Scientific Research Publishing

Open Journal of Pediatrics, 2024, 14, 1079-1089
https://www.scirp.org/journal/ojped
ISSN Online: 2160-8776
ISSN Print: 2160-8741

Epidemiological, Diagnostic and Evolutionary Profile of Seizures in Young Infants at Albert Royer (Dakar/Senegal)

Cissé Djénéba Fafa[1], Dieng Yaay Joor[2], Diagne Guillaye[1], Sow Ndeye Fatou[3], Kane Awa[1], Mbaye Aminata[2], Faye Papa Moctar[2], Ly Fatou[1], Gueye Modou[4], Diagne-Gueye Ndeye Rama[4], Sylla Assane[5], Ndiaye Ousmane[2]

[1]Pediatrics Department, Pikine National Hospital, Dakar, Senegal
[2]Neonatal Department, Albert Royer National Children's Hospital, Dakar, Senegal
[3]Pediatrics Department, Dalal Jamm National Hospital, Dakar, Senegal
[4]Neonatal Department, Diamniadio Children's Hospital, Dakar, Senegal
[5]Pediatrics Department, Abass Ndao National Hospital, Dakar, Senegal
Email: fafcisse17@hotmail.com

How to cite this paper: Fafa, C.D., Joor, D.Y., Guillaye, D., Fatou, S.N., Awa, K., Aminata, M., Moctar, F.P., Fatou, L., Modou, G., Rama, D.-G.N., Assane, S. and Ousmane, N. (2024) Epidemiological, Diagnostic and Evolutionary Profile of Seizures in Young Infants at Albert Royer (Dakar/Senegal). *Open Journal of Pediatrics*, **14**, 1079-1089.
https://doi.org/10.4236/ojped.2024.146104

Received: October 10, 2024
Accepted: November 12, 2024
Published: November 15, 2024

Abstract

Introduction: Seizures are one of the most common neurological complications in the infant period. The aim of our study was to describe the epidemiological, clinical, therapeutic and prognostic features of seizures in infants at the Albert Royer Children's Hospital (Senegal). **Materials and Methods:** This was a retrospective, descriptive study from 1 January 2012 to 30 September 2018 of infants aged 0 days to 2 months who presented with seizures. **Results:** The hospital rate was 8.5%. Almost all the mothers (99.1%) had undergone at least 3 antenatal visits. Urogenital infection, gestational arterial hypertension and funicular anomalies were the main pregnancy-related pathologies. Delivery was vaginal in the majority of cases (80.9%). Most infants (43.6%) had not cried at birth. The majority of infants (63%) were born at term. Trophicity was normal in 68% of cases. The average age of the infants was 6.7 days. The main causes of seizures were hypoxic-ischemic encephalopathy (48.7%), metabolic disturbances (48.1%) and central nervous system infections (15.6%). Phenobarbital was the 1st-line anticonvulsant. The case fatality rate was 39.5%. The main sequela observed were delayed psychomotor development (20.6%). **Conclusion:** Optimal management of infant seizures requires early diagnosis and etiological treatment by improving the quality of perinatal care to ensure better management of risk factors, as well as increasing the availability of neuroimaging equipment.

Keywords

Seizures, Infant, Albert Royer Hospital

1. Introduction

The neonatal period is a high-risk period for neurological morbidity and mortality, one of the most common manifestations of which is seizures [1] [2]. The exact prevalence of neonatal seizures is difficult to estimate, due to a wide variability in its frequency in most studies worldwide (1.5‰ - 5.5‰ in newborns). This could be explained by the disparity in inclusion criteria, the diversity in the methodology used to identify seizures and the lack of description of the clinical presentations of seizures [3]-[5]. Investigating the etiology of an infant's seizures is a crucial step in ensuring appropriate therapeutic management. Thanks to early and accurate detection of the underlying cause of the seizures, recent advances in neuroimaging techniques, particularly electroencephalographic monitoring, have significantly improved the prognosis, as well as new neuroprotective strategies such as hypothermia. The management of seizures is often problematic in developing countries, as resuscitation equipment and anticonvulsants are sometimes lacking due to their unavailability or unsuitable galenic presentations. In sub-Saharan Africa, particularly Senegal, the main studies concern perinatal asphyxia. The aim of our study was to describe the epidemiological, clinical, therapeutic and prognostic characteristics of seizures in young infants in the neonatology department of the Albert Royer National Children's Hospital (Senegal).

