Neonatal Encephalopathy in the Term Newborn

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Abstract

Introduction: Perinatal brain injury is the third leading cause of child mortality globally.

Purpose: Evaluation of perinatal risk factors for encephalopathy in neonates in order to prevent deaths and disabilities

Method: This is a prospective, case-control study conducted in the Maternity Hospital "K. Gliozheni" during the time period 2012 - 2016. 65 newborns at term ≥37 weeks diagnosed with encephalopathy according to the Thompson classification >5 within 12 hours of birth were compared with a control group, infants without encephalopathy in a 1:1 ratio selected casual and gender-appropriate.

Results: Total antepartum risk factors were found in (70.8%) of cases and (18.5%) of controls (p<0.01). Sentinel events were found in 38.5% of cases and in 9.2% of controls. (p<0.01). Acute intrapartum events in total were found in (38.5%) of cases and (9.2%) of controls (p<0.01). 43.1% of babies had a combination of antepartum and intrapartum factors (p<0.01). Significant and independent predictive factors of risk for neonatal encephalopathy resulted: from maternal factors, mother's age >35 years (p=0.03). Of the intrapartum factors: pregnancy with twins (p<0.01), hypertension/preeclampsia (p<0.01), non-reactive FHR before delivery (p<0.01).

From intrapartum factors: breech birth (p=0.01), emergency cesarean section (p=0.01), meconial amniotic fluid (p=0.02), prolonged birth (p=0.01).

Conclusion: Knowledge of perinatal risk factors associated with neonatal encephalopathy is essential for developing interventions to prevent neonatal death and disability.

Key words: *neonatal encephalopathy, hypoxic ischemic encephalopathy, etiological factors*

Introduction

Neonatal encephalopathy is estimated to affect 2-9:1000 term newborns, while EHI affects 1.5-2.6:1000 term newborns. As the term "neonatal encephalopathy" became increasingly favored, studies show that the diagnosis of "birth asphyxia" declined between 1991 and 2000 (1-3). It is essential for health care providers to understand that the term "neonatal encephalopathy" is simply a descriptive term for the neurological condition of the newborn, and does not determine the underlying etiology of the condition. Unfortunately, the term hypoxic-ischemic encephalopathy (EHI) is the most common term still used to describe any newborn showing signs of encephalopathy, but this term may not be accurate (4). The term Hypoxic-Ischemic Encephalopathy should not be used, if there is no evidence of perinatal asphyxia as the primary cause of the encephalopathy (5). EHI is a frequent cause of neonatal encephalopathy, but the differential diagnosis should also be made with other causes such as infections, epilepsy, genetic, maternal, metabolic or toxic, so health care providers should be familiar with the evaluation, diagnosis and treatment of various causes of Neonatal Encephalopathy (6,7).

The use of the term neonatal encephalopathy and Hypoxia Ischemia is often contradictory. It has been proposed that the term neonatal encephalopathy should be used for full-term and near-term infants who have not shown any "sentinel" events (8,9). It is difficult to prove the presence of cerebral hypoxia except in animal models or in cases of neonatal cerebral ischemia. All currently used clinical and laboratory parameters including umbilical blood pH and seizures are nonspecific (10). Some of the cerebral lesions shown in the MRI of EN patients can be provoked in animal models by inducing hypoxia/ischemia, but this again does not prove that the entire spectrum of EN manifestations is a consequence of cerebral hypoxia (11-13). There are few studies conducted on a population basis that have shown that there are antepartum risk factors, and not just asphyxia, that are associated with EN (14). On the contrary, some authors state that EHI is the cause of EN in 50-80% of cases, based on clinical criteria, EEG and MRI (15). The purpose of the

study is to evaluate perinatal risk factors for encephalopathy in neonates in order to prevent deaths and disabilities.

Method

Type of study

This is a prospective, case-control study. The study was conducted at the Maternity Hospital "K. Gliozheni" during the time period 2012 - 2016.

