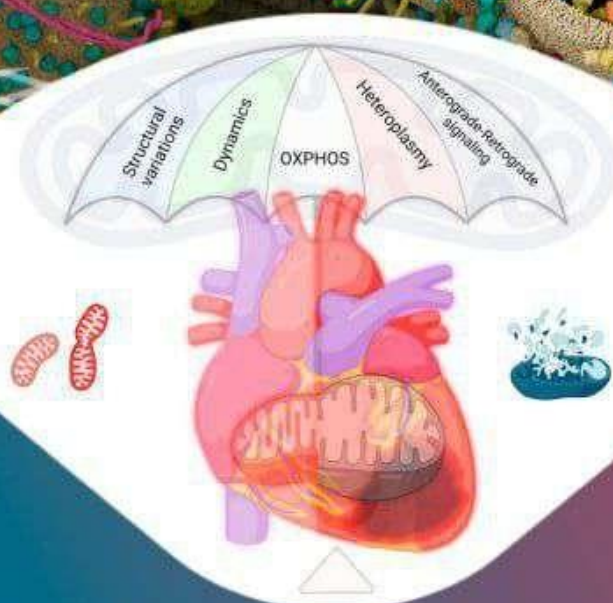


**КАРТИНА ИЗМЕНЕНИЙ УРОВНЯ ФЕТУИНА-A НА РАЗНЫХ СТАДИЯХ ХРОНИЧЕСКОЙ БОЛЕЗНИ ПОЧЕК**

**МИКРОБНЫЕ МЕТАБОЛИТЫ КАК МЕДИАТОРЫ МЕЖДУ ОРАЛЬНОЙ МИКРОБИОТОЙ И СЕРДЕЧНО-СОСУДИСТЫМИ ЗАБОЛЕВАНИЯМИ**

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**ЭКСТРАКОРПОРАЛЬНОЕ ОПЛОДОТВОРЕНИЕ: НАУЧНАЯ ЭВОЛЮЦИЯ, ТЕХНОЛОГИИ И ПЕРСПЕКТИВЫ РЕПРОДУКТИВНОЙ МЕДИЦИНЫ**



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**CLINICAL AND IMMUNOLOGICAL DESCRIPTION OF EPILEPTIC ENCEPHALOPATHY IN EARLY CHILDHOOD AND DEVELOPMENT OF CRITERIA FOR ITS EARLY DIAGNOSIS**

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**КЛИНИКО-ИММУНОЛОГИЧЕСКАЯ ХАРАКТЕРИСТИКА ЭПИЛЕПТИЧЕСКОЙ ЭНЦЕФАЛОПАТИИ У ДЕТЕЙ РАННЕГО ВОЗРАСТА С РАЗРАБОТКОЙ КРИТЕРИЕВ РАННЕЙ ДИАГНОСТИКИ**

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**ERTA BOLALIK DAVRIDA EPILEPTIK ENSEFALOPATIYANING KLINIK-IMMUNOLOGIK TAVSIFI VA ERTA TASHXISLASH MEZONLARINI ISHLAB CHIQUISH**

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**ABSTRACT**

This article provides a comprehensive study of the clinical and immunological characteristics of early childhood epileptic encephalopathy. Within the framework of the research, diagnostic criteria were developed to enable early identification of epileptic encephalopathy and its differential diagnosis from other forms of epilepsy. Immunological markers — interleukin-1 (IL-1), interleukin-10 (IL-10), and tumor necrosis factor-alpha (TNF- $\alpha$ ) — and their relationship with clinical manifestations were analyzed. Based on the obtained results, scientific and practical recommendations were developed to improve the effectiveness of early diagnosis and treatment.

**Keywords:** epileptic encephalopathy, seizure, West syndrome, Lennox–Gastaut syndrome, Ohtahara syndrome.

**АННОТАЦИЯ**

В данной статье подробно изучены клинические и иммунологические особенности эпилептической энцефалопатии раннего детского возраста. В рамках исследования были разработаны критерии, позволяющие раннюю

диагностику эпилептической энцефалопатии и проведение её дифференциальной диагностики с другими формами эпилепсии. Были проанализированы иммунологические показатели — интерлейкин-1 (IL-1), интерлейкин-10 (IL-10), фактор некроза опухоли альфа (TNF- $\alpha$ ), а также их взаимосвязь с клиническими проявлениями. На основе полученных результатов разработаны научно-практические рекомендации по повышению эффективности ранней диагностики и терапии.

**Ключевые слова:** эпилептическая энцефалопатия, судороги, синдром Веста, синдром Леннокса–Гасто, синдром Отахара.

### ANNOTATSIYA

Ushbu maqolada erta bolalik davrida uchraydigan