2. Materials and Methods

2.1. Study Setting

The study took place in the neonatology unit of the Albert Royer Children's Hospital, a national referral service, which receives and admits infants aged 0 - 2 months, all from other health facilities in the regions of Senegal.

2.2. Type, Period and Study Population

This was a retrospective, descriptive and analytical study, conducted from 1 January 2012 to 30 September 2018, of infants admitted who presented with seizures.

2.3. Inclusion Criteria

All infants aged 0 days to 2 months with seizures diagnosed at the clinic examination during the study period were included.

2.4. Data Collected and Parameters Studied

Data were collected on a pre-established survey form after consultation with hospital records, the health record and the liaison form for referred children. The

parameters studied were epidemiological (age, sex, geographical origin), diagnostic (clinical and paraclinical signs, etiologies), therapeutic (ventilatory support, etiological treatment) and evolutionary (mortality, complications), relating to the characteristics of the mother and the infant.

2.5. Data Entry and Statistical Analysis

Data were entered and analyzed using SPSS software version 20.0. Qualitative variables were expressed as percentages and quantitative variables as means or medians with their ranges. For statistical comparisons, we used Pearson's Chi-squared and the p-value (p), with a 95% confidence interval when the p-value was significant ($p < 0.05$), depending on the conditions of application.

3. Results

3.1. Epidemiological and Socio-Demographic Data

A total of 351 infants were included, representing a hospital frequency of 8.5%. The most common maternal age group was between 18 and 35 years. The majority of mothers (66%) were from the suburbs of Dakar. The socio-economic level was low in half the cases (50.0%).

3.2. Maternal Medical and Gynecological-Obstetric Data

The average gestational age was 2.5 and the average parity was 1.9. Primiparous women accounted for 46.1% of the total, compared with 53.9% of multiparous women. Almost all the mothers (99.1%) had made at least 3 antenatal visits. Urogenital infections (6.3%), gravid hypertension (2.8%) and funicular abnormalities (3.1%) were the main medical and gynecological-obstetric pathologies associated with pregnancy. Prolonged labor lasting more than 12 hours occurred in 10.5% of cases. Delivery was by non-instrumental vaginal way in the majority of cases (80.9%).

3.3. Clinical Data

Most of the infants (43.6%) had not cried at birth and had been resuscitated in the delivery room. The Apgar score at 5 minutes was less than 7 in 12.8% of cases. The majority of infants (63%) were born at term, compared with 3.1% of premature babies and 4% of post-mature babies (**Figure 1**).

Trophicity was normal in 68% of cases. The sex ratio (M/F) was 1.4. The mean age of the infants was 6.7 days [0 days - 2 months]. Half of the cases (52.7%) were admitted before 72 hours of life. The clinical features of the seizures were dominated by focal tonic seizures (47.3%), multifocal clonic seizures (41.9%), subtle seizures as oral-buccal-lingual movements (19.9%) and abnormal eye movements (15.9%). A status epilepticus was noted in 8% of cases. The total duration of seizures was less than 72 hours in the majority of cases (70.3%). Other neurological abnormalities were dominated by abnormal primitive reflexes (74.6%) and lethargy (35.8%). Other clinical signs associated with seizures were dominated by

disturbances in thermal regulation (66.2%) and respiratory distress (50.2%). The main causes of seizures were hypoxic-ischemic encephalopathy (48.7%), metabolic disturbances (48.1%), particularly dysnatremia, central nervous system infections (15.6%), and bilirubin encephalopathy (4.5%) (as shown in Table 1).

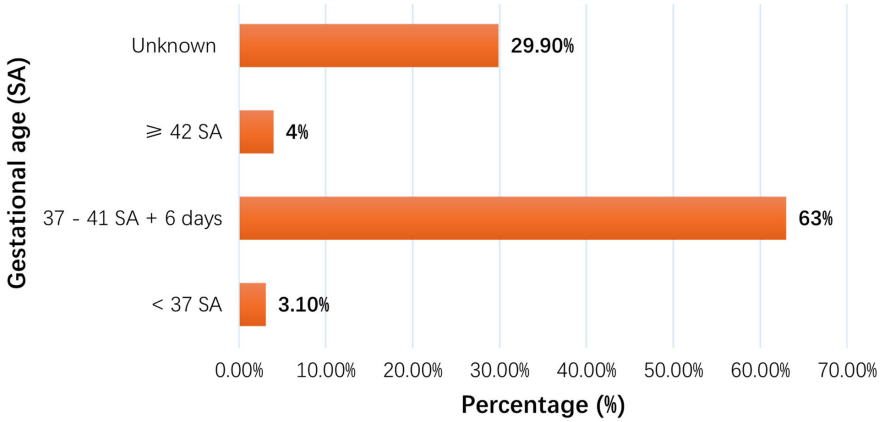

Figure 1. Distribution of cases according to gestational age.

