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Neonatal seizures and outcome in NICU

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Abstract

Background: Neonatal seizure is a relatively common pediatric emergency and it is critical to determine the etiology and other factors that determine the outcome. Our study aimed to delineate the Clinco-etiologic profile of neonatal seizures and the neurodevelopmental Outcome in a sample of Egyptian newborns. Methods: This prospective cohort study was conducted in Neonatal Intensive Care Units (NICUs) at Banha University Hospital and Benha Children Hospital between January 2018 and December 2020. The study protocol was approved by the Ethical Scientific Committee of Faculty of Medicine, Banha University conferring to the World Medical Association Declaration of Helsinki, and informed consent was obtained from parents/guardians before enrollment in the study. Eligibility criteria were a birth gestational age 37 weeks or less and clinically evident neonatal seizures (i.e., within the first 28 days of life). The diagnosis of clinical neonatal seizures was made by a pediatric neurologist and neonatologist. Our study population consisted of 65 term and preterm infants, of whom 50 neonates (76.9%) met the inclusion criteria. All neonates were subjected to detailed history included sex, mode of delivery, gestational age, maternal risk factors, Apgar score at 1 and 5 minutes, seizure onset age, seizure type. Etiology, antiepileptic drugs, cranial ultrasonography findings and outcome of seizures were identified. Seizure types were categorized according to Volpe classification schema,1 based on the paroxysmal clinical phenomena. It included subtle, clonic, tonic and myoclonic presentations. Results: Hypoxic ischemic encephalopathy was the most common etiology noted and was identified in 14(28.0%) infants. Second most common was intracranial hemorrhage 11(22.0%) infants, followed by infection 9(18.0%). This study showed that, subtle seizures were the most common clinical type of seizures noted in 29 (58.0%) infants followed by clonic type in 11(22.0%) and tonic type in 9(18.0%) infants. This study showed that, regarding outcome of the studied neonates: of 50 infants, 25(50.0%) infants had a normal outcome and 9(18.0%) infants survived with a neurodevelopmental impairment, while 16(32.0%) infants died. In the present work, there was highly significant Correlation between clinical type of seizures and Apgar score at 5 minutes. And There was significant association between treatment of cases during admission and clinical type of seizures Conclusion: Hypoxic ischemic encephalopathy is the most common etiology of neonatal seizures. Subtle seizure was the most common pattern in their observation. High risks for unfavorable neurological outcomes. The mortality rate was high.

Key words: Neonatal seizures, outcome, NICU.

1. Introduction

Neonatal seizure is a relatively common pediatric emergency and it is critical to determine the etiology and other factors that determine the outcome. Even with advanced perinatal care, mortality and morbidity of neonatal seizure remains high. There are a number of problems in diagnosis and management of neonatal seizures underscoring the dynamic nature of the study of neonatal seizures. [1] The incidence of seizures is higher in the neonatal period than in any other period of life and is estimated at approximately three per 1000 live births [2]. Yet their clinical recognition is difficult, therefore true incidence of neonatal seizures is difficult to determine. Seizures are often the first sign of neurological dysfunction in newborn but their clinical expression at this age is quite variable, poorly organized and often subtle [3]. Seizures are a potentially life-threatening problem with a variety of causes. Studies from different low-income countries showed that perinatal asphyxia with hypoxic-ischemic encephalopathy (HIE) is the most common cause. [4] Metabolic abnormalities, infection, intracranial hemorrhage, developmental anomalies, and others like inborn errors of metabolism are rare causes of neonatal seizures. [5] Seizures are one of the immediate neonatal emergencies, where diagnostic and therapeutic plans are necessary because delay in therapy often results in poor neurological outcome [5].Our study aimed to delineate the Clinco-etiologic profile of neonatal seizures and the neurodevelopmental Outcome in a sample of Egyptian newborns.

2. Subjects and methods

Study design and population

This prospective cohort study was conducted in Neonatal Intensive Care Units (NICUs) at Banha University Hospital and Banha Children Hospital between January 2018 and December 2020. The study protocol was approved by the Ethical Scientific Committee of Faculty of Medicine, Banha University conferring to the World Medical Association Declaration of Helsinki, and informed consent was obtained from parents/guardians before enrollment in the study. Eligibility criteria were a birth gestational age 37 weeks or less and clinically evident neonatal seizures (i.e., within the first 28 days of life). The diagnosis of clinical neonatal seizures was made by a pediatric neurologist and neonatologist. .Exclusion criteria were cerebral malformation and genetic syndromes. All patients had at least 6 months of neurologic follow-up data. Our study population consisted of 65 term and preterm infants, of whom 50 neonates (76.9%) met the inclusion criteria. All

