ANDES PEDIATRICA
REVISTA CHILENA DE PEDIATRÍA
www.scielo.cl

Andes pediatr. 2024;95(2):165-173
Doi: 10.32641/andespediatr.v95i2.4604

ORIGINAL ARTICLE

Extremely preterm infants with severe intraventricular hemorrhage: neurological evolution and long-term and educational status

Niños muy prematuros con hemorragia intraventricular extensa: evolución neurológica y escolaridad a largo plazo

Rodrigo Salas Núñez[a], Raquel Gaete Sepúlveda[b], Javier Salas Fontecilla[c], Nelson Suárez Urieles[d], Felipe Salas Fontecilla[e]

[a]Servicio de Neonatología, Complejo Asistencial Barros Luco. Santiago, Chile.
[b]Servicio de Neurología, Hospital Dr. Exequiel González Cortés. Santiago, Chile
[c]Facultad de Medicina y Ciencias, Universidad San Sebastián. Santiago, Chile.
[d]Programa de Formación de Especialistas en Neurología Pediátrica, Universidad de Chile, Hospital Dr. Exequiel González Cortés. Santiago, Chile.
[e]Ingeniero Civil. Magister en Ciencias de la Ingeniería, Universidad Católica de Chile. Santiago, Chile.

Received: November 25, 2022; Approved: January 24, 2024

What do we know about the subject matter of this study?

Extensive intraventricular hemorrhage in very premature newborns causes varied, frequent, and severe neurological sequelae in the long term, mainly affecting motor functions such as gait or mobility, intellectual capacity, and therefore cognitive performance, which impacts health, autonomy, and family and social integration.

What does this study contribute to what is already known?

Through a neuro-pediatric follow-up program until school age, it was possible to clinically observe in children with history of being very premature and with extensive intraventricular hemorrhage, the functional performance in mobility (according to gait) and in the cognitive area (according to intellectual capacity), grouping them by levels of functionality. This work provides a more optimistic view in relation to the expectations of neurological functionality and autonomy in very preterm newborns with extensive intraventricular hemorrhage in the long term.

Abstract

Extensive intraventricular hemorrhage (IVH) in very preterm newborns (VPNB) is associated with mortality and severe long-term neurological sequelae. **Objectives:** To know the most frequent neurological pathologies associated with extensive IVH, to determine the functional outcomes of mobility in the motor area and intellectual capacity in the cognitive area, to analyze the association between both areas and to know the schooling achieved. **Patients and Method**: Descriptive and longitudinal study in VPNB with extensive IVH born between 2001 and 2014. They underwent protocolized

Keywords:
Preterm Newborn;
Cerebral Intraventricular Hemorrhage;
Chronic Brain Damage;
Educational Status;
Follow-up

Correspondence:
Rodrigo Salas Núñez
rodrigosalas80@yahoo.cl

Edited by:
Patricia Mena Nannig

How to cite this article: Andes pediatr. 2024;95(2):165-173. Doi: 10.32641/andespediatr.v95i2.4604

neurological follow-up until school age. The functional outcomes in mobility and intellectual capacity were categorized into 4 levels: level 1 corresponds to good functionality and autonomy; level 2, functionality that allows independence, with support in some tasks; level 3 requires constant external support; and level 4 where there is total dependence. The association was analyzed using Chi-square and Cramer's V coefficient. **Results:** 74 children completed the follow-up; the most frequent associated neurological pathologies were neurodevelopmental disorders, hypertensive hydrocephalus, and epilepsy. Independent mobility (normal or with limitations) reached 74.4% while 24.3% used wheelchairs. 51.3% was categorized as normal to borderline intellectual range, 12.2% as mild intellectual disability (ID), 17.6% as moderate ID, and 19.9% as severe to profound ID. There was a strong statistical association between functional levels of mobility and intellectual capacity ($p < 0.000$ and $V = 0.62$). Schooling was proportional to intellectual capacity: 56.8% attended regular schools, 27.0% attended special schools, and 16.2% had no schooling. **Conclusions**: 2/3 VPNB with extensive IVH showed positive functional outcomes, from normal to mild limitations that allow an almost autonomous life; in 1/3 the outcomes were unfavorable in mobility and cognitive performance, and there was a strong statistical correlation between both areas studied. Schooling was consistent with the intellectual level.