Table 1. Distribution of cases by causes.

Causes	Number (n)	Percentage (%)
Hypoxic-ischemic encephalopathy	171	48.7
Metabolic disturbances	169	48.1
Central nervous system infections	55	15.6
Bilirubin encephalopathy	16	4.5
Intracranial hemorrhage	10	2.7
Ischemic stroke	8	2.2
Neonatal epilepsy	6	1.7
Congenital hydrocephalus	3	0.7
Congenital malaria	2	0.5
Viral encephalitis	2	0.5
Aminoacidopathy	1	0.2
Unknown	20	5.7

3.4. Paraclinical Data

Laboratory tests abnormalities included hyponatremia (17.1%), hypernatremia (9.4%), renal failure (9.9%), hepatic cytolysis (6.8%), hypomagnesaemia (6.5%), hypocalcaemia (4.5%), hyperkaliemia (1.4%) and hepatocellular failure (0.2%). The most common Transfontanellar ultrasound abnormalities were hemorrhagic lesions (6.1%) and hypoxic-ischemic white matter lesions (3.1%).

3.5. Therapeutic Data

Phenobarbital was administered as the first line anticonvulsant in the majority of cases (84%), followed by diazepam (19.9%) (Figure 2).

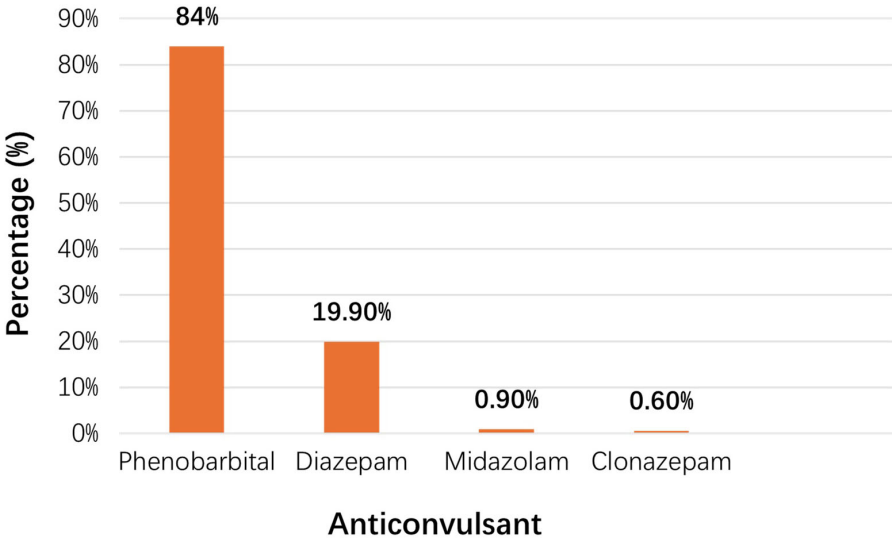

Figure 2. Distribution of cases according to anticonvulsant treatment.

An oral relay was instituted in 16.5% of cases, and sodium valproate was used most frequently. The associated therapeutic measures are shown in the following table **(Table 2).**

Table 2. Associated therapeutic measures.

Other therapeutic measures	Number (n)	Percentage (%)
Invasive ventilation	86	24.5
Magnesium sulphate	9	2.5
Correction of hypoglycemia	20	5.7
Correction of hyponatremia	45	12.8
Correction of hypocalcaemia	8	2.28
Rehydration	49	13.9
Phototherapy	14	3.9
Antibiotic therapy	38	10.8

3.6. Evolutionary Data

The case fatality rate was 39.5%. The majority of deaths (59.2%) occurred within 72 hours of hospitalization. The etiologies and clinical signs associated with the highest mortality were stroke (62.5%), dehydration (48.1%), hypernatremia (45.5%) and EAI (35.1%). The main sequela observed were delayed psychomotor development (20.6%), cerebral palsy (6.0%), epilepsy (4.8%) and neurological sequela (1.2%). Cerebral palsy occurred more frequently in infants who had convulsed for more than 48 hours (28.6% cases).