neonates were subjected to detailed history included sex, mode of delivery, gestational age, maternal risk factors, Apgar score at 1 and 5 minutes, time of admission to NICU and occurrence of jaundice. Seizure types were categorized according to Volpe classification schema' [6] based on the paroxysmal clinical phenomena. It included subtle, clonic, tonic and myoclonic. The primary etiology of the seizure was determined through the clinical history, neuroimaging studies [computed tomography (CT), cranial ultrasonography findings and magnetic resonance imaging (MRI)], and laboratory tests (cbc, electrolytes, ABG, blood glucose, blood and CSF cultures, (TORCH) screen for congenital infection or workup for inborn error of metabolism.. Intrapartum asphyxia required 5-minute Apgar score of _6 and fetal distress. The diagnosis of infection (bacterial or viral) had confirmatory laboratory evidence on CSF or blood culture. Intracranial hemorrhage included epidural, subarachnoid, subdural, parenchymal, and/or intraventricular hemorrhage. Almost all infants had serial cranial ultrasonography examinations. Some had at least one additional modality of imaging, such as cranial CT or MRI.

We divided the etiologies to 7 groupes: (1) Hypoxic ischemic encephalopathy, (2) Intracranial hemorrhage, (3) infection, (4) Inborn error of metabolism, (5) Electrolyte disturbance, (6) Trauma, (7) Miscellaneous

The drug of first choice was phenobarbital at a loading of 20 - 40 mg/kg and a maintenance dose of 3 - 8 mg/kg/day intravenously administered. If the seizures persisted or recurred, then we administered phenytoin at a loading dose of 20 mg/kg and a maintenance dose of 4-8 mg/kg/day intravenously then third line was levetiracetam with loading dose 40 mg/kg divided on two doses followed by maintenance dose of 40-60 mg/kg/day intravenously. The neurologic outcome recorded at the last follow-up was included in the subsequent data analysis. And it was divided to survivors with normal outcome, survivors with late complications and non-survivors.

2.1Statistical Analysis

Data analysis was performed using the software SPSS (Statistical Package for the Social Sciences) version 24. Quantitative variables were described using their means and standard deviations. Categorical variables were described using their absolute frequencies and were compared using Chi square test and fisher exact test when appropriate. Kolmogorov-Smirnov (distribution-type) tests were used to verify assumptions for use in parametric tests. To compare continuous quantitative data of two groups, Mann whitney test (for non-normally distributed data) and independent sample t test (for normally distributed data) were used. The level statistical significance was set at 5% ($P<0.05$). [7]

3. Results

We studied group of 50 neonates there were 30 male and 20 female. The mean gestational age was 34.6± 3.2 weeks. The mean birth weight was 2.2 ± 0.75. Nine infants were born by vaginal delivery9 (18%) and 41(82%) by cesarean section Table (1).

Of the 50 study participants, subtle seizures were the most common seizures type 29(58.0%) followed by clonic seizures 11(22.0%) and tonic seizures 9(18.0%) Table (2).

hypoxic ischemic encephalopathy was the most common etiology noted and was identified in 14 (28.0%) Followed by intracranial hemorrhage 11(22.0%) and infection 9 (18.0%) Table (3).

- Regarding anticonvulsant therapy of the studied neonates during admission: Of 50 infants there were 25(50.0%) infants treated with monotherapy (Phenobarbital only), 10(20.0%) infants received double therapy (Phenobarbital plus phenytoin) and 15(30.0%) infants received triple therapy (Phenobarbital, phenytoin and levetiracetam) Table (6).

There were 25(50.0%) Survivors with normal outcome, 9(18.0%) Survivors with late complications and 16(32.0%) non-survivors Table (4).

- There was highly significant Correlation between clinical type of seizures and mean APGAR score at 5 minutes (p value 0.002) Table (5).

- There was significant association between treatment of cases during admission and clinical type of seizures (p value 0.024) Table (6).

Table (1) Perinatal history of the studied neonate.

perinatal history	Range	Mean ±SD
Gestational age (weeks)	29-41	34.6± 3.2
Birth weight (kg)	0.96-3.8	2.2 ± 0.75
Sex		
Male	30	60
Female	20	40
Mode of delivery		
vaginal delivery	9	18
cesarean section	41	82

Table (2) clinical type of Seizures.

Seizures	Range	Mean ±SD
Clinical type		
Subtle	29	58
clonic	11	22
tonic	9	18
Myoclonic	1	2

Table (3) Etiology of the studied neonates.