Sample

Patients included in the study:

- Newborns at term ≥37 weeks diagnosed with encephalopathy according to the Thompson classification >5 within 12 hours of birth.
- Babies with encephalopathy were compared with a control group, babies without encephalopathy in a 1:1 ratio, randomly selected and adjusted according to gender.
- Control babies were included in the study if they were at term and the Thompson score was <3.
- Neurological assessment was performed at the beginning of the study for cases and controls and then every day for 5 days (cases only).
- Encephalopathy was graded (mild, moderate, or severe) on the most severe day between days 1 and 5, according to the modified Sarnat classification.

Exclusion criteria from the study:

- Preterm babies (< 37 weeks);
- babies with marked dysmorphia or babies with at least one major congenital anomaly;
- babies with hepato-splenomegaly, cataract and thrombocytopenia indicative of intrauterine infection;
- babies with microbiological evidence of early neonatal infection with positive bacteriological cultures of blood or cerebrospinal fluid collected within 24 hours of birth; and infants whose neurological condition normalizes with correction of hypoglycemia
- Babies, cases and controls who have used antibiotics

Examinations

Umbilical cord blood gas examination, including pH and base excess values, was routinely obtained at the time of delivery in all neonates, including controls.

Assessment of amniotic fluid volume at term; oligohydramnios was defined as an amniotic fluid index <5 cm and polyhydramnios as a vertical pocket >8 cm.

Small for gestational age was defined as a birth weight <10th percentile adjusted for sex and gestational age according to WHO.

Physiological variables monitored:

- Heart rate
- Respiratory frequency, saturation
- Arterial pressure
- The temperature

Clinical evaluations include:

- Neurological status on admission and during NICU stay,
- Type of respiratory support required,
- Determining the degree of encephalopathy,
- The presence of seizures and the time of their onset,
- Time of full initiation of oral feeding,
- Neurological examination at discharge.

Results

65 babies with encephalopathy and 65 controls - babies without encephalopathy - took part in the study.

Regarding the clinical characteristics for Apgar score 1 min and Apgar score 10 min, the values were smaller in the cases with a significant difference with the controls ($p<0.01$).

For Apgar score 1 min <3 there were 60 (92.3%) of cases and 2 (3.1%) of controls, for score 4-7 there were 5 (7.7%) of cases and 52 (80%) of controls and for score > 7 were only 11 (17%) of controls and none of the cases.

For Apgar score 10 min <3 there were 33 (50.8%) of the cases and none of the controls, for score 4-7 there were 32 (49.2%) of the cases and 7 (10.8%) of the controls and for score >7 there were only 58 (89.2%) of the controls and none of the cases.

The need for resuscitation prevails in cases compared to controls (p<0.01).

There was no need for resuscitation in only 1 (1.5%) of the cases and 58 (89.2%), of the controls, inhalation, oxygen mask or both were applied in 23 (35.4%) of the cases and 7 (10.8%) of the controls, positive pressure ventilation was applied in 23 (35.4%) of the cases and 1 (1.5%) of the controls, while only endotracheal intubation and intubation accompanied by cardiac massage was applied in 5 (7.7%) and 14 (21.5%) respectively. in cases. Birth trauma affected 12 (18.5%) of the cases and 1 (1.5%) of the controls (p<0.01). Table 1 presents the characteristics of encephalopathic infants and controls.

TABLE 1. Characteristics of encephalopathic infants and controls

Characteristics	Encephalopathic infants (n=65)	Controls (n=65) P	P
Apgar score min. 1			
<3	60 (92.3)	2 (3.1)	<0.01
4-7	5 (7.7)	52 (80.0)	
>7	0	11 (17.0)	
Apgar score min. 10			
<3	33 (50.8)	0	<0.01
4-7	32 (49.2)	7 (10.8)	
>7	0	58 (89.2)	
Resuscitation			
Jo	1 (1.5	58 (89.2)	
Suction reflex, oxygen mask or both	23 (35.4)	7 (10.8)	<0.01
ventilation	23 (35.4)	1 (1.5)	
Endotracheal intubation	5 (7.7)	0	
Intubation and cardiac massage	14 (21.5)	0	
Birth trauma			
Yes	12 (18.5)	1 (1.5)	<0.01
No	53 (81.5)	64 (98.5)	

Clinical characteristics of babies with neonatal encephalopathy: in relation to the degree of encephalopathy, the average degree predominates in 36 (55.4%) of the cases, followed by the severe degree in 21 (32.%) and the mild degree in 7 (10.8%) of the cases (p <0.01).

