Clinically diagnosed neonatal seizures in Al- Diwanyah, an epidemiological study

Rahman K. Al-jeboori[1], Aqeel K. Abd[2] , Thuraya H. Farhan[2]* , Hamid S. Dhaher[2]**
[1]Department of pediatrics, College of medicine, Al- Qadisiyah University, Iraq
[2]Maternity and Children Teaching Hospital In Al- Diwanyah, Iraq

Abstract

INTRODUCTION

Neonatal seizures are the most frequent and distinctive manifestations of neurological disturbances during the neonatal period. This retrospective study aimed to determine the incidence rate, causes and risk factors for neonatal seizures in Al-Diwanyah Province during one calendar year from the 1st of January, 2016 to 31st December, 2016

METHODS.

Data were extracted from the records at Maternity and children Teaching Hospital in Al-Diwaniyah. All neonates who had developed clinically recognized seizures before 28 days of life were enrolled in the study. These data included gestational age (full or pre-term infant), maternal diseases and drug intake during the last trimester, family history of seizures, number of parities, consanguinity, mode of delivery (normal vaginal delivery or caesarian section) age and gender of neonate, body weight at birth (normal or low body weight), and age at which seizure has developed (early onset or delayed onset). Biochemical tests were blood sugar and serum calcium.

RESULTS

Out of 3167 recorded birth in the hospital, 113 neonates have developed seizure with overall incidence rate of 3.57%. Four main causes of seizures were recognized which were: asphyxia (34.5%), hypoglycemia (23%), hypocalcemia (14.16%) and intraventricular hemorrhage (7.08%). However, in 21.42% of cases, the cause(s) was/were undiagnosed.

DISCUSSION

Three risk factors (gender, family history of seizures and number of parities) were found to have no significant association with any of these causes of seizures. The other risk factors associated with these causes in different modes. Each of early onset of seizure, mother's disease during pregnancy, caesarian section delivery and full term infant were significantly associated with hypoglycemia. Hypocalcemia, on the other hand, was significantly associated with delayed onset of seizures and preterm infants with low body weight, while there was very significant association between asphyxia and normal vaginal delivery. Although less frequent than other causes of seizure, intraventricular hemorrhage was found to be significantly associated with three risk factors (delayed onset of seizures, normal vaginal delivery and preterm infants). Finally, a positive significant association was found between consanguinity and undiagnosed causes of seizures

CONCLUSION.

These results pointed out the importance of asphyxia and hypoglycemia as the main causes of neonatal seizures. The most important risk factors associated with these causes are normal vaginal delivery, mother's disease during pregnancy, and low body weight at birth.

Keywards: neonatal seizures, hypoxic ischemic encephalopathy, hypoglycemia,Hypocalcemia,intreventricular haemorrhage

Introduction

Neonatal Seizures

Neonatal seizures may be defined as paroxysmal electrical discharges from central nervous system manifested clinically by transitory stereotype muscular activity, alteration in conciousness or other signs and symptoms related to brain dysfunction [(1)].

Seizures are the most frequent and ditinctive manifestation of neurological disturbance in the neonatal period, and the major risk for death or subsequent neurological disability. Moreover, it could confer an adverse neurodevelopmental outcome in high risk neonates [(2)].

Epidemiology

The exact incidence of neonatal seizures in the general newborn population is difficult to estimate because this incidence has been largely estimated depending on clinical observations and abnormal movements, although there is an increasing trends towards using electrodiagnostic techniques. It is well known that the clinical presentation of seizures in neoborn are subjective with wide interventional variation. Eventhough, most of the published studies used clinical criteria to diagnose neonatal seizures, and therfore, there is both over- and under-estimation of the frequency of seizures in most of these studies [3].

Family history in neonatal seizure is mainly associated with benign familial neonatal seizure (BFNS) which may present in the current series but without molecular detection. This type of neonatal seizure is associated with certain mutations.

The first study in this regard is that of Holden et al. [4] who investigated 54000 pregnacies in USA between 1959-1966 . They found the incidence of neonatal seizures to be 5 per 1000 live births. After this study, large number of studies have been performed worldwide including Iraq and some neighboring countries [5,6,7].