Introduction

In newborns younger than 32 weeks of gestation, one complication is intraventricular hemorrhage (IVH), defined as bleeding from the subependymal germinal matrix adjacent to the caudate nucleus into the lateral ventricles, which are irrigated mainly by perforating branches from the anterior and middle cerebral arteries[1,2]. Its pathogenesis is multifactorial and is associated with the severe immaturity of the vessels at birth. The vascular fragility of the germinal matrix, caused by immature vessels, is a key factor as they are undifferentiated, without a basement membrane, and vulnerable to variations in cerebral blood flow and blood pressure[3], worsened by frequent coagulation disorders, as well as respiratory and hemodynamic instability that usually come along with multiple pre- and post-natal complications[4,5]. 80-90% of IVHs occur within the first 72 hours of life, and virtually 100% within the first 10 days[6]. In recent decades, survival of very preterm newborns (VPNB) has increased and IVH has become a pathology of great interest due to its incidence and neurological sequelae.

Cranial ultrasound has been a good and useful tool to identify the onset and evolution of IVH in VPNB, offering the advantages of being a painless, non-invasive test, which is performed in the neonatal intensive care unit, can be repeated whenever necessary, without harmful effects on children, and can be complemented with a brain CT scan or MRI when there are doubts or when surgery is required[7].

The Papile et al. classification is commonly used to determine the extent of IVH. This classification is divided into four grades according to severity[8]:

- Grade I: Subependymal hemorrhage
- Grade II: IVH without ventricular dilatation
- Grade III: IVH with ventricular dilatation
- Grade IV: IVH with ventricular dilatation and extension to parenchyma

The neurological evolution and clinical prognosis are proportional to its extension, with favorable outcomes in IVH grades I and II and of high risk of neurological sequelae in IVH grades III and IV[7], also called extensive IVH (EIVH), which, in the short term, can determine the appearance of epilepsy, hydrocephalus, among others and, in the long term, motor, cognitive, and neurodevelopmental disorders due to damage in the parenchyma and germinal matrix[9,10,11]. In addition, other lesions or malformations such as periventricular leukomalacia, *ex vacuo* ventriculomegaly, hydrocephalus, etc., can be detected[12,13]. The incidence and severity are directly related to the degree of immaturity and lower birth weight. In Chile, the latest data published in 2007 showed that 28% of VPNBs present some degree of IVH, and 13% present EIVH[14].

VPNBs with EIVH present motor, sensory, and cognitive sequelae, and other neurological pathologies such as epilepsy, extrapyramidal symptoms, learning and speech disorders, and autism, among others[15,16]. The objectives of this study are to recognize the most frequent pathologies or neurological complications diagnosed in VPNB with EIVH, to determine in school children with a history of VPNB with EIVH the functionality in the gross motor area according to mobility level and in the cognitive area according to intellectual capacity, to analyze whether there is a statistical association between the outcomes of functional levels of mobility and intellectual capacity in VPNB with EIVH, and to know the type of schooling achieved by the children according to the cognitive level.

Patients and Method

Observational, descriptive, longitudinal, and ambispective study that included all VPNB with gestational age from 24 to 31 weeks born in the Neonatology Service of the *Hospital Barros Luco* between 2001 and 2014 that presented EIVH in the neonatal period and survived, and whose pathology was defined as IVH grade III or IV of uni- or bilateral location. The diagnosis was made by brain ultrasound performed before 7 days of life, at 30 days, and at discharge or 40 weeks of corrected age.

The population assigned to our hospital, including pregnant women, is geographically located in the southern area of Santiago, is considered of medium-high to high social priority[17], users of the public health system and seen in Institutional Care Modality; and presents socio-economic, cultural, and genetic proximity homogeneity[18].

All premature infants weighing < 1,500 grams and/or < 32 weeks who were born at the *Hospital Barros Luco* are referred to the Prematurity Follow-up Program upon discharge from the hospital, whose protocol establishes serial medical check-ups from 40 weeks of corrected age up to 7 years of age or more if necessary; both pediatric check-ups in the Neonatology Service and neurological and rehabilitation visits at the *Hospital Exequiel Gonzalez Cortéz*[19]. The VPNB with EIVH underwent a neurological examination according to the standardized guidelines of the specialty to evaluate the abilities, conditions, and functionalities in the different areas of the specialty such as the motor, sensory, cognitive, behavioral, and neurodevelopmental ones, among others, and all pertinent information was recorded in the respective follow-up clinical records.

