FREQUENCY CORRELATIONS BETWEEN THE NEUROLOGICAL AND THE EPILEPTIC ENCEPHALOPATHY SYNDROMES

C. MICHEU[1]

[1]*County Clinical Hospital Mureş*

Keywords: *epileptic encephalopathy, West syndrome, Lennox-Gastaut syndrome, epileptic encephalopathy continuum, cerebral palsy*

Abstract: *Objective of the study: Based on the observations made on a period of 10 years regarding the most common form of epileptic encephalopathy (EE), namely, the West syndrome (WS), the Lennox-Gastaut syndrome (LGS), or the epileptic encephalopathy continuum form (EEC), LGS derived from WS (WS-LGS), we found a statistically significant association frequency between the hypotonic forms of cerebral palsy (CP) and LGS and between the spastic forms of CP and WS respectively. Materials and methods: The study comprised a group of 30 patients, aged between 2 months and 6 years old. Two patients were diagnosed with other forms of EE (Dravet syndrome and Landau-Kleffner syndrome), the rest of 28 with the above mentioned forms, as follows: 12 with WS, 8 with LGS and 8 with WS-LGS. The patients were included in the study based on the inclusion criteria. They benefited from general examination, neurological and psychiatric examinations, blood tests, EEG records, imagistic investigation as well as optic fundus examination. Results: After the application of the specific statistical methods, a close correlation with significant values of the parameter p has resulted, representing the association between the hypotonic and spastic forms of PC and the most common forms of EE (SW, SLG and SW-SLG). Also, significant frequency correlations were revealed between psychomotor retardation or regression and the syndromes listed. Conclusions: Although EE is defined as a heterogeneous group of entities, with well-defined individual characteristics, in addition to some common characteristics such as: polymorphous character of the seizures, resistance of seizures to treatment and variability of EEG patterns, we can add the identified neurological syndromes and their association in statistically significant proportions with WS, LGS and WS-LGS.*

Cuvinte cheie: *encefalopatii epileptice, sindrom West, sindrom Lennox-Gastaut, continuum epileptic encefalopatic, paralizii cerebrale*

Rezumat: *Obiectivul studiului. Pe baza observaţiilor efectuate într-o perioadă de 10 ani pe un lot de studiu cuprinzând 30 de pacienţi cu formele cel mai frecvent întâlnite de encefalopatii epileptice (EE), şi anume sindrom West (SW), sindrom Lennox-Gastaut (SLG) şi forma de continuum epileptic encefalopatic (CEC), respectiv SLG evoluat din SW (SW-SLG), am constatat o frecvenţă semnificativă statistic a asocierii dintre formele hipotone de paralizie cerebrală (PC) şi SLG, respectiv a formelor spastice de PC şi SW. Material şi metodă: Lotul studiat a cuprins în total 30 de pacienţi, cu vârste cuprinse între 2 luni şi 6 ani. Dintre aceştia, 2 pacienţi au fost diagnosticaţi cu alte forme de EE (sindrom Dravet şi sindrom Landau-Kleffner), restul de 28 cu formele amintite, după cum urmează: 12 cu SW, iar câte 8 cu SLG, respectiv SW-SLG. Pe baza aplicării criteriilor de includere, pacienţii au fost admişi în măsura în care au îndeplinit aceste criterii. Pacienţii au beneficiat de examen clinic general, examen neurologic, examen psihic, analize de sânge, înregistrări EEG seriate, investigaţii imagistice, examen de fund de ochi. Rezultate: După aplicarea metodelor statistice specifice au rezultat corelaţii strânse cu valori semnificative ale parametrului p reprezentând asocierea între formele hipotone şi cele spastice de PC şi formele cele mai frecvente de EE (SW, SLG şi SW-SLG). De asemenea, corelaţii de frecvenţă semnificative au fost relevate şi între retardul sau regresul psihomotor şi sindroamele menţionate.Concluzii: Cu toate că aşa cum sunt definite EE ca un grup heterogen de entităţi, cu caracteristici individuale bine conturate, pe lângă câteva trăsături comune, cum ar fi caracterul polimorf al crizelor, rezistenţa mare la tratament a crizelor şi variabilitatea patternurilor EEG, se adaugă şi sindroamele neurologice identificate şi asocierea acestora în proporţii semnificative statistic cu SW, SLG şi SW-SLG.*