Etiology	Frequency	%
Hypoxic ischemic encephalopathy	14	28.0
Intracranial hemorrhage	11	22.0
infection	9	18.0
Inborn error of metabolism	4	8.0
Electrolyte disturbance	5	10.0
Trauma	3	6.0
Miscellaneous etiologies (Benign neonatal convulsions, Neonatal abstinence syndrome, Congenital muscular dystrophy, mass	4	8.0

Table (4) Outcome & late complications among neonates with different types of seizures.

Outcome& late complications	TOTAL	Clinical type of seizures				FET test	P-value
		Subtle n=29	Tonic n=11	Clonic n=9	Myoclonic n=1		
Survivors with normal outcome	25(50%)	10	8	7	0		
Survivors with late complications:	9(18%)	7	0	2	0	36.95	0.057
Non survivor	16(32%)	12	3	0	1		

Table (5) Relation between APGAR score & clinical type of seizure.

APGAR score	Clinical type of seizures				F test	P-value
	Subtle n=29	Tonic n=11	Clonic n=9	Myoclonic n=1		
At one minute Mean ±SD	5.27±1.48	5.54±1.5	6.66±1.11	4.00	2.56	0.06
At five minutes Mean ±SD	8.24±1.09	9.09±0.83	10.55±2.8	8.00	5.62	0.002**

Table (6) Treatment protocols used for neonates with clinical types of seizures.

Treatment	total	Clinical type of seizures				FETtest	P-value
		Subtlen=29	Tonic n=11	Clonicn=9	Myoclonic n=1		
Phenobarbital	25(50%)	10(34.5%)	7(63.6%)	8(88.9%)	0(0%)		
Phenobarbital + phenytoin	10(20%)	7(24.1)	1(9.1%)	1(11.1%)	1(100%)	12.28	0.024*
Phenobarbital + phenytoin +levetiracetam	15(30%)	12(41.4%)	3(27.3%)	0(0%)	0(100%)		

4. Discussion

In this study, hypoxic ischemic encephalopathy was the most common etiology noted and was identified in 14(28.0%) infants. Second most common was intracranial hemorrhage 11(22.0%) infants, followed by infection 9(18.0%).

This was in accordance with that reported by Ghanshyambhai et al. [8] who found the most common cause of neonatal seizure was hypoxic ischemic encephalopathy (HIE)

This was in agreement with Baudou et al. [8] who found the frequencies of etiologies of neonatal seizures were: hypoxic-ischemic encephalopathy (HIE) (n = 91; 37%). In their population, the incidence of each etiology was: 37% hypoxic-ischemic encephalopathy, 12% ischemic infarction, 15% intracranial hemorrhage, 8% intracranial infections, 3% metabolic or electrolyte disorder, 2% inborn errors of metabolism, 5% congenital malformations of the central nervous system, and 11% epileptic syndromes.

This study showed that, 16(32.0%) of the studied neonates died.

This was higher than that reported by Baudou et al. [9] who found 18.5% of the studied patients died.

And also, higher than previous publications of Mastrangelo et al. [10] (21%) and Glass et al. [11] (17%).

This study showed that, subtle seizures were the most common clinical type of seizures noted in 29(58.0%) infants followed by clonic type in 11(22.0%) infants and tonic 9(18.0%) infants

In agreement with Sabzehei et al. [12] who found regarding terms of clinical type, subtle seizure was the most common type, which was seen in 39 (38.2%) neonates, followed by tonic in 30 (29.4%), clonic in 27 (26.4%), and myoclonic in 6 (5.9%)

Similar results were reported by moayedi et al. and Tekgul et al. [13, 14].

In contrast to these results, Fiaz et al. studied 101 neonates with seizures, of whom 39.6% had both tonic and clonic seizures [15].

This study showed that, regarding outcome of the studied neonates: of 50 infants, 25(50.0%) infants had a normal outcome and 9(18.0%) infants survived with a neurodevelopmental impairment, while 16(32.0%) infants died.

This is consistent with Lai et al. [16] who found among the 232 enrolled infants, 125 had a normal outcome and 14 had mild functional disability (59.9%), and 55 (23.7%) survived with one or more neurodevelopmental impairments and 38 (16.4%) died. Forty-seven (23.0%) of the 204 patients who survived after the first discharge had epilepsy.

Conclusion

Based on the results of the current study, it can be concluded that hypoxic ischemic encephalopathy is the most common etiology of neonatal seizures. Subtle seizure was the most common pattern in their observation. High risks for unfavorable neurological outcomes. The mortality rate was high.

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