From these studies, the overall incidence of seizures is about 1-4 per 1000 live births in term infants, while in preterm/low body weight infants the estimates vary significantly but are generally 10 times more common than in term infants [8] and ranged from 57.5 to 132 per 1000 live births [7].

Factors like inclusion criteria, ethnic diversity among the study population, variation in the methods used in seizure diagnosis, the lack of clear description of clinical seizure presentation (especially for subtle seizures) and differing referral pattern may influence the incidence rate [9].

Regarding time of occurrence, most neonatal seizure occur very early in the life with nearly occuring within the first day of life, and another occuring within the first weeks [6].

Patients and Methods

This retrospective study covered 12 months period from the 1st of January to 31st of December 2016. Data were based on the medical records of 113 neonates diagnosed with neonatal seizures and admitted to the neonatal care unit in Maternity and Children Teaching Hospital AL Diwaniyah.

Inclusion criteria : were all neonates who developed clinically recognized seizure before 28 days of life.

exclusion criteria : were neonates having gross congenital malformations like anencephaly or large occipital meningomyelocele, and those who had the first seizure > 28 days of life..

Diagnosis of neonatal seizures relied on clinical features, para-clinical investigations (laboratory studies) and observations recorded by resident doctors. The clinical types of seizures were confirmed by the pediatrician according to criteria of Volpe [14].

.Statistical Analysis

Graphpad prism software was used for data analysis. Continuous variables were expressed as mean standard deviation, while categorical variables were expressed as percentage. Chi-square test was used to compare. Variables P value was considered significant if less than 0.05

Result

Association of Different Risk Factors with Causes of neonatal Seizures

Association of Neonate Sex with Different Causes of Neonatal Seizures

Despite females were more frequently associated with asphyxia and hypocalcemia than males, the asociations were non-significant (table 2-1).

Association of Family History with Different Causes of Seizures

The majority of cases did not have family history of seizure. Although there were 25% of hypocalcemic neonates with positive family history, the association did not differ significantly when compare with other causes. (table 2-1).

Association of Consanguinity with Different Causes of Neonatal Seizures

There is significant association with high percentage (79.17%) of neonates from consanguineous marriage with hypoglycemia and undiagnosed cause(s) of seizure ($p<0.05$) as shown in table (2-1).

Association of Maternal Diseases with Different Causes of Neonatal Seizures

Table (2-1) shows that neonates delivered from diabetic mother were prone to seizures caused by hypoglycemia (100%) with significant differences compared with other causes of neonatal seizures. (P<0.05).

Association of Parities with Different Causes of Neonatal Seizures

Neonates suffering from asphyxia referred to higher percentage of mothers with ≤ 2 children compared with other causes of neonatal seizures. However, the differences were not significant (table 2-1).

Association of Seizure Onset with Different Causes of Neonatal Seizures

Early onset of seizure (≤3 days) was significantly associated with hypoglycemia since 92.31% of hypoglycemic neonates developed seizures with the 3 days of life (P<0.05). On the other hand, delayed onset (>3 days) was significantly associated with IVH and hypocalcemia where 87.5% and 75% of neonates, respectively, developed seizures after 3 days of life (table 2-1).

Association of Mode of Delivery with Different Causes of Neonatal Seizures

Table (2-1) shows that normal vaginal delivery was significantly associated with both asphyxia (97.44%) and IVH (87.5%), while C/S was significantly associated with hypoglycemia (92.31%) as shown in table (2-1).

Association of Gestational Age with Different Causes of Neonatal Seizures

Twenty-two hypoglycemic neonates (92.31%) had full term pragnancy which is far greater than the other causes of neonatal seizures, while both IVH (87.5%) and hypocalcemia (75%) were significantly associated with preterm pregnancy (P<0.05) as shown in table (2-1).