3.7. Factors Associated with Mortality

Mortality was significantly associated with prematurity ($p = 0.002$), macrosomia ($p = 0.006$), intrauterine growth restriction ($p = 0.006$), resuscitation at birth ($p =$

0.003), dehydration (p = 0.005), shock (p = 0.008), postnatal age greater than 48 hours (p < 0.003) and status epilepticus (p = 0.01) **(**Table 3**)**.

Table 3. Factors associated with mortality.

Parameters	Survival		Death		OR	p-value
	Number	%	Number	%		
Term						
< 37 SA	2	18	9	82	6.99	**0.002***
> 37 SA	141	61	90	39	-	-
Trophicity						
Eutrophy	146	61	92	39	-	
Macrosomia	23	82	5	18	0.34	**0.006***
Hypotrophy	24	51	23	49	1.52	**0.006***
Type of seizures						
Generalized	46	71	19	29	-	-
Localized	87	63	52	37	1.45	0.05
Resuscitation at birth						
Yes	99	66	52	34	0.63	**0.003***
No	213	58	154	42	-	**-**
Dehydration						
Yes	32	62	20	38	0.75	**0.005***
No	250	54	209	46	-	**-**
Shock						
Yes	7	27	19	73	3.55	**0.008***
No	275	57	210	43	-	**-**
Postnatal age						
≤ 48h	111	63	65	37	-	**-**
> 48h	99	58	72	42	1.24	**0.003***
Status epilepticus						
Yes	14	50	14	50	0.63	**0.01***
No	196	61	123	39	-	**-**

***:** significant p-value (< 0.05); **SA =** week of amenorrhea

4. Discussion

In our study, the frequency of hospitalization was high at around 8.5%, demonstrating its relatively common occurrence in the infant period in our regions. A lower result was found in Morocco in 2017 (4.5%) [6]. However, this difference can be explained by our longer study period. The most represented maternal age group was between 18 and 35 years, in contrast to a study conducted in California where maternal age over 40 years was an independent risk factor associated with the occurrence of infant seizures [7]. Throughout the literature, primiparity is associated with a higher risk of childbirth difficulties [8]. In our study, most of the mothers were primiparous. Almost all the mothers had undergone at least 3 antenatal visits. However, these pregnancies were insufficiently monitored and this situation was correlated with the socio-economic level, which was considered low in the majority of cases. In our series, we noted medical and gyneco-obstetric complications such as urogenital infection, gravid arterial hypertension, funicular

anomalies and prolonged labor, thus demonstrating their role in the genesis of neonatal complications. These results are comparable to those of other studies on the subject [7] [9]. In our study, vaginal delivery predominated (80.9%), unlike in Morocco, where the caesarean section rate was higher (45%). This would reduce the risk of childbirth complications, particularly perinatal asphyxia [6]. Most of the infants (43.6%) had required resuscitation in the delivery room, a result consistent with the presence of hypoxic-ischemic encephalopathy as the main cause of seizures. This situation would appear to be linked to poor resuscitation, which worsens the neurological prognosis and the incidence of seizures.

