

## NEONATAL SEIZURES: ETIOLOGY AND FREQUENCY

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### Abstract

#### Objective

The aim of the present study was to evaluate the etiology and frequency of neonatal seizure in hospitalized neonates.

#### Materials and Methods

In this descriptive, cross-sectional study, we evaluated 1295 neonates with seizures admitted to neonatal and NICU wards in our center. Data was collected on age, sex, birth weight, serum levels of calcium, glucose, and sodium, CT scan findings, history of maternal opium abuse, blood and cerebrospinal fluid culture, and analyzed using SPSS 13.

#### Results

Of a total of 1295 patients, 34 (2.62%) had seizure. Mean age was  $14.03 \pm 10.05$  days (range, 1 to 29 days); twenty-five (73.5%) neonates were boys and 9 (26.5%) were girls. Of 34 neonates with neonatal seizures, 12 (35.3%), 11 (32.4%), 9 (26.5%), 7 (20.6%), and 3 (8.8%) had hypocalcemia, asphyxia, hypoglycemia, intracranial hemorrhage, and hypernatremia, respectively. Maternal addiction, meningitis, and sepsis were found in 3 (8.8%), 1 (2.9%) and 1 (2.9%) of neonates, respectively.

#### Conclusion

The incidence rate of neonatal seizure in the neonates in our NICU and neonatal ward was 2.62%. Common causes of seizure in this study included hypocalcemia, asphyxia, hypoglycemia, intracranial hemorrhage, and hypernatremia. Maternal addiction, meningitis and sepsis had the lowest prevalence.

**Keywords:** Neonate, Seizure, Etiologies.

### Introduction

The neonate's central nervous system is anatomically and functionally immature. Although division of the cortical neurons stops at the second trimester of the pregnancy, it seems that glial cells, dendritic processes, and myelination increase after birth and during the neonatal period (1). Numerous pathophysiologic mechanisms may adversely affect the growing and developing brain of neonates during this period; some of these conditions, possibly permanent, may include hypoxia, ischemia, infections, inflammations, malformations, maternal drug abuse, coagulative disorders and postpartum injuries such as birth trauma, hypoxia, ischemia, hypothyroidism, hyperthyroidism, polycythemia, hemorrhage, and meningitis(1-3). Neonatal seizures may have different causes with clear background and clinical manifestations. Seizures due to hypoxic-ischemic encephalopathy

usually occur within 12 to 24 hours after a history of asphyxia. The risk for seizures, due to intraventricular hemorrhage (IVH), exists with bulged fontanel, bloody cerebro-spinal fluid, anemia, lethargia, and coma (1-4). Seizures due to hypoglycemia occur when the blood sugar decreases to the lowest level after delivery(1). Seizures due to hypocalcemia and hypomagnesaemia occur in high-risk neonates and respond fairly well to treatment with calcium or magnesium(1-5). Seizures in the delivery room usually occur due to direct injection of the local anesthetic drugs in the neonatal scalp and are accompanied by bradycardia and fixed dilated pupils. Seizures with weakness, acidosis, and family history of neonatal death may be attributed to inborn errors of metabolism(1). If one of the neonate's parents has a history of neonatal convulsion, the neonate will be at the risk of benign neonatal convulsion (1-6). An abrupt onset of a short, non-repeating convulsion in a healthy neonate between the 1<sup>st</sup> and 3<sup>rd</sup> day of the birth may be due to subarachnoid hemorrhage. Focal convulsion is often due to focal brain infarction(1). Any form of clinical signs may represent a primary or secondary central nervous system abnormality(1-7). Finding the precise cause of convulsions is of crucial importance because it helps determine the appropriate treatment and clarifies the prognosis of the disease(1-16). On the other hand, low gestational age and neonatal disease may increase risk of convulsions (1-17). Numerous studies reveal that convulsions occurring in the neonatal period, play a major role in neonatal health and also later in life, as seen in developing countries (2-16). Considering the limited literature available on the subject from our country, this study on hospitalized neonates was carried out to determine the prevalence of the seizure and the underlying diseases.

### Materials and Methods

In this descriptive, cross-sectional study, 1295 hospitalized cases were studied from September 2004 to September 2006 in neonatal and NICU wards in Ekbatan Hospital of Hamedan University of Medical Sciences. Data including information on age, sex, birth weights, serum calcium, glucose and sodium, CT scan

findings, history of the maternal addiction, blood and cerebrospinal fluid cultures in patients with seizure were documented in questionnaires and analyzed using SPSS 13. All cases of jitteriness were excluded from the study. We considered the subtle, tonic, clonic, and myoclonic seizures as a neonatal seizure in the study. Other inclusion criteria were Asphyxia, considered as PH below 7; 5<sup>th</sup> minute Apgar score between 0 and 3, decreased muscle tone and consciousness, seizure and cortical atrophy in brain CT scan.

Hypoglycemia was defined as blood sugar less than 35 mg/dL during the first three hours of the birth, less than 40 mg/dL between 3 to 24 hours of the birth, and less than 45 mg/dL after the first 24 hours of the birth. Hypocalcemia was defined as the total serum calcium less than 8 mg/dL in term and less than 7.5 mg/dL in preterm neonates. Hyponatremia was considered as the serum sodium values over 150 meq/dL. Intracranial hemorrhage was determined according to the brain CT scan findings. Drug withdrawal was confirmed by the mother having a history of opiate use. Bacterial meningitis was determined based on the positive cerebrospinal fluid culture and sepsis was confirmed if the blood culture was positive.

