term babies. In our study subtle seizures (48.78%) were the commonest of all types followed by tonic seizures (39.02%). Shah GS *et al*., [20] Mizrahi & Kellaway [38], Scher *et al*. [47], Cloherty [29] and Meharban Singh [33] also reported that subtle seizures are the commonest type accounting for over 50% of seizures. Ajay *et al*. [19] reported multifocal seizures as commonest of all types. Birth asphyxia (42.6%) was the most common cause of neonatal seizures in our study, like studies done by Shah GS *et al*. [20]. This is because ours is a tertiary centre and cases were referred with improper antenatal care, untreated or partially treated PIH, ante partum haemorrhage, varying presentations of baby, fetal distress with meconium-stained liquor, undue prolongation of stages of labour.

Table 1: Incidence of neonatal Seizures among inborn patients

Total NICU admission	Inborn (Included in the Study)	Outborn (Excluded from Study)	Cases who Developed Seizures (among inborn)	Percentage
1617	756	861	82	10.84

Table 2: Sex wise distribution of neonatal seizures

Gender	No. of cases (n=82)	Percentage
Male	45	54.8%
Female	37	45.12%
Total	82	100%

Table 3: Distribution of neonatal seizures according to Gestational age

Gestational Age	No of cases (n=82)	Percentage
Preterm Babies	50	60.9%
Term babies	28	34.14%
Post term babies	4	4.87%
Total	82	100%

Table 4: Birth weight wise distribution of neonatal seizures

Birth weight	No of cases (n=82)	Percentage
Low birth weight	45	54.8%
Normal birth weight	37	45.12%
Total	82	100%

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Table 5: Distribution of neonatal seizures according to Time of onset

Time of onset	No of cases	Percentage
<24 hours	35	42.6%
24-72 hours	28	34.14%
>72 hours	19	23.17%
Total	82	100%

Table 6: Distribution of cases with different types of neonatal seizures

Types of neonatal seizures	No. of cases (n=82)	Percentage (%)
Subtle	40	48.78%
Tonic	32	39.02%
Focal clonic	8	9.75%
Multifocal clonic	2	2.43%
Total	82	100%

Table 7: Etiology of neonatal seizures

Etiology of neonatal seizures	No. of cases (n=82)	Percentage (%)
Birth asphyxia	35	42.6%
Hypoglycemia (isolated)	15	18.29%
Neonatal meningitis/Septicemia	10	12.19%
Hypocalcemia (isolated)	9	10.9%
Intracranial haemorrhage (ICH)	10	12.19%
Unknown	3	3.65%
Total	82	100%

Table 8: Outcome of neonatal seizures and number of cases

Outcome	No of pt	Percentage
Discharge	58	70.7%
Expiry	24	29.26%
Total	82	100%

Conclusion

Based on our study we conclude that neonatal seizures is very common in NICU setup.
All efforts should be taken to recognise seizures early so that damage to developing brain can be avoided by early recognition & timely action.

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Limitations

In our study, we have identified neonatal seizures based on clinical criteria alone. In our setup where continuous video EEG monitoring is not available, which is necessary for confirming abnormal electroencephalogram discharge, there may be chances that we could have missed the electrographic seizures, so that the real magnitude of neonatal seizures is not known. Moreover, there may be overdiagnosis or underdiagnosis of cases based on inter-observer variation and lack of continuous in-function cerebral monitor.

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