In our study, seizures mainly concerned full-term infants. Indeed, term and post-term infants are more exposed to the consequences of anoxo-ischemia, such as seizures [6] [7]. With regard to trophicity, hypotrophy and macrosomia may expose the baby to complications that can lead to seizures, such as metabolic disorders (hypoglycemia, hypomagnesaemia), obstetric trauma or ischemic lesions (leucomalacia) [10]. As reported in the literature, we noted a slight male predominance, reflecting the excess male morbidity in the neonatal period [6] [11] [12]. The majority of infants (64.1%) were less than 7 days old. Similar results have been reported by some authors, with greater susceptibility during the first week of life, particularly the first 48 hours [3] [6] [7] [13]. Neonatal seizures have unique clinical features compared with those of older infants and children. In addition to their discreet nature, which may escape the scrutiny of medical staff, they were focal in two-thirds of cases, in line with the literature [14]. In our study, they were focal tonic, multifocal clonic or subtle seizures as in the majority of cases, or of the chewing or eye-revulsion type, a result similar to that noted in Morocco [6]. The frequency of atypical seizures is also a feature of the neonatal period [15]. Archaic reflexes were blunted in most cases and hypotonia was often present. The main other associated signs were disturbances in thermal regulation and respiratory distress. These clinical signs were related to the etiology and were sometimes part of a multivisceral failure. Perinatal asphyxia, the cause of hypoxic-ischemic encephalopathy, is a worldwide public health problem. Metabolic disturbances are the 2nd leading cause of seizures, namely dysnatremia, hypoglycemia, hypomagnesaemia and hypocalcaemia, and central nervous system infections are in 3rd place [16]. In our context, the main causes of infant seizures were anoxic-ischemic encephalopathy, metabolic disturbances and meningitis. These results are similar to those of other studies on the subject [6] [17]-[19]. Diagnosis and investigation in infants are made difficult by the non-accessibility of certain complementary examinations. The main finding was that the essential test for confirming seizures, the electroencephalogram, was not available, and none of the children were able to benefit from it at the initial stage. Electroencephalogram plays an essential role in detecting subclinical seizures, confirming the epileptic nature of the seizures, assessing the prognosis, guiding treatment and sometimes contributing to the diagnosis [20]. Its unavailability is therefore a real obstacle to the monitoring and management of infant seizures. In addition, magnetic resonance imaging is rarely performed in the

neonatal period for reasons of availability, accessibility and organization. It is also an essential test for determining the prognosis in the event of seizures and neurological damage in the newborn [21] [22]. In our context, the most available examination is the Transfontanellar ultrasound, which has been able to demonstrate a certain number of lesions related to seizures. It is available on the ward at the patient's bedside. The standard biochemical work-up is also available, enabling the detection of a number of metabolic disorders associated with seizures.

Phenobarbital was the main anticonvulsant used in our study and in the study conducted in Morocco in 2017 [6]. It remains the treatment of choice for neonatal seizures, as shown by recent European and American surveys [17] [23]-[27]. Unfortunately, its shortage during the study period resulted in the use of diazepam, which is not recommended in the neonatal period. The drugs most commonly used in cases of infant seizures refractory to phenobarbital are phenytoin, levetiracetam, lidocaine and midazolam, but the majority remain unavailable. In addition to anticonvulsant treatment, the following therapeutic means have been used: correction of metabolic disturbances, administration of antibiotics and various means of resuscitation. Therapeutic hypothermia is not used, even though two large studies have demonstrated its efficacy in neuroprotection [28] [29]. In our study, neonatal convulsions are marked by a very high mortality rate of around 39.5%. A lower result (9%) was reported in Morocco in 2017 [6]. This situation could be explained by late referrals with a serious clinical picture, poor quality of initial management, inadequate technical facilities and unavailable drugs. Most deaths (59.2%) occurred within 72 hours of hospitalization. There was a high incidence of premature death associated with neonatal seizures [17] [30]. In survivors, the most common sequela reported across studies are neurological disorders, developmental delays and postnatal epilepsy [31]-[38]. In our work, the evolution was marked by the occurrence of epilepsy and neurological sequela such as cerebral palsy, language disorders, blindness and delayed psychomotor development. These sequela are relatively frequent and pose the problem of long-term follow-up. In our context, the socio-cultural realities and low socio-economic level make this care difficult. The following risk factors for death were identified: prematurity ($p = 0.02$), macrosomia ($p = 0.006$), intrauterine growth retardation ($p = 0.006$), the presence of dehydration ($p = 0.005$) or shock ($p = 0.008$), age greater than 48 hours and status epilepticus ($p = 0.01$). The association between the presence of status epilepticus and mortality supports the hypothesis that optimal seizure control in terms of both detection and treatment improves the neurological prognosis in these infants. Furthermore, improving short- and long-term neurological outcomes requires correct management of the risk factors of prematurity and intrauterine growth retardation, as well as fluid and electrolyte disturbances [17] [30] [39] [40].