INTRODUCTION

Epileptic encephalopathy (EE) is a heterogeneous group of epilepsies and epileptic syndromes characteristic of infancy and childhood which have several common features: a) the multiform character of the seizures which defines them clinically; b) EEG patterns specific to almost every entity; c) pre-existing cognitive impairment or progressively installed after seizures and as a consequence d) resistance to treatment, in most cases antiepileptic drug combinations (AED) in bi-therapy or poly-therapy are required.(1) Of all types of epilepsy, EE proved most difficult to be classified but syndromes such as Lennox - Gastaut (sometimes evolved from the West syndrome, other times de novo), West syndrome, severe myoclonic epilepsy of infants (Dravet's syndrome), acquired epileptic aphasia (Landau-Kleffner syndrome) and epilepsy with myoclonic-astatic seizures (Doose syndrome) are well

[1]Corresponding author: Cristian Micheu, Str. Baladei, Nr. 6, Târgu-Mureş, România, E-mail: micheucristian@yahoo.com, Tel: +4074 5660526
Article received on 15.03.2012 and accepted for publication on 23.05.2012
ACTA MEDICA TRANSILVANICA September 2012;2(3):182-187

defined.(9)

West syndrome (WS) usually starts in the first year of life, but seizures mostly occur between 3 and 7 months. In addition to seizures whose emblem is represented by infantile spasms, the diagnostic triad involves an electroencephalographic pattern called hypsarrhythmia and initial psychomotor retardation or psychomotor regress after the onset and during the seizure's development.(3,5) The etiologic factors represent a heterogeneous group and in 40% of cases they cannot be classified. A great variety of factors was identified such as: brain malformations, infections (especially those opportunistic, grouped under the acronym TORCH) intra-natal (during delivery), cerebral hemorrhage, hypoxic-ischemic states, metabolic disturbances and genetic syndromes such as Down syndrome. In this context, it worth mentioning a record percentage of psychomotor development progress, which in case of symptomatic forms account for only 6%, while in case of possible symptomatic forms (replacing the term obsolete, abandoned, cryptogenetic), it represents 51%(4, 6, 8).

Lennox-Gastaut syndrome (LGS) can be defined as a mixture of epileptic seizures with onset in childhood and a very poor prognosis, both in terms of seizures' development and psychomotor development which leads to a severe psychomotor and language regression.(7) The most frequently encountered seizure types are the tonic seizures, atonic and atypical absences ones. The characteristic interictal pattern is represented by the slow-wave complex discharges (usually with frequencies of 1.5-2 Hz), often with multifocal epileptiform discharges.(10) The ictal appearance is dependent on the type of seizure that it correlates with. The symptomatic forms predominate in a percentage of 70-78%, and the etiologic factors are represented by a wide variety, some congenital, others acquired, brain malformations, hypoxic-ischemic injuries and encephalitis being statistically representative. The prognosis for the symptomatic forms is very poor, fact which increases the risk of severe psychomotor retardation, considered as a disturbing percentage of 100%. In this context, we must mention that the risk for the above mentioned retardation is augmented by a positive history of infantile spasms with a very early onset (before 3 months).(9)

Epileptic encephalopathy continuum (EEC) is a concept that was and is still supported by records showing the "transformation" from a form of EE to another form of EE, both clinically (with reference to epileptic seizures) and in terms of EEG. Thus, West syndrome may evolve from Ohtahara syndrome, Lennox-Gastaut syndrome may evolve from West syndrome, Doose syndrome from Lennox-Gastaut syndrome.(2)