Given the great diversity and disparity in the clinical diagnoses and magnitude of the sequelae in the motor and cognitive areas, it was decided to evaluate the functional outcomes in gross motor skills according to independence and gait quality, as well as to evaluate the cognitive functional outcomes according to intellectual capacity. The functional outcomes in both areas were categorized into 4 levels: Level 1 represents good functionality and autonomy; Level 2 has a functionality that allows independence but with slight limitations and the need for support in some tasks; Level 3 requires constant and greater external support to develop this motor or cognitive function; and Level 4 has poor functionality with total dependence on others (table 1).

To categorize the level of mobility through gait, the 2008 Gross Motor Function Classification System-Extended and Revised (GMFCS-E&R) for cerebral palsy by Palisano et al.[20] was applied and adapted to 4 functional levels: Level 1 presents independent and normal gait; Level 2 presents independent gait but with functional limitations; Level 3 presents independent gait only if they use assistive devices such as canes, crutches, or walkers; in Level 4, mobility with devices is very reduced and/or requires a wheelchair.

The categorization of cognitive level according to intellectual capacity was obtained by clinical assessment and, in some cases, by individual standardized tests. Based on the guidelines for intellectual development disorders of the Diagnostic and Statistical Manual of Mental Disorders DSM-5[21], intellectual capacity was clinically determined considering the evaluation of receptive and expressive language, literacy acquisition, memory, academic skills, learning, executive functions, and abstract thinking.

The Wechsler Intelligence Scale for Children (WISC) is the most widely used test and is validated in children over 6 years of age. It allows an objective evaluation of the development of verbal comprehension, visual-spatial, fluid reasoning, working memory, and processing speed, establishing an IQ score with automatic categorization of the cognitive level[22]; however, considering that it is a very limited resource, it was indicated in selected cases when there was clinical uncertainty about the capacity or intellectual level. In those who did not undergo the WISC test, a homologation was performed in the IQ score ranges of this test based on the clinical evaluation and DSM-5 criteria[23] where the children were categorized in a cognitive level according to the following guideline:

Level 1 or normal to borderline IQ (IQ ≥ 70): normal intellectual performance; in the case of borderline intelligence, there is a deficit in the adaptive capacity in at least two areas such as academic, social, interpersonal, occupational, family, and self-care, therefore, they require intermittent support at different stages of their development.

Table 1. Functionality Levels of mobility and intellectual capacity

Functionality Level	Gait Autonomy (Motor Area)	Intellectual Capacity (Cognitive Area)
1	Normal	Normal to Slight Limitations
2	Independent with slight limitations	Mild ID
3	Requires assistive devices	Moderate ID
4	with devices is very reduced or using wheelchairs	Severe ID

ID: Intellectual Deficit.

Level 2 or mild intellectual disability (ID) (IQ 50-69): individuals often present expressive and receptive language delay, difficulties in learning reading, writing, and mathematics, are socially immature, manage to learn appropriate social skills, and need support in many tasks.

Level 3 or moderate ID (IQ 36-49): individuals can achieve language or learn to communicate, have limited social and comprehension skills, maintain a good degree of independence, need constant support, and can attend elementary or special school with help.

Level 4 or severe to profound ID (IQ < 35): individuals present limited spoken language with only a few words or mostly nonverbal with little understanding and maladaptive behavior. Also, extreme cognitive limitations, often with sensory and/or physical impairments, and continued support and supervision in any basic, daily activity are essential.

The type of schooling achieved by the children in the different cognitive levels was determined, identifying whether they attended regular schools, regular schools with School Integration Program, special schools, or no attend to school at all. Along with the motor and cognitive categorization, the neurological pathologies that appeared in the long-term follow-up were recorded, such as epilepsy, ataxia, blindness, hypoacusis, autism, and attentional and language deficit disorder, among others.

To determine whether there is a statistical association between the levels of mobility functionality and intellectual capacity, a contingency table was used to test the hypothesis of independence based on the chi-square distribution with a significance level of 5%. The Cramer's V association coefficient was used to determine the strength of the association.

Patients were excluded from the study if they had died or dropped out of follow-up before 6 years of age after discharge. This study was approved by the Scientific Ethical Committee of the South Metropolitan Health Service (code 03-14012022).

Results

During the period studied, 1,784 VPNB were born in the Neonatology Service, of which 1,312 survived (73.5%); 19.5% of the deceased VPNB had EIVH as an associated diagnosis. Among the survivors, there were 86 children with EIVH (6.6%) who were included in the study and entered the Preterm Follow-up Program; of these, 25 (29.1%) were female, 14 (16.3%) were small for gestational age, and 40 (46.5%) had a gestational age < 28 weeks. During the period of check-ups and observation up to school age, 6 children died and 6 patients did not continue attending the check-ups, so finally the study and neurological follow-up were completed with 74 patients out of 80 possible (92.5%).