Regarding neurological signs > 48 hours, weakening of tone and reflexes was observed in 41 (63.1%) cases, agitation in 28 (43.1%) cases and MODS appearance in 44 (67.7%) cases (p=0.4).

Convulsions were observed clinically in 29 (44.6%) cases, lack of absorption in 51 (78.5%) cases (p<0.01), metabolic acidosis in 27 (41.5%),

16 (24.6%) of the cases ended in exitus before exit.

Neurological condition at discharge was normal in 22 (45%) cases, abnormal tone in 14 (28.6%), abnormal tone and absorption in 5 (10.2%) and abnormal tone, absorption and level of consciousness in 8 (16.3%)) in cases, (p<0.01).

TABLE 2. Multivariate analysis of intrapartum risk factors for encephalopathy. Logistic regression

Intrapartum factors	OR	aOR	95%CI	P
Cord prolapse	1.0	1.12	0.41 – 5.12	0.9
Detachment of the placenta	11.6	2.28	0.85 - 4.75	0.1
Amniotic fluid embolus	7.3	1.76	0.68 - 2.99	0.4
Shoulder dystocia	7.3	1.80	0.80 - 2.86	0.2
Acute onset of bradycardia	16.7	2.38	0.83 - 5.85	0.1
Podalic birth	7.3	3.35	1.38 - 8.11	0.01
Uterine rupture	6.5	1.73	0.68 - 3.44	0.1
Emergency cesarean section	4.6	3.91	1.96 - 7.84	0.01
Meconial amniotic fluid	5.8	3.04	1.56 - 9.47	0.02
PROM > 18 hours	6.7	2.12	0.87 – 3.12	0.1
Prolonged labor	4.7	3.84	1.56 - 9.47	0.01

Discussion

Total antepartum risk factors were found in 46 (70.8%) cases and 12 (18.5%) controls (p<0.01). Significant factors resulted:

- Diabetes mellitus
- Hypertension/preeclampsia
- Chorioamnionitis
- Obesity
- Non-reactive prenatal Fetal Heart Rate
- Of the prenatal risk factors with diabetes, there are 8 (12.3%) of the case mothers and 2 (3.1%) of the controls (p=0.05),
- Hypothyroidism in 3 (4.6%) of cases and 1 (1.5%) of controls (p=0.3),
- Hypertension/preeclampsia in 13 (20%) of cases and 3 (4.6%) of controls (p<0.01), -
- Chorioamnion in 6 (9.2%) of cases and 1 (1.5%) of controls (p=0.05),

- Marked anemia during pregnancy in 4 (6.2%) of cases and 1 (1.5%) of controls (p=0.01).
- Obesity in 10 (15.4%) cases and 2 (3.1%) controls (p=0.01),
- Previous cesarean delivery in 12 (18.5%) of cases and 5 (7.7%) of controls (p=0.07),
- Neurological pathology (hemiparesis) in 3 (4.6%) cases and none of the controls (p=0.08),
- No prenatal care in 3 (4.6%) of the cases and none of the controls (p=0.08), SGA in 7 (10.8%) of the cases and 4 (6.2%) of the controls (p=0.3),
- Oligohydramnios in 5 (7.7%) of cases and 2 (3.1%) of controls (p=0.2),
- Polyhydramnios in 5 (7.7%) of cases and 1 (1.5%) of controls (p=0.09).
- Non-reactive FHR before delivery was found in 21 (32.3%) cases and 1 (1.5%) of controls (p<0.01).
- Urinary infection was found in 6 (9.2%) cases and 2 (3.1%) controls (p=0.1).
- Streptococcus GBS + was found in 7 (10.8%) of cases and 3 (4.6%) of controls (p=0.2).
- Dysmorphic features / mother or father was found in 1 (1.5%) cases and none of the controls and
- Marked anemia of the baby at birth was found in 2 (3.1%) of the cases and 1 (1.5) of the controls (p=0.6).