Cerebral palsy (CP) or Infantile Chronic Encephalopathy (ICE) is defined as a group of disorders characterized by motor dysfunction caused by non-progressive brain damage early installed. The motor dysfunctions are frequently associated with cognitive dysfunctions, psychiatric and language disturbances, agnosia, dyspraxia, sensory disturbances.(1) The identified etiologic factors include brain malformations, anoxia, intracerebral hemorrhage, hypoxic-ischemic neonatal encephalopathy, hypoglycemia, opportunistic infections (TORCH) or others. All these etiologic factors act during pre, peri and in the immediate postnatal period. The clinical picture has three main aspects: retardation in the development of new acquisitions corresponding to the chronological age; the persistence of reflexes that should have been abolished and the absence of the pathological pattern corresponding to the specific chronological age. All these are due to hypertonic, hypotonic or dystonic state, resulting from the motor neuron lesions.(1) The classification of cerebral palsy can be done using topographic criteria and it includes: quadriplegic, diplegic and hemiplegic forms. There are triplegic forms too, in the situation when an upper limb "seems" functional or paraplegic forms, when the upper limbs "seem" functional. They can be also classified into spastic, athetoide (diskinetic), hypotonic and at.xic forms.(1)

PURPOSE

The purpose of the study is to identify the clinical-epidemiological correlations between the type of neurological syndrome and the type of epileptic encephalopathy.

METHODS

The studied group included a total number of 30 patients, aged between 2 months and 6 years old. The patients were hospitalized in the Children Neuropsychiatry Clinic of Tirgu-Mures between 1999 and 2009. Of these, 2 patients were diagnosed with other forms of EE (Dravet syndrome and Landau-Kleffner syndrome), the remaining 28 with the already mentioned forms, as follows: 12 with WS, 8 with LGS and 8 with WS-LGS. To support the preliminary diagnosis for being included in the group, all the patients underwent history taking. Within this area, the greatest interest consisted in the identification with the highest accuracy of the factors acting during pregnancy and considered potential generators of severe brain insults as well as of those acting intranatally and perinatally. Great attention was given to the type of seizures present upon onset and to an accurate description of their characteristics (their beginning, content and end, including the post-ictal period). The patients' examination involved a general clinical examination (skin lesions characteristic to the neurocutanate syndromes were carefully looked for, as well as malformations), neurological and psychiatrical examination and language performance. Blood tests were mainly focused on antivirus antibodies titers (cytomegalovirus, herpes simplex virus , rubella virus) and on Toxoplasma gondii. Repeated EEG recordings were performed to capture the dynamic evolution of different patterns. Almost in all cases, the recordings were performed in natural sleep (when possible) and drug-induced sleep with chloral hydrate, 10% 1ml./kg.corp. All patients underwent radiological and imagistic investigations: computed tomography (CT), magnetic resonance imaging (MRI), ultrasound examination (US) and received an optic fundus examination. The diagnostic classification and thus, the inclusion in the study group were possible as a result of applying and accomplishing the inclusion criteria. The inclusion criteria corresponding to the two entities which belong to EE are the following:

Inclusion criteria for West syndrome:

Types of seizures: spasms (s) in flexion or extension, combined s. (in flexion and extension), asymmetric s., asynchronous s., spasm preceded by short atony, spasm preceded by asymmetric partial seizures during epilepsy, focal s., subtle s. subclinical s.;

The onset of seizures: between 3 and 7 months (before 1 year, rarely before 3 months);

EEG patterns: hypsarrhythmia, with its different variants (asymmetric, altered, atypical, fragmentary, unilateral);

Evolution of EEG abnormalities: organization of rhythms during the process, between 2 and 4 years the H pattern is replaced by the slow-wave complex pattern of SLG;

Psychomotor development: initially delayed or installed (regression) only after the onset of spasms. It was maintained in most cases by the lack of control or poor control of seizures.

Neurological syndrome: variable (spastic forms, hypotonic or diskinetic of tetraplegia, hemiplegia, paraplegia).

Inclusion criteria for Lennox-Gastaut syndrome:

Seizure types: tonic seizures, atonic seizures, absence seizures, myoclonic seizures, drop attacks, status epilepticus (sometimes persistence of infantile spasms or their early appearance).

The onset of seizures: after the age of 1 year (if they derive from WS) and between 3 and 5 years old in the de novo forms;

EEG patterns: a) paroxysms of rapid rhythms or fast sharp-wave characteristic of tonic seizures, most frequently noticed in slow wave sleep; b) generalized discharges of slow-wave complex, bilateral, synchronous, symmetrical and of high amplitude on frontal derivations, characterizing atypical absences; c) interictal spikes and multifocal or slow-wave complex, predominant in the frontal and occipital areas; d) multiple independent foci of spikes in the transition from the H pattern to slow-wave pattern.