The most frequent neurological complications were neurodevelopmental disorders (45.9%) which, in decreasing order, were: attention deficit, learning disorders, mixed language disorders, and autism spectrum disorders; epilepsy (36.5%), and hypertensive hydrocephalus with ventricular shunt placement in 26 patients (35.1%) (table 2).

Table 3 shows the outcomes in the levels of motor and cognitive functionality. In the motor area, 74.4% presented independent gait (with or without limitations); mobility using a wheelchair or mobility aids (Level 4) reached 24.3%.

In relation to the cognitive area, 51.3% of the VPNB were categorized in Level 1 or normal to borderline intellectual range, 12.2% in Level 2 or mild ID, 17.6% in Level 3 or moderate ID, and 18.9% of the children in Level 4 or severe to profound ID. Schooling in the VPNB with EIVH reached 56.8% attendance at regular schools (with or without School Integration Program), 27.0% at special schools, and 16.2% had no schooling (table 4). If we observe this distribution according to

Table 2. Neurological pathologies diagnosed in very preterm newborn (VPNB) with extensive intraventricular hemorrhage (EIVH)

Pathologies	n	%
Neurodevelopmental disorders	34/74	45.9
Epilepsy	27/74	36.5
Hydrocephalus with ventricular shunt placement	26/74	35.1
Periventricular leukomalacia multicystic	8/74	10.8
Hypoacusis requiring hearing aids	6/74	8.1
Blindness < 20/200	3/74	4.1
Cerebelar disorder	1/74	1.4

Table 3. Outcomes in levels of motor and cognitive functionality in very preterm newborn (VPNB) with extensive intraventricular hemorrhage (EIVH) at school age

Area	Motor Area		Cognitive Area	
Levels	n	%	n	%
Level 1	44	59.5	38	51.3
Level 2	11	14.9	9	12.2
Level 3	1	1.3	13	17.6
Level 4	18	24.3	14	18.9

Table 4. Distribution outcome of schooling in very preterm newborn (VPNB) with extensive intraventricular hemorrhage (EIVH) according to cognitive level

Type of Schooling	Level 1		Level 2		Level 3		Level 4		Total	
	n	%	n	%	n	%	n	%	n	%
Regular School	27	71.1	0	0.0	0	0.0	0	0.0	27	36.5
Regular School with integration program	11	28.9	4	44.4	0	0.0	0	0.0	15	20.3
Special School	0	0.0	5	55.6	12	92.3	3	21.4	20	27.0
Not attending to school	0	0.0	0	0.0	1	7.7	11	78.6	12	16.2
Total	38	100	9	100	13	100	14	100	74	100

Table 5. Correlation between levels of motor and cognitive functionalities in very preterm newborn (VPNB) with extensive intraventricular hemorrhage (EIVH)

			Levels of Cognitive Functionality				Total n (%)	χ^2 (gl) p-value	V-Cramer*
			Level 1 n (%)	Level 2 n (%)	Level 3 n (%)	Level 4 n (%)			
Levels of motor functionality	Level 1	n (%)	36 (48.6)	4 (5.4)	4 (5.4)	0 (0.0)	44 (59.4)	84.86 (9) p < 0.00	0.62
	Level 2	n (%)	2 (2.7)	4 (5.4)	5 (6.8)	0 (0.0)	11 (14.9)		
	Level 3	n (%)	0 (0.0)	1 (1.4)	0 (0.0)	0 (0.0)	1 (1.4)		
	Level 4	n (%)	0 (0.0)	0 (0.0)	4 (5.4)	14 (18.9)	18 (24.3)		
	Total	n (%)	38 (51.3)	13 (12.2)	14 (17.6)	15 (18.9)	74 (100)		

*Outcome between 0,6 and 1 indicates a strong association.

cognitive level, we can see that all children in cognitive Level 1 attend regular schools and mostly without a school integration program, of the children in cognitive Level 2, 44.4% were able to attend regular schools with school integration support, and the rest attended special schools; those in Level 3 attended only special schools and, finally, most children in Level 4 (78.6%) did not attend school at all.