Association of Birth Weight with Different Causes of Neonatal Seizures

The only neonatal seizure cause which significantly associted with normal body weight was hypoglycemia. The vast majority (92.31%) of hypoglycemic neonates had a body weight of ≥ 2500 grams, which is far more greater than the other causes of neonatal seizures. On the other extreme, body weight < 2500 grams was significantly associated with IVH (P<0.05) as shown in (table 2-1).

Association of Maternal Drug History with Different Casuses of Neonatal Seizures

Logically, the association of mother's drug history should be closely similar to that of mother's health, and that was true in the majority of cases of neonates from drug using mothers like (insulin ,phenobarbital , magnesium sulphate) were have hypoglycemia , Asphyxia and other with undiagnosed neonatal seizures compared with the other causes (table 2-1).

Table (2-1) show variable risk factors with different causes of neonatal seizures

Variables	Asphyxia (39)	IVH (8)	Hypoglycemia (26)	Hypocalcemia (16)	Other Causes (24)
Sex Male (52)	18(46.15%)	3(37.5%)	14(53.85%)	5(31.25%)	12(50%)
Female (61)	21(53-85%)	5(62.3%)	12(46.15%)	11(68.75%)	18(50%)
P value	0.1	0.7	0.3	0.2	0.8
Family history Positive (11)	2(5.13%)	1(12.5%)	2(7.69%)	4(25%)	2(8.33%)
Negative(102)	37(94.87%)	7(87.5%)	24(92.31%)	12(75%)	22(91.67%)
P value	0.3	0.5	0.1	0.4	0.1
Consguinity Positive (64)	21(53.5%)	6(75%)	6(23.08%)	12(75%)	19(74.17%)
Negative (49)	18(46-15%)	2(25%)	20(76.92%)	4(25%)	5(20.83%)
P value	0.6	0.4	0.001	0.17	0.01
Maternal disease diseased (55)	11(28-21%)	(1(12.5%)	26(100%)	9(56-25%)	8(33.33%)
healthy (58)	28(71.79%)	7(87.5%)	0(0%)	7(43.75%)	16(66.67%)
P value	0.07	0.06	0.001	0.5	0.1

Parity ≤ 2 children (62)	24(61-54%)	4(50%)	9(34.62%)	5(31-25%)	10(41.67%)
≥ 3 children (51)	15(38-46%)	4(50%)	17(65-28%)	11(68.75%)	14(58.33%)
P value	0.3	0.1	0.2	0.2	0.6
Age of onset of seizure ≤ 3 days (65)	22(56.41%)	1(12.5%)	24(42.31%)	4(25%)	14(58.33%)
> 3 days (48)	17(43.59%)	7(87.5%)	2(7.69%)	12(75%)	10(41.67%)
P value	0.001	0.01	0.001	0.006	0.1
Mode of delivery ND (65)	38(97.44%)	7(87.5%)	2(7.69%)	8(50%)	10(41.67)
C/S (48)	1(2.56%)	1(12.5%)	24(92.31%)	8(50%)	14(58.33%)
P value	0.001	0.001	0.001	0.1	0.2
Gestational age Full term (49)	11(58.97%)	1(12.5%)	22(92.31%)	4(25%)	9(58.33%)
Preterm (64)	28(41.03%)	7(87.5%)	4(7.69%)	12(75%)	15(41.67%)
P value	0.06	0.02	0.001	0.003	0.6
Body weight ≥ 2500 gm (57)	14(35.9%)	1(12.5%)	24(92.31%)	6(37.5%)	12(50%)
< 2500 gm (56)	25(64-1%)	7(87.5)	2(7.64%)	10(62.5%)	12(50%)
P value	0.07	0.003	0.001	0.2	0.1
Maternal drug history Positive (48)	9(23.08)	1(12.25%)	25(96.15%)	8(50%)	5(20.83%)
Negative (65)	30(76.92%)	7(87.75%)	1(3.85%)	8(50%)	19(79.17%)
P value	0.002	0.13	0.001	0.5	0.019