Psychomotor development: relatively good before the onset of seizures (despite the fact that there are only symptomatic forms).

Neurological syndrome: variable (hypotonic syndrome in a significant proportion).

RESULTS

The general clinical examination revealed characteristic skin lesions typical for 3 of the neurocutanate syndromes that occur more frequently, namely: neurofibromatosis type I (2 cases), Bourneville tuberous sclerosis (3 cases) and Sturge-Weber disease (1 case). Neurological examination revealed 25 cases in CP, predominantly hypotonic and spastic forms (the first in 13 cases, the others in 15 cases, the rest 4 cases were distonic forms including 3 cases associated with hypotonic forms and 1 with spastic forms, and 3 ataxic syndromes, two of them associated with hypotonic and one with spastic form). (see table I). Microcefaly were found in 12 cases, being more commonly associated with spastic forms and craniosynostoses in six cases. The psychiatric examination in 19 cases showed initial retardation while in the remaining 11 cases, a regress was noticed after the onset of the seizures with progressive increase in persistence of seizures to a severe degree. Antibodies titre of CMV (cytomegalovirus) was identified in 8 cases, anti-HSV (herpes simplex virus) in 7 cases, anti TG (Toxoplasmosis gondii) in 4 cases, and anti RV (rubella virus) in 2 cases. In 3 of the 30 patients associations were identified, as follows: HSV + TG + VR, CMV + HSV+ TG, CMV + HSV each of them in 1 case. Electroencephalographic recordings revealed characteristic aspects in the studied entities, underlining their characteristic patterns (classic hipsarrhythmia in more than 50% of cases, the rest being its variants, especially fragmentary hipsarrhythmia, rarely unilateral; classical discharges of generalized or predominantly frontal complexes of slow-wave were also noticed. Increasing relevance in cases in which drug-induced sleep EEG recording was performed (which sometimes required initial sleep deprivation) should be mentioned. Imagistic investigations by cranial computed-tomography examination (CT) were performed in 20 patients, and by magnetic resonance images (MRI) in 10 patients. In 8 patients, both were practiced. One patient received MRI with angiographic sequences (in Sturge-Weber disease). Ultrasound examination (US) was performed in 10 patients. On these occasions the following were revealed: cerebral atrophy in 18 cases, in 8 of them it was focused in most cases frontally and temporally, in 4 cases ventriculomegaly (consistent with the US appearance), intracranial calcification in 3 cases, hydrocephaly respectively, and in one case, arterio-venous malformation and left porencephalic cyst (FT) respectively in 2 cases. Statistical analysis was performed using the SPSS software version 19. and GRAPH PAD PRISMA. For the univariate analysis of the data, we used $\chi 2$ test (dichotomous variables). Multivariate regression was also used where confidence intervals strongly suggested the presence of risk factors for various combinations. Tables of frequency were used to obtain numerical data and the percentage ones. Averages and SD were also calculated. Differences were considered statistically significant at a value of the parameter p less than 0.05. After applying the above tests and their inclusion in the graphics program, significant associations resulted with p values less than 0.05 betwen the tetraplegic form of CP and novo Lennox-Gastaut syndrome (p = 0.01) or Lennox-Gastaut syndrome evolved from West syndrome(WS-LGS) (p = 0.034).

Figure no. 1. Frequency combination of ESI and West syndrome

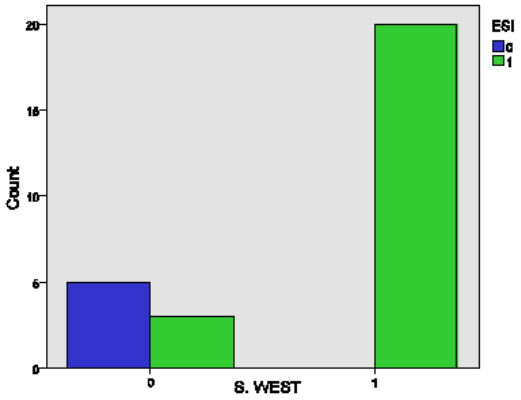


Table no. 2. Frequency combination of ESI and West syndrome

Total	**Count**	5	23	28
	% within S. WEST	17.9%	82.1%	100.0%
	% within ESI	100.0%	100.0%	100.0%
	% of Total	17.9%	82.1%	100.0%