Regarding the correlation between functional levels of mobility and intellectual capacity in VPNB with EIVH, table 5 shows a tendency to group the children categorized in the best functional levels in both areas and the same occurs with the worst functional levels; 48.6% were categorized in functional Level 1 in both areas and 18.9% of the total were categorized in Level 4 in both areas (wheelchair users and severe to profound ID). The statistical analysis of the same table shows that the hypothesis of independence (no association) between the variables mobility level and cognitive level was ruled out by the Chi-square test with a chance probability < 1 per 100,000 ($p < 0.000$), thus confirming an association or interdependence between the outcomes of intellectual functionality and mobility in VPNB with EIVH in the long term. The value of Cramer's V association coefficient was 0.62 indicating a strong relationship between both areas.

Discussion

The Neonatology Service of the *Hospital Barros Luco* and the Pediatric Neurology Service of the *Hospital Exequiel González Cortés* have worked together and in coordination for more than two decades in the follow-up of premature infants to avoid, reduce, or reverse neurological problems, especially in the motor and cognitive-behavioral spheres, with the follow-up protocol of the Ministry of Health according to the technical guidelines of 2,000[19]. Premature infants represent a population at high neurobiological risk, and with EIVH they are at even higher risk of presenting neurological sequelae in frequency and severity[24,25]. Studies show that 50-75% of preterm infants with EIVH have some variety and degree of long-term cerebral palsy and 45-85% have some degree of ID and will require significant special education support[26,27].

Neurodevelopmental disorders were the most frequently diagnosed neurological pathologies in VPNB with EIVH (45.9%), their frequency could be higher if we admit that ID interferes with or masks these diagnoses; in addition, one-third of the children under study presented epilepsy and hypertensive hydrocephalus (36.5% and 35.5%, respectively),

pathologies that can produce long-term neurological problems. These figures coincide with published results[28].

When observing the outcomes of independent mobility, without aid devices (mobility Levels 1 and 2), we found that 74.4% of the children presented an independent gait. The literature and clinical practice teach us that efficient rehabilitation and early intervention allow for improving motor, intellectual, and neurodevelopmental outcomes[29,30]. 82.4% of the children received neuromotor rehabilitation mostly for more than one year and those who did not receive it generally corresponded to children with very severe neurological damage where therapy was directed to medical survival goals.

In the cognitive area, it was observed that half of the children (51.3%) presented normal to borderline intellectual capacity (Level 1), which is a good functional outcome, given that they are independent, attend regular schools, and are integrated in family and social life with productive work. On the contrary, children in cognitive Level 4 or with severe to profound ID (18.9%), are dependent on help in all aspects, being the cognitive functional outcome definitely unfavorable.

Cognitive Levels 2 and 3 corresponding to mild and moderate ID fall between the outcomes of normal and very limited intellectual capacity. These children present a variable deficit in social, conceptual, practical, and executive skills; however, they can develop simple cognitive tools for everyday challenges with reasonable expectations in a favorable environment, which produces in the families and community a sense of satisfaction for the outcomes achieved, even if they are not objectively the best. This makes us reflect on the intellectual performance of children with intermediate cognitive level since functionality is not only given by the IQ scale, but how their intellectual skills and limitations are integrated in an environment that is unique in expectations and demands for each child, in other words, the cognitive deficit depends on the difficulties produced by the ID in daily life[31].

It is always useful to remember the discouraging expectations of survival and neurological prognosis in the neonatal period and to confront it with the functional outcomes in the long term. Both for the relatives and for the professional team, most of the time there is a feeling of "it was better than expected"; we cannot forget the high neurological risk to which the VPNBs were exposed due to immaturity, hypoxic-ischemic phenomena, hemorrhage and perinatal brain injuries, neurological complications, socio-economic problems, and difficult access to rehabilitation and special education, among others[23].

Reports in publications with patients in similar conditions show that between 60-80% of good cognitive range was obtained[32]. It should be clarified that it was difficult to obtain published data to compare our results, given that the study design was very particular in selecting only VPNB with EIVH and not the total number of preterm newborns in cohorts, and due to selecting only functional outcomes in gait and IQ, in addition to categorizing the outcomes in levels.

One of the weaknesses of our work was not being able to universally use the WISC test as a tool to determine IQ and as a criterion to define the degree of ID. The main reason was the professional resource of psychologists at the institutional level; therefore, it was only applied to certain children when there were doubts about their IQ range. However, its application in patients with clinically normal intellectual ability is not necessary, and in cases of moderate to profound ID, it is not as useful. The measurement of IQ is frequently used to determine intellectual capacity and thus the degree of ID; however, its use is currently more directed to document the presence of ID, which becomes very suggestive if the IQ is < 70[23]. The homologation of the IQ ranges of the WISC test obtained according to the clinical cognitive assessment guideline based on the DSM-5 to support the categorization of the intellectual level in children seems to us a valid and replicable strategy to respond to the objectives of the work.