5. Conclusion

Neonatal seizures have unique clinical features and are often subclinical. This requires immediate assessment to determine the cause, institute emergency treatment

specific to the etiology and limit cerebral dysfunction. Hence there is a need to equip neonatology departments with continuous video-EEG equipment in order to refine the detection of electrographic seizures, but also to optimize the quality of perinatal care for better management of risk factors for neonatal seizures.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Volpe, J.J. (2008) Neonatal Seizures. In: Volpe, J.J., Ed., *Neurology of the Newborn*, Elsevier, 203-244. https://doi.org/10.1016/b978-1-4160-3995-2.10005-6

[2] Clancy, R.R. (2006) Summary Proceedings from the Neurology Group on Neonatal Seizures. *Pediatrics*, **117**, S23-S27.

[3] Lanska, M.J., Lanska, D.J., Baumann, R.J. and Kryscio, R.J. (1995) A Population-Based Study of Neonatal Seizures in Fayette County, Kentucky. *Neurology*, **45**, 724-732. https://doi.org/10.1212/wnl.45.4.724

[4] Ronen, G.M., Penney, S. and Andrews, W. (1999) The Epidemiology of Clinical Neonatal Seizures in Newfoundland: A Population-Based Study. *The Journal of Pediatrics*, **134**, 71-75. https://doi.org/10.1016/s0022-3476(99)70374-4

[5] Saliba, R.M., Annegers, J.F., Waller, D.K., Tyson, J.E. and Mizrahi, E.M. (1999) Incidence of Neonatal Seizures in Harris County, Texas, 1992-1994. *American Journal of Epidemiology*, **150**, 763-769. https://doi.org/10.1093/oxfordjournals.aje.a010079

[6] Kojmane, W., Hmami, F. and Atmani, S. (2019) Convulsions néonatales (À propos de 96 cas). *Journal de Pédiatrie et de Puériculture*, **32**, 259-261. https://doi.org/10.1016/j.jpp.2019.06.008

[7] Glass, H.C., Pham, T.N., Danielsen, B., Towner, D., Glidden, D. and Wu, Y.W. (2009) Antenatal and Intrapartum Risk Factors for Seizures in Term Newborns: A Population-Based Study, California 1998-2002. *The Journal of Pediatrics*, **154**, 24-28.E1. https://doi.org/10.1016/j.jpeds.2008.07.008

[8] Munan, R., Kakudji, Y., Nsambi, J., Mukuku, O., Maleya, A., Kinenkinda, X., *et al*. (2017) Accouchement chez la primipare à Lubumbashi: Pronostic maternel et périnatal. *Pan African Medical Journal*, **28**, Article No. 77. https://doi.org/10.11604/pamj.2017.28.77.13712

[9] Hall, D.A., Wadwa, R.P., Goldenberg, N.A. and Norris, J.M. (2006) Maternal Risk Factors for Term Neonatal Seizures: Population-Based Study in Colorado, 1989-2003. *Journal of Child Neurology*, **21**, 795-798. https://doi.org/10.1177/08830738060210092001

[10] Kohelet, D., Shochat, R., Lusky, A. and Reichman, B. (2006) Risk Factors for Seizures in Very Low Birthweight Infants with Periventricular Leukomalacia. *Journal of Child Neurology*, **21**, 965-970. https://doi.org/10.1177/08830738060210111301

[11] Saliba, R.M. (2001) Risk Factors for Neonatal Seizures: A Population-Based Study, Harris County, Texas, 1992-1994. *American Journal of Epidemiology*, **154**, 14-20. https://doi.org/10.1093/aje/154.1.14

[12] Kohelet, D., Shochat, R., Lusky, A. and Reichman, B. (2004) Risk Factors for Neonatal Seizures in Very Low Birthweight Infants: Population-Based Survey. *Journal of Child Neurology*, **19**, 123-128. https://doi.org/10.1177/08830738040190020701

[13] Kellaway, P. and Hrachovy, R.A. (1983) Status Epilepticus in Newborns: A Perspective on Neonatal Seizures. In: Delgado-Escueta, A.V., Wasterlain, C.G., Treiman, D.M. and Porter, R.J., Eds., *Advances in Neurology*, *vol* 34: *Status Epilepticus*, Raven Press, 93.

[14] Kaminska, A., Mourdie, J., Barnerias, C., *et al*. (2007) Management of Neonatal Seizures. *Archives de Pédiatrie*, **14**, 1137-1151.

[15] Laugier, J. and Rozé, J.C. (2006) Soins aux nouveau-nés avant pendant et après la naissance. 2ème Édition, Elsevier.