p- 0,001

Figure no. 2. Frequency combination of ESI and Lennox-Gastaut

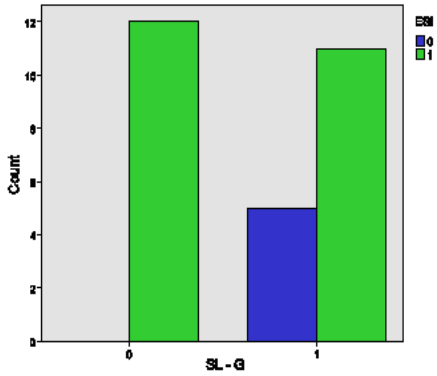


Table no. 3. Frequency combination of ESI and Lennox-Gastaut

Total	**Count**	5	23	28
	% within SL - G	17.9%	82.1%	100.0%
	% within ESI	100.0%	100.0%	100.0%
	% of Total	17.9%	82.1%	100.0%

p- 0,05

Table no. 1. Evolution of psychomotor development in EE

Sub. no.	EE forms	Motor development	Speech and mental development	Neurological syndromes
S1	S L - G	good initially, decline after 2.6 years	mild retardation, speech disturbance	hypotonic quadriplegia,
S2	S L - G	good initially, decline after 6 months	rett syndrome, severe retardation	hypotonic quadriplegia,
S3	S. WEST	initially severe retardation	severe retardation	spastic quadriplegia, microcephaly
S4	S. WEST	good initially, decline after 4 months	severe retardation, autistic syndrome	hypotonic quadriplegia, brachycephaly, cerebellar syndrome
S5	S L - G	initially severe retardation	severe retardation	spastic quadriplegia, dystonic syn.
S6	SL - G	normal limits up to 3 years	initially mild retarded, severely after	right spastic hemiparesis
S7	SW-SLG	initially severe retardation	severe retardation, autistic syndrome	hypotonic quadriplegia, brachycephaly,
S8	S L - G	Severe mental decline after four years	severe retardation, autistic syndrome	hypotonic quadriplegia
S9	S L - G	Severe mental decline after 6 years	severe retardation	hypotonic quadriplegia
S10	S. WEST	psychomotor regression after 8 months	severe retardation	spastic quadriplegia,
S11	SW-SLG	initially severe retardation	severe retardation, autistic syndrome	hypotonic quadriplegia
S12	S. WEST	initially severe retardation	severe retardation	spastic quadriplegia,
S13	SW-SLG	initially severe retardation	severe retardation	hypotonic quadriplegia, dystonic syn.
S14	S. WEST	initially severe retardation	severe retardation	spastic quadriplegia, microcephaly
S15	SW-SLG	initially severe retardation	severe retardation	hypotonic quadriplegia, dystonic syn., microcephaly
S16	S. WEST	initially severe retardation	severe retardation	hypotonic quadriplegia,
S17	SW-SLG	initially severe retardation	severe retardation	spastic quadriplegia, dystonic syn., scafocefaly
S18	SW-SLG	initially severe retardation	severe retardation	hypotonic quadriplegia, dystonic syn.
S19	S L - G	mentally regress after 2.6 years	moderate retardation	hypotonic quadriplegia, cerebellar syn.
S20	S. WEST	initially severe retardation	moderate retardation	hypotonic quadriplegia, microcephaly
S21	SW-SLG	initially severe retardation	severe retardation	spastic quadriplegia, dystonic syn.,
S22	S. WEST	initially severe retardation	moderate retardation	hypotonic quadriplegia,
S23	S. WEST	initially severe retardation	severe retardation	spastic quadriplegia,
S24	S. L-K	initially discrete retardation, moderate decline after four years	mental and language severe retardation (aphasia)	cerebellar syn.
S25	S. WEST	severe retardation, microcephaly	severe retardation	spastic quadriparesis, dystonic-dyskinetic syndrome
S26	S. WEST	moderate regression after 4 months	moderate retardation	flaccid tetraparesis
S27	S. WEST	initially severe regression	severe retardation	spastic quadriplegia
S28	SW-SLG	initially mild regression	mild retardation	flaccid tetraparesis + ataxic syndrome
S29	SL - G	initially normal development until the onset of crisis (5 years) regression (disabilities, dyspraxia)	severe regression after 5 years old, progressively	ataxic syndrome installed after five years, evolving progressively
S30	S. DRAVET	good initial development until the onset of crisis (2 months)	regression after 2 months, progressively (severe in the end)	asymmetric flaccid tetraparesis (predominantly right)