Half of the children (48.6%) developed a good functional level both in mobility and IQ (Level 1) and 18.9% of the children showed the lowest outcomes in both areas (Level 4). These figures agree with similar studies but of different designs[11]. One of the objectives was to verify if there is an association between the variables studied in the VPNB with EIVH, confirming the dependence between the functional outcomes of mobility and IQ with a strong intensity of relationship (table 4). This association of long-term neurological sequelae was expected given that EIVH and other brain injuries occur in a critical period of rapid growth and encephalic development[33]. In related publications, it is mentioned that the high rates of neurological sequelae in these patients are attributable to some extent to prematurity[34], but that poor outcomes are exacerbated in those who also have EIVH[15,35]. A point of controversy was to have made the diagnosis of EIVH without distinguishing between unilateral and bilateral lesions. Some articles do not find significant differences in long-term outcomes, while others do[36,37].

The VPNBs require specialized school attention[38] and we did not have great expectations of the school goals of these patients who also suffered from EIVH[39]. It was interesting to observe that 56.8% of the children evaluated received regular education, although a third of them were supported by a school integration program, and almost all of them belong to Level 1 or

normal to borderline intellectual range. It was expected that the schooling received by children with lower cognitive levels of intellectual performance would be only special education or none at all since the type of schooling or teaching received depends on the intellectual level of each child. This information is similar to the data provided by other groups of researchers where the rates of educational and learning problems exceed 50%[27,40]. Just as additional information, it is interesting to know that the academic performance of those who received regular education was generally low; in addition, the implementation of school integration programs is usually not enough for the pedagogical support and/or rehabilitation of children with special educational needs[41].

Given the homogeneity of the population, we did not consider other external factors that influence neurological outcomes in the long term, such as socioeconomic status, mental and emotional situation of parents or caregivers, family dysfunction, or others. Finally, the outcomes obtained in VPNB with EIVH in motor and intellectual functionality, including schooling, provide relevant information in the long-term follow-up of premature infants, since this is the most vulnerable subgroup with the highest bio-neuro-psycho-social risk, and allow recommendations to be made to improve health services and educational tasks.

Conclusions

This study shows the long-term outcomes of the neurological area in VPNB with a diagnosis of EIVH. Most of the children (two out of three) achieved positive or favorable functional outcomes given that Level 1 was normal and Level 2 corresponds to limitations that allow them to develop an independent, productive, and integrated life in society and family and one-third of the children obtained functional outcomes classified as unfavorable (Levels 3 and 4), if we consider that the latter are not autonomous and require constant external support depending on the degree of intellectual and/or mobility deficit. There is a strong statistical association between the functional outcomes achieved in the motor and cognitive areas. Most of the children received schooling and the type of schooling was concordant and proportional to the cognitive level. Premature infants in general, and even more so those with perinatal EIVH, require support in the medical, rehabilitation, educational, and social areas throughout their development, given the high neurobiological risk conditions.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

Authors state that no economic support has been associated with the present study.