[16] Verboon-Maciolek, M.A., Groenendaal, F., Hahn, C.D., Hellmann, J., van Loon, A.M., Boivin, G., *et al*. (2008) Human Parechovirus Causes Encephalitis with White Matter Injury in Neonates. *Annals of Neurology*, **64**, 266-273. https://doi.org/10.1002/ana.21445

[17] Glass, H.C., Shellhaas, R.A., Wusthoff, C.J., Chang, T., Abend, N.S., Chu, C.J., *et al*. (2016) Contemporary Profile of Seizures in Neonates: A Prospective Cohort Study. *The Journal of Pediatrics*, **174**, 98-103.E1. https://doi.org/10.1016/j.jpeds.2016.03.035

[18] Rennie, J.M., de Vries, L.S., Blennow, M., Foran, A., Shah, D.K., Livingstone, V., *et al*. (2018) Characterisation of Neonatal Seizures and Their Treatment Using Continuous EEG Monitoring: A Multicentre Experience. *Archives of Disease in Childhood—Fetal and Neonatal Edition*, **104**, F493-F501. https://doi.org/10.1136/archdischild-2018-315624

[19] Lynch, N.E., Stevenson, N.J., Livingstone, V., Murphy, B.P., Rennie, J.M. and Boylan, G.B. (2012) The Temporal Evolution of Electrographic Seizure Burden in Neonatal Hypoxic Ischemic Encephalopathy. *Epilepsia*, **53**, 549-557. https://doi.org/10.1111/j.1528-1167.2011.03401.x

[20] Glass, H.C. and Shellhaas, R.A. (2019) Acute Symptomatic Seizures in Neonates. *Seminars in Pediatric Neurology*, **32**, Article ID: 100768. https://doi.org/10.1016/j.spen.2019.08.004

[21] Boylan, G.B. (2002) Phenobarbitone, Neonatal Seizures, and Video-EEG. *Archives of Disease in Childhood—Fetal and Neonatal Edition*, **86**, F165-F170. https://doi.org/10.1136/fn.86.3.f165

[22] Lamblin, M.D., André, M., Auzoux, M., Bednarek, N., Bour, F., Charollais, A., *et al*. (2004) Indications de l'électroencéphalogramme en période néonatale. *Archives de Pédiatrie*, **11**, 829-833. https://doi.org/10.1016/j.arcped.2004.01.031

[23] Hellström-Westas, L., Boylan, G. and Ågren, J. (2014) Systematic Review of Neonatal Seizure Management Strategies Provides Guidance on Anti-Epileptic Treatment. *Acta Paediatrica*, **104**, 123-129. https://doi.org/10.1111/apa.12812

[24] Dilena, R., De Liso, P., Di Capua, M., Consonni, D., Capovilla, G., Pisani, F., *et al*. (2019) Influence of Etiology on Treatment Choices for Neonatal Seizures: A Survey among Pediatric Neurologists. *Brain and Development*, **41**, 595-599. https://doi.org/10.1016/j.braindev.2019.03.012

[25] Dizon, M.L.V., Rao, R., Hamrick, S.E., Zaniletti, I., DiGeronimo, R., Natarajan, G., *et al*. (2019) Practice Variation in Anti-Epileptic Drug Use for Neonatal Hypoxic-Ischemic Encephalopathy among Regional NICUs. *BMC Pediatrics*, **19**, Article No. 67. https://doi.org/10.1186/s12887-019-1441-7

[26] Le, V.T., Abdi, H.H., Sánchez, P.J., Yossef, L., Reagan, P.B., Slaughter, L.A., *et al*. (2019) Neonatal Antiepileptic Medication Treatment Patterns: A Decade of Change. *American Journal of Perinatology*, **38**, 469-476. https://doi.org/10.1055/s-0039-1698457

[27] Keene, J.C., Morgan, L.A., Abend, N.S., Bates, S.V., Bauer Huang, S.L., Chang, T., *et al*. (2022) Treatment of Neonatal Seizures: Comparison of Treatment Pathways from

11 Neonatal Intensive Care Units. *Pediatric Neurology*, **128**, 67-74. https://doi.org/10.1016/j.pediatrneurol.2021.10.004