SLG- syndrome Lennox-Gastaut, SLK- syndrome Landau-Kleffner, SW-SLG- syndrome West evolved in Lennox-Gastaut syndrome;

Figure no. 3. Frequency of association between West syndrome and initially severe psychomotor retardation

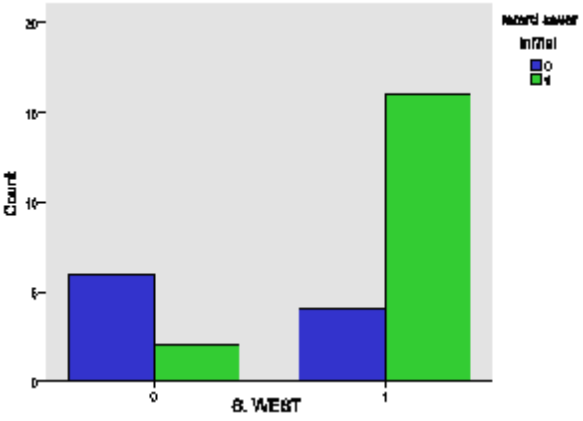


Table no. 4. Frequency of association between West syndrome and severe psychomotor retardation initially

Total	**Count**	10	18	28
	% within S. WEST	35.7%	64.3%	100.0%
	% within initial severe retardation	100.0%	100.0%	100.0%
	% of Total	35.7%	64.3%	100.0%

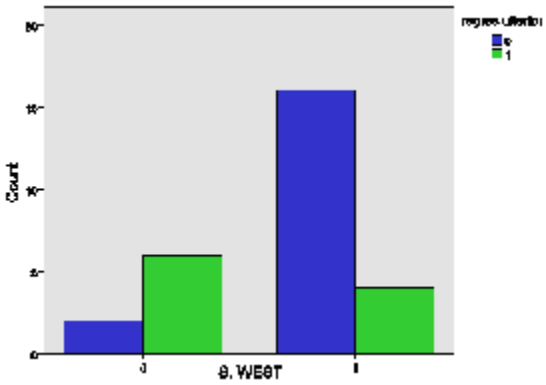
p-0,011

Table no. 5. Frequency of association between West syndrome and psychomotor regression after

Total	**Count**	18	10	28
	% within S. WEST	64.3%	35.7%	100.0%
	% within subsequent	100.0%	100.0%	100.0%
	% of total	64.3%	35.7%	100.0%

p-0,011

Figure no. 4. Frequency of association between West syndrome and psychomotor regression after



Picture no. 5. Frequency of association between West syndrome and flaccid tetraparesis

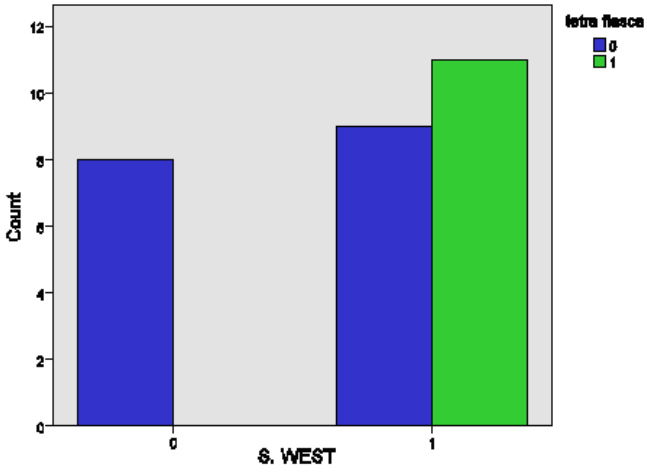


Table no. 6. Frequency of association between West syndrome and flaccid tetraparesis