### Results

Of a total of 1295 hospitalized neonates studied, from the NICU and neonatal wards, 34 (2.62%) were found to have seizures. Mean age of the neonates was  $14.03 \pm 10.05$  days (range 1 to 29 days). Of the 34 neonates with seizure, 25 (73.5%) were boys and 9 (26.5%) were girls (male: female ratio was 3:1).

Of the 34 neonates, twenty-three (67.6%), 6 (17.6%), and 5 neonates (14.7%) had normal (2500 to 4000 gr), low (1500 to 2500 gr), and very low birth weight (less than 1500 gr), respectively (Table 1); 12 (35.3%) had hypocalcemia, 11 (32.4%) had asphyxia, 9 (26.5%) suffered from hypoglycemia, 7 (20.6%) had intracranial hemorrhage (ICH), and 3 (8.8%) had hyponatremia. Maternal addiction, meningitis, and sepsis were found in 3(8.8%), 1 (2.9%), and 1(2.9%) neonates, respectively (Table 2).

Table 1: Birth weights of the neonates with seizure

Birth Weight	Number (N=34) / Percent
Normal (2500 - 4000 gr)	23(67.6)*
Low Birth Weight (1500 – 2500 gr)	6(17.6)
Very Low Birth Weight (less than 1500 gr)	5(14.7)

\* Numbers in parenthesis are percents.

Table 2: Causes of seizures in hospitalized neonates

Causes	Number (N=34) / Percent
Hypocalcemia	12(35.3)*
Asphyxia	11(32.4)
Hypoglycemia	9(26.5)
Intracranial hemorrhage	7(20.6)
Hypernatremia	3(8.8)
Maternal addiction	3(8.8)
Meningitis	1(2.9)
Sepsis	1(2.9)

\* Numbers in parenthesis are percents.

### Discussion

A number of pathophysiologic mechanisms can damage the developing brain of the neonates during their perinatal period; these include hypoxia, ischemia, infections, malformations, drug abuse by mother, coagulative disorders, and also postpartum events such as delivery injuries, hypoxia, ischemia, hypothyroidism, hyperthyroidism, polycythemia, bleeding, and meningitis(1). Every clinical presentation of the neonatal seizure implies the existence of a primary or secondary central nervous system disturbance(1- 4). Numerous studies in neonatal seizure field reveal that it has different causes with different history and clinical presentations. Determining the cause of the seizure is very important because it helps choose the treatment and also determines the prognosis(2-16). In the present study, 2.62% of the evaluated neonates suffered from seizure, less than that reported by Manoel and Saliba; in Manoel’s study, seizure incidence was 6.9%, while in Saliba’s, it was 8.6%;(5,6) these differences may be due to the low socio-economic conditions of the populations evaluated and lack of access to NICU. In our study, the seizure incidence was lower compared to Brunquell’s(7). Kohelet and colleagues revealed that in Israel the incidence rate of seizure was 5.6% in very low birth weight neonates(8). Kawakami and coworkers in Japan reported an incidence of 0.25% neonatal seizure, which is less than our findings(9).

Of 34 neonates with seizure, 25 (73.5%) were boys and 9 (26.5%) were girls, the male to female ratio being 3:1, a finding compatible to those documented in textbooks; Kohelet and associates also mention that male sex is regarded to be one of the risk factors for seizure (1,8,10 -17).

Other findings observed, accompanying seizure in our study included hypocalcemia (35.3%), asphyxia (32.4%), hypoglycemia (26.5%), intracranial hemorrhage (subarachnoid and intraventricular; 20.6%), hypernatremia (8.8%), addiction of the mother to opiates (8.8%), and meningitis and sepsis (2.9%). Calcicoliary and colleagues in USA and Ronen and associates in Canada revealed that hypoxic-ischemic encephalopathy in 60% and 40% of the cases was determined to be the most

common cause of neonatal seizure;(10,11) whereas our study revealed this to be the main cause in 32.4% of neonates. We found hypocalcemia to be the most frequent cause of neonatal seizure, a finding not in agreement with other studies and text books, which show hypoxic-ischemic encephalopathy to be the most frequent cause of neonatal seizures (12-17). This difference may be due to the asymptomatic cases of grade 1 hypoxic-ischemic encephalopathy. Diagnosis of grade 1 hypoxic-ischemic encephalopathy is based on Apgar score, but Apgar score was not definitely recorded in the patients' files. Hypocalcemia is one of the most frequent complications of hypoxic-ischemic encephalopathy. In the other word, neonatal seizure due to hypocalcemia could have been due to neonatal asphyxia in majority of our cases.

### Conclusion

According to our results, the rate of occurrence of the seizure in neonates hospitalized in the NICU and neonatal wards of Ekbatan hospital was 2.62%. Based on the causes of seizure reported in this investigation, we recommend preventive programs for delivery injuries, premature delivery and low birth weight, congenital malformations, infections and inflammations which must be programmed in four stages: preconception, during pregnancy, peripartum, and postpartum.

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