Sentinel events were found in 38.5% of cases and in 9.2% of controls, with a significant difference between them (p<0.01).

Acute intrapartum events in total were found in 25 (38.5%) of the cases and 6 (9.2%) of the controls, with a significant difference (p<0.01) of which:

- Cord prolapse in 1 (1.5%) case and in 1 (1.5%) control,
- Detachment of the placenta in 10 (15.4%) of the cases and 1 (1.5%) of the controls (p<0.01),
- Amniotic fluid embolism in 3 (4.6%) cases and none of the controls (p=0.08),
- Shoulder dystocia in 3 (4.6%) cases and none of the controls (p=0.08),
- Acute onset of bradycardia in 7 (10.8%) cases and none of the controls (p<0.01),
- Podal birth in 8 (12.3%) cases and none of the controls (p<0.01),
- Uterine rupture (external or burden-related factors) in 6 (9.2%) cases and 1 (1 (1.5)%) of controls p=0.05.
- Emergency cesarean section in 15 (23.1%) of cases and 1 (1 (1.5%) of controls, 4 (6.2%) p<0.01.
- Meconial amniotic fluid in 18 (27.7%) of cases and 4 (6.2%) of controls p<0.01, -PROM > 18 hours in 16 (24.6%) of cases and 3 (4.6%) of controls p<0.01,

- Prolonged labor in 16 (21 (32.3%) of cases and 6 (9.2%) of controls p<0.01.
- 27 (43.1%) of the babies had a combination of antepartum and intrapartum factors compared to 4 (6.2%) of the controls, (p<0.01).

Regarding the maternal factors, the average age of the mothers of the cases is greater M=28.7 (±5.2) years compared to the age of the control mothers M=26.5 (±4.8) years, p=0.01.

In cases, a low economic level prevails in 16 (24.6%) compared to 3 controls (4.6%), with a significant difference between them (p<0.01).

Also, the low level of education prevails in 15 cases (23.1%) compared to 5 controls (7.7%), with a significant difference between them (p=0.02).

Assisted fertilization was performed in 19 (29.2%) of the cases and 4 (6.2%) of the controls, with a significant difference between them (p=0.02).

Previous neonatal death occurred in 7 (10.8%) of the cases and 1 (1.5%) of the controls, with a significant difference between them (p=0.03).

Twin pregnancy occurred in 10 (15.4%) of the cases and 1 (1.5%) of the controls (p<0.01).

Metabolic disorders of the fetus were found in 17 (26.2%) of the cases and 2 (3.1%) of the controls, with a significant difference between them (p<0.01).

Myopathy was found in 7 (10.8%) of the cases and 1 (1.5%) of the controls, with a significant difference between them (p=0.03).

The results of our study are similar and comparable with other studies reported in literature (16-18). Accurate prediction of the severity of long-term complications of neonatal encephalopathy is difficult, although clinical, laboratory and imaging criteria have been used (19,20).

Conclusion

Correct recognition and interpretation of the term neonatal encephalopathy and not confusing it with the term hypoxic-ischemic encephalopathy is important for diagnosis and treatment. Identification of risk factors before birth and timely intervention in such cases can minimize fetal injury and occurrence of NE Introduction of advanced methods of treating encephalopathy such as hypothermia will improve the survival and outcome of the infants. The use of advanced imaging methods for diagnosis such as magnetic resonance is will provide more accurate diagnosis.

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