Total	**Count**	17	11	28
	% within S. WEST	60.7%	39.3%	100.0%
	% within flaccid tetraperesis	100.0%	100.0%	100.0%
	% of total	60.7%	39.3%	100.0%

p-0,01

Figure no. 6. Frequency of association between West syndrome and ataxic syndrome

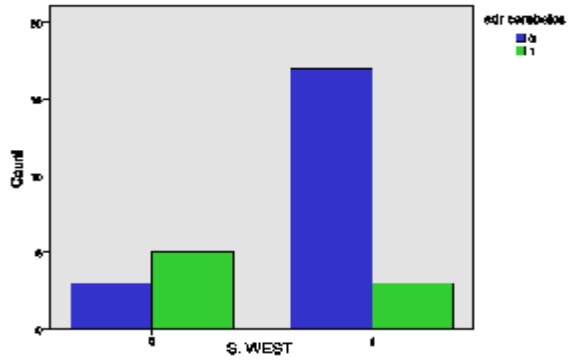


Table no. 7. Frequency of association between West syndrome and ataxic syndrome

Total	**Count**	20	8	28
	% within S. WEST	71.4%	28.6%	100.0%
	% within ataxic syndrome	100.0%	100.0%	100.0%
	% of Total	71.4%	28.6%	100.0%

p-0,022

Figure no. 7. Frequency of association of Lennox-Gastaut syndrome and spastic tetraparesis

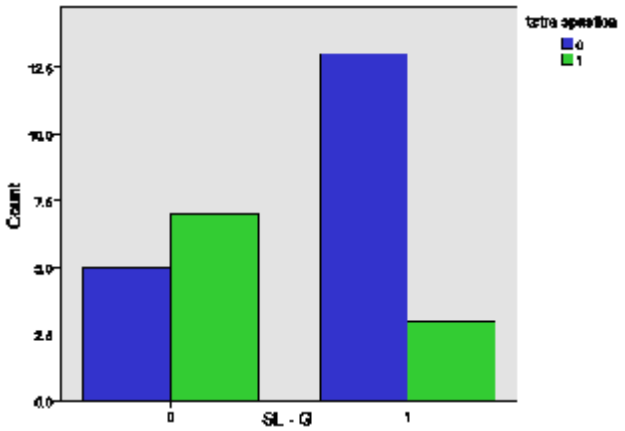


Table no. 8. Frequency of association of Lennox-Gastaut syndrome and spastic tetraparesis

Total	**Count**	18	10	28
	% within SL - G	64.3%	35.7%	100.0%
	% within tetra spastica	100.0%	100.0%	100.0%
	% of Total	64.3%	35.7%	100.0%

p-0,05

Statistically significant associations also emerged between the severe degree of retardation (especially in the mental and language functions) with values of p of 0.022, a percentage higher in WS evolved SLG than in de novo LGS as it can be seen from the graphic.

Despite the fact that the evidence is so clear, especially regarding the association between the quadriplegia form of CP and de novo Lennox-Gastaut syndrome (p = 0.01), we could not find a plausible explanation considering that further studies are needed in this field.

DISCUSSIONS

As you can see, the association between the various forms of ESI (especially spastic and hypotonic) with West syndrome and Lennox-Gastaut syndrome have equivalent statistical significance. Although the evidence is so clear in terms of retardation in development, statistical significance resulted only in association with West syndrome, although the data summarized in Table 1 shows the most cases of severe degree later psychomotor regression (especially mental and language development).

Comorbid states represented by neurocutaneous syndromes can be considered maintenance factors worsening the clinical pictures, especially in terms of persistent seizures due to inadequate drug control, in spite of different antiepileptic drug combinations (MAE), double, triple or even quadruple. The etiological factors identified a high proportion by opportunistic infections (TORCH syndrome), represented only one possible

explanation of the issues captured imaging (brain atrophy, hypoplasia of various locations, ventriculomegalii, cysts porencefalice), cranial malformations (microcefalii, craniosynostosis). The limited possibilities of investigation did not allow a definite diagnosis of neurocutaneous syndromes (another possible explanation for the maintenance and worsening factor of the studied forms of epileptic encephalopathy) by molecular genetic analysis.