[28] Gluckman, P.D., Wyatt, J.S., Azzopardi, D., Ballard, R., Edwards, A.D., Ferriero, D.M., *et al*. (2005) Selective Head Cooling with Mild Systemic Hypothermia after Neonatal Encephalopathy: Multicentre Randomised Trial. *The Lancet*, **365**, 663-670. https://doi.org/10.1016/s0140-6736(05)17946-x

[29] Shankaran, S., Laptook, A.R., Ehrenkranz, R.A., Tyson, J.E., McDonald, S.A., Donovan, E.F., *et al*. (2005) Whole-Body Hypothermia for Neonates with Hypoxic-Ischemic Encephalopathy. *New England Journal of Medicine*, **353**, 1574-1584. https://doi.org/10.1056/nejmcps050929

[30] Lemmon, M.E., Bonifacio, S.L., Shellhaas, R.A., Wusthoff, C.J., Greenberg, R.G., Soul, J.S., *et al*. (2020) Characterization of Death in Infants with Neonatal Seizures. *Pediatric Neurology*, **113**, 21-25. https://doi.org/10.1016/j.pediatrneurol.2020.08.002

[31] Tekgul, H., Gauvreau, K., Soul, J., Murphy, L., Robertson, R., Stewart, J., *et al*. (2006) The Current Etiologic Profile and Neurodevelopmental Outcome of Seizures in Term Newborn Infants. *Pediatrics*, **117**, 1270-1280. https://doi.org/10.1542/peds.2005-1178

[32] Ortibus, E.L., Sum, J.M. and Hahn, J.S. (1996) Predictive Value of EEG for Outcome and Epilepsy Following Neonatal Seizures. *Electroencephalography and Clinical Neurophysiology*, **98**, 175-185. https://doi.org/10.1016/0013-4694(95)00245-6

[33] Blume, W.T., Lüders, H.O., Mizrahi, E., Tassinari, C., Van Emde Boas, W. and Engel, J. (2001) Glossary of Descriptive Terminology for Ictal Semiology: Report of the ILAE Task Force on Classification and Terminology. *Epilepsia*, **42**, 1212-1218. https://doi.org/10.1046/j.1528-1157.2001.22001.x

[34] Brunquell, P.J., Glennon, C.M., DiMario, F.J., Lerer, T. and Eisenfeld, L. (2002) Prediction of Outcome Based on Clinical Seizure Type in Newborn Infants. *The Journal of Pediatrics*, **140**, 707-712. https://doi.org/10.1067/mpd.2002.124773

[35] Ronen, G.M., Buckley, D., Penney, S. and Streiner, D.L. (2007) Long-term Prognosis in Children with Neonatal Seizures: A Population-Based Study. *Neurology*, **69**, 1816-1822. https://doi.org/10.1212/01.wnl.0000279335.85797.2c

[36] Mizrahi, E.M., Clancy, R.R., Dunn, J.K., *et al*. (2001) Neurological Impairment, Developmental Delay and Postnatal Seizures 2 Years after EEG-Video Documented Seizures in Near-Term and Term Neonates: A Report of the Clinical Research Centers for Neonatal Seizures. *Epilepsia*, **42**, 102.

[37] Davis, A.S., Hintz, S.R., Van Meurs, K.P., Li, L., Das, A., Stoll, B.J., *et al*. (2010) Seizures in Extremely Low Birth Weight Infants Are Associated with Adverse Outcome. *The Journal of Pediatrics*, **157**, 720-725.E2. https://doi.org/10.1016/j.jpeds.2010.04.065

[38] Uria-Avellanal, C., Marlow, N. and Rennie, J.M. (2013) Outcome Following Neonatal Seizures. *Seminars in Fetal and Neonatal Medicine*, **18**, 224-232. https://doi.org/10.1016/j.siny.2013.01.002

[39] Glass, H.C., Shellhaas, R.A., Tsuchida, T.N., Chang, T., Wusthoff, C.J., Chu, C.J., *et al*. (2017) Seizures in Preterm Neonates: A Multicenter Observational Cohort Study. *Pediatric Neurology*, **72**, 19-24. https://doi.org/10.1016/j.pediatrneurol.2017.04.016

[40] Buraniqi, E., Sansevere, A.J., Kapur, K., Bergin, A.M., Pearl, P.L. and Loddenkemper, T. (2017) Electrographic Seizures in Preterm Neonates in the Neonatal Intensive Care Unit. *Journal of Child Neurology*, **32**, 880-885. https://doi.org/10.1177/0883073817713918