Discussion

The current study revealed an overall incidence of 3.57% of neonatal seizures among all admitted neonates during a whole of one calendar year. This result is comparable with global studies. In India, Dzhala et al. [11] reported 0.7-2.7%.. In Iraq , Al-Yasiri [12] found (3.9%) were having seizures, while Al-Zawini et al. [13]

These variations in the incidence rate are attributed to several factors the most important of which is the method of diagnosis. The clinical presentation of seizures during the neonatal period is subjective, leading to considerable variability in the recognition and diagnosis [14]. The current study depended only on the clinical diagnosis while many other studies, especially those which reported high rate used EEG beside clinical characteristics for diagnosis which is more precise and reliable. In this regard, one study revealed that 80% of EEG documented seizures were not accompanied by observable clinical signs [15]. In another study, only 27% of clinical seizures were correctly identified by EEG, while 73% of presumed clinical seizures were negative [16]. The study design also affects the result. Digra and Gupta [17] found that incidence was 19.2% in hospitalized neonates. which is comparable to that obtained by Seay and Bray [18] who estimated that 20% of neonates in the ICU had evidence of seizure activity at some time.

The most common cause of neonatal seizures in this study was asphyxia (34.5% of cases) followed by hypoglycemia (23% of cases).

Family history in neonatal seizure is mainly associated with benign familial neonatal seizure (BFNS) which may present in the current series but without molecular detection. This type of neonatal seizure is associated with certain mutations. Grinton et al. [21] reported KCNQ2 gene mutation in 27 families, SCN2A mutation in 2 families and KCNQ3 mutation in one family. Because there were no adequate facilities, Iraqi hospitals cannot detect such mutation and the incidence of BFNS.

The parents of more than half (56.64%) of the babies with neonatal seizures in this study are of consanguineous marriage.Very few studies addressed this issue worldwide, because it is only prevalent in some developing countirs. This high percentage reflects the presence of recessive gene which exert their effects only when presents in homozygous genotype.

The study revealed significant association between the undiagnosed cause(s) of neonatal seizure and consanguineous marriage. This result implies inhereted causes of neonatal seizure and support the assumption of presence of benign familial neonatal seizures cases among certain families. Howvere, more investigations are required to endore this assumption.

Among the 55 ill mothers, the vast majority (52) was diabetic taking insulin in different forms, and this was reflected by 100% of neonates with hypoglycemia. Generally, diabetes in mother was found to increase the risk of neonatal seizures more than 4-fold mainly through causing hypoglycemia in infants [22].

Interestingly, early onset of seizure (≤3 days) was significantly associated with hypoglycemia while delayed onset (>3 days) was significantly associated with IVH and hypocalcemia. Infants suffering from hypoglycemia will have seizure in early life probably because the hypoglycemia has already developed during late stages of pregnancy (in mother with diabetes). Hypocalcemia, on the other hand usually develop due to several factors, the most important of which are vitamin D status of the mother and using formula for infant feeding especially that containing high percentage of phosphorus. These factors are associated with delayed (>3days) onset of hypocalcemia [23].

In our study we found that full term infants with normal body weight were significantly associated with hypoglycemia, while preterm and low body weight infant was significantly associated with IVH and hypocalcemia. While other studies considered preterm , low body weight, delay in the breast feeding for more than 2 hrs postnatal, large for gestational age (LGA) and cold stress as risk factor for neonatal hypoglycemia [24]. This disparity may be due to the vast majority of hypoglycemic neonates were born from diabetic mothers .

For the significant association of preterm and low body weight infants with asphyxia, it is a logical result because preterm infant fail to initiate breathing at time of delivery causing hypoxia leading to hypoxic ischemic encephalopathymore . [25].

Conclusions

1- There is a relatively high incidence of neonatal seizures in Al-Diwaniyah
2- Four main causes are responsible for the majority of cases which are perinatal asphyxia, hypoglycemia, hypocalcemia and intraventricular hemorrhage.
3- Early onset of seizure, mother's illness during pregnancy, normal vaginal delivery, and low birth weight baby are the most important risk factors for developing seizures in neonates.
4- Consanguinity may predispose for neonatal seizures through certain genes that are prevalent among certain families.

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