References

1. Egesa W, Odoch S, Odong R, et al. Germinal Matrix-Intraventricular Hemorrhage: A Tale of Preterm Infants. International Journal of Pediatrics. 2021, Article ID 6622598, 14 pages. doi. org/10.1155/2021/6622598
2. Ballabh P. Pathogenesis and prevention of intraventricular hemorrhage. Clin Perinatol. 2014;41:47-67. doi: 10.1016/j. clp.2013.09.007
3. Lekic T, Klebe D, Poblete R, et al. Neonatal brain hemorrhage of prematurity: translational mechanisms of the vascular-neural network. Curr Med Chem. 2015;22:1214-38. doi: 10.2174/0929867322666150114152421.
4. Gilard V, Tebani A, Bekri S, et al. Intraventricular Hemorrhage in Very Preterm Infants: A Comprehensive Review. J. Clin. Med. 2020;9:2447. doi: 10.3390/jcm9082447.
5. Segura M, Rivera M, Fernández L, et al. Factores de riesgo asociados para el desarrollo de hemorragia intraventricular en recién nacidos < 1.500 g ingresados a una UCIN. Perinatol Reprod Hum. 2017;31:174-79. doi.org/10.1016/j. rprh.2018.03.010
6. Volpe J. Intracranial Hemorrhage: Germinal Matrix–Intraventricular Hemorrhage of the Premature Infant. Volpe J, 5th Ed. Neurology of the newborn. Philadelphia, Elsevier-Health Sciences Division. 2008: 517.
7. Dorner R, Burton V, Allen M, et al. Preterm neuroimaging and neurodevelopment outcome: a focus on intraventricular hemorrhage, post-hemorrhagic hydrocefalus and associated brain injury. J Perinatol. 2018;38:1431-43. doi: 10.1038/s41372-018-0209-5
8. Papile L, Burstein J, Burstein R, et al. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weigth less than 1,500 g. J Pediatr. 1978;92:529-34. doi:10.1016/ s0022-3476(78)80282-0
9. Papile L, Munsick–Bruno G, Schaefer A. Relationship of cerebral intraventricular hemorrhage and early childhood neurologic handicaps. J Pediatr. 1983;103:273-6.
10. Narberhaus A, Segarra M, Pueyo R, et al. Long-term cognitive dysfunctions in preterm subjects with intraventricular haemorrhage. Rev Neurol. 2008;47:57-60. doi: https://doi.org/10.33588/ rn.4702.2007506
11. Bolisety S, Dhawan A, Abdel-Latif M. Intraventricular hemorrhage and neurodevelopmental outcomes in extreme preterm infants. Pediatrics. 2014;133(1):55-62. doi: 10.1542/ peds.2013-0372.
12. Hinojosa M, Harmonya T, Carrillo C, et al. Clinical neuroimaging in the preterm infant: Diagnosis and prognosis. NeuroImage Clinical. 2017;16:355-68 http://dx.doi.org/10.1016/j. nicl.2017.08.015
13. D'Apremont I, Marshall G, Musalem C, et al. Trends in Perinatal Practices and Neonatal Outcomes of Very Low Birth Weight Infants during a 16-year Period at NEOCOSUR Centers. J Pediatr. 2020;225:44-50. doi: 10.1016/j. jpeds.2020.05.040
14. Ministerio de Salud Subsecretaría de Redes Asistenciales. "Análisis Epidemiológico de los Recién nacidos con menos de 32 semanas en la red pública de salud de Chile". Quinquenio 2000-2004. Red de Seguimiento Neonatal Chilena. Dra. Mónica Morgues. 2007.
15. Radic J, Vincer M, McNeely D. Outcomes of intraventricular hemorrhage and posthemorrhagic hydrocephalus in a population-based cohort of very preterm infants born to residents of Nova Scotia from 1993 to 2010. J Neurosurg Pediatr. 2015;15:580-8. doi: 10.3171/2014.11. PEDS14364
16. Smithers-Sheedy H, Badawi N, Blair E, et al. What constitutes cerebral palsy in the twenty-first century? Dev Med Child Neurol. 2014;56:323-8. doi:10.1111/ dmcn.12262
17. Región Metropolitana de Santiago: Índice de Prioridad Social de Comunas 2019. Seremi de Desarrollo Social y Familia Metropolitana. Santiago Gajardo Polanco, Área de Estudios e Inversiones.
18. Rocco P, Morales C, Moraga M, et al. Composición genética de la población chilena. Distribución de polimorfismos de DNA mitocondrial en grupos originarios y en la población mixta de Santiago. Rev Méd Chile. 2002;130:125-31. http://dx.doi.org/10.4067/S0034-98872002000200001.
19. Orientaciones técnicas para el seguimiento del recién nacido < 1.500 g o < 32 sem al nacer. Programa de Salud del Niño. Ministerio de Salud. 2000.
20. Palisano R, Rosenbaum P, Barlett D, et al. "Content validity of the expanded and revised Gross Motor Function Classification System". Dev Med Child Neurol. 2008;50:744-50. Doi: 10.1111/j.1469-8749.2008.03089.x
21. Asociación Americana de Psiquiatría. Manual Diagnóstico y Estadístico de las Trastornos Mentales (DSM-5®), 5ª ed. España, Panamericana. 2014.
22. Frankenburg W, Camp B and Van Natta P. Validity of the Denver Developmental Screening Test. Child Development. 1971;42(2):475-85. https://doi. org/10.2307/1127481
23. Campo A, Hernández A, Pérez A, et al. Discapacidad intelectual. Protoc diagn ter pediatr. 2022;1:51-64. https://www. aeped.es/sites/default/files/documentos/ pdf_final_protocolos_aep-senep_2022.pdf
24. Morgues M, Henríquez MT, Tohá D, et al. Sobrevida del niño menor de 1500 g en Chile. Rev chil obstet ginecol. 2002;67(2):100-5. http://dx.doi. org/10.4067/S0717-75262002000200003
25. Tsai A, Lasky R, John S, et al. Predictors of neurodevelopmental outcomes in preterm infants with intraparenchymal hemorrhage. J Perinatal. 2014;34:399-404. doi: 10.1038/jp.2014.21.
26. McCrea H, Ment L. The diagnosis, management, and postnatal prevention of intraventricular hemorrhage in the preterm neonate. Clin Perinatol. 2008;35(4):777-92. https://doi. org/10.1016/j.clp.2008.07.014
27. Vohr B, Allan W, Westerveld M, et al. School age outcomes of very low birth weight infants in the indomethacin intraventricular hemorrhage prevention trial. Pediatrics. 2003;111:e340. https:// doi.org/10.1542/peds.111.4.e340
28. Lesión cerebral en el niño prematuro. Fernando Cabañas y Adelina Pellicer. Protocolos Diagnóstico Terapeúticos de la AEP: Neonatología. 2008;27.
29. Fucile S, Gisel E. Sensorimotor interventions improve growth and motor function in preterm infants. Neonatal Netw. 2010;29:359-66. doi: 10.1891/0730-0832.29.6.359.
30. Avilés C, Madariaga P, Fuentes P, et al. Intervención temprana en prematuros, una experiencia de trabajo. Revista Chilena De Terapia Ocupacional 2004;4:11-8. https://doi.org/10.5354/0719-5346.2004.157
31. Lee K, Cascella M, Marwaha R. Intellectual disability. Treasure Island (FL): StatPearls Publishing 2020. PMID: 31613434. https://www.ncbi.nlm.nih.gov/ books/NBK547654/
32. Roze E, Van Braeckel K, van der Veere C, et al. Functional outcome at school age of preterm infants with periventricular hemorrhagic infarction. Pediatrics 2009;123:1493-500. https://doi. org/10.1542/peds.2008-1919
33. Volpe JJ. The encephalopathy of prematurity--brain injury and impaired brain development inextricably intertwined. Semin Pediatr Neurol. 2009;16(4):167-78. doi: 10.1016/j. spen.2009.09.005.
34. Aarnoudse-Moens C, Weisglas-Kuperus N, Van Goudoever J, et al. Meta-analysis of neurobehavioral outcomes in very preterm and/or very low birth weight children. Pediatrics 2009;124:717-28. doi: 10.1542/peds.2008-2816.
35. Narberhaus A, Segarra-Castells A, Pueyo-Benito R, et al. Disfunciones cognitivas