CONCLUSIONS

Although EE are defined as a heterogeneous group of entities with individual features well-shaped, besides some common features, such as polymorphous character of the crisis, high resistance to treatment variability crisis and EEG patterns, the identified neurological syndromes are also added, and their association in statistically significant proportion with SW and SW-SLG SLG. The etiologic factors recognized as having a significant involvement in determining these syndromes, are mostly those who work during pre, peri and immediate postpartum. The effect of different degrees are asphyxia syndromes, which are designed to fragile anyway immature brain and provide the conditions for the development of serious conditions often irreversible. Maintaining constant concern for the etiological factors, the opportunistic infections have a decisive role in determining powerful lesions of the brain, depending on the moment in which they act on the embryo or fetus. Records from processing sensitive data show equal percentages for cytomegalovirus and herpes viruses (26 and 23%) and lower percentages (13%) for Toxoplasma gondii. Epileptic encephalopathies comorbidities are multiple, but a very significant proportion is due to *infant chronic encephalopathies* in the different above-mentioned forms, involving a severe degree of retardation and different neurological syndromes (spastic and hypotonic forms over 60%, ataxia and diskinetic forms). Retardation in development may precede the onset of encephalopathy in a percentage of 64%, while the decline is installed after the onset of crisis and is now at 34%. The first is more common in West syndrome, the second in Lennox-Gastaut syndrome. As important comorbidities not statistically but determining, the neurocutaneous syndromes, autistic syndrome, microcephaly, and craniosynostosis should also be mentioned. The detection of these clinical pictures as early as possible will allow the early intervention by establishing complex neuropsychomotor recovery programmes (both the drug therapy, physiotherapy, ludotherapy, speech therapy, art therapy, music therapy), treatment of epilepsy associated with how to achieve a better control of the epileptic seizures that always need to adjust the treatment schemes in order to achieve a good psychomotor performance evolution.

REFERENCES

1. Levitt S. The clinical picture and therapy for management, in: Treatment of cerebral palsy and motor delay, 4th ed., Blackwell Publishing; 2009. p. 1-6.
2. Djukic A, Lado FA, Shinnar S, et al. Are early myoclonic encephalopathy (EME) and the Ohtahara syndrome (EIEE) independent of each other? Ep Res. 2006;70:S68-S76.
3. Guzzetta F, Cioni G, Mercuri E, et al. Neurodevelopmental evolution of West syndrome: A 2-year prospective study, J Paed Neurol. 2007;12:387-397.
4. Hrachovy RA, Frost JD Jr. Severe epileptic encephalopathies in infants; infantile spasms (West syndrome), in: Pellok J, Bourgeois BFD. (Eds.) Pediatric epilepsy, diagnosis and therapy (3thd ed.), New York, Demos Medical Publishing; 2008. p. 249-266.
5. Kobayashi K, Oka M, Inoue T, et al. Characteristics of Slow Waves on EEG Associated with Epileptic Spasms Epilepsia. 2005;46:1098-1105.
6. Ohtahara S. Epileptic encephalopathies of infancy. Neurol Asia. 2007;12:1-3.
7. Okumura A, Watanabe K, Hayakawa F, et al. The Timing of Brain Insults in Preterm Infants Who Later Developed West Syndrome. Neuroped. 2001;32:245-249.
8. Parisi P, Spalice A, Nicita F, et al. Epileptic Encephalopathy of Infancy and Childhood: Electro-Clinical-Pictures and Recent Understanding, Curr Neurophar. 2010;8:409-421.
9. Morita DA, Glauser TA. Lennox-Castaut syndrome, in: Pellok J., Bourgeois BFD (Eds.), Pediatric epilepsy, diagnosis and therapy (3thd ed.), New York, Demos Medical Publishing; 2008. p. 307-323.
10. Kim A, Nordly RD Jr, Lennox-Gastaut Syndrome in: Panayotopoulos CP (Ed.) Atlas of Epilepsies, vol. 2, Springer-Verlag London Limited; 2010. p. 899-905.