a largo plazo en sujetos prematuros con hemorragia intraventricular. Rev Neurol. 2008;47:57-60. Doi: https://doi.org/10.33588/rn.4702.2007506

36. Roze E, Kerstjens J, Maathuis C, et al. Risk Factors for Adverse Outcome in Preterm Infants With Periventricular Hemorrhagic Infarction. Pediatrics. 2008;122:e46-e52. https://doi.org/10.1542/peds.2007-3305
37. Maitre N, Marshall D, Price W, et al. Neurodevelopmental outcome of infants with unilateral or bilateral periventricular hemorrhagic infarction. Pediatrics 2009:124:e1153-e1160. doi: 10.1542/peds.2009-0953.
38. Luu T, Ment L, Schneider K, et al. Lasting effects of preterm birth and neonatal brain hemorrhage at 12 years of age what's known on this subject. Pediatrics. 2009;123:1037-44. https://doi.org/10.1542/peds.2008-1162
39. Marlow N, Wolke D, Bracewell M, et al. Neurologic and developmental disability at six years of age after extremely preterm birth. N Engl J Med. 2005;352:9-19. doi: 10.1056/NEJMoa041367.
40. Msall ME, Tremont M. Measuring functional outcomes after prematurity: developmental impact of very low birth weight and extremely low birth weight status on childhood disability. Ment Retard Dev Disabil Res Rev. 2002;8:258-72. doi:10.1002/mrdd.10046.
41. Arriagada C, Jara L, Calzadilla O. La co-enseñanza desde enfoques inclusivos para los equipos del Programa de Integración Escolar. Estudios Pedagógicos XLVII. 2021;1:175-95. Doi: 10.4067/S0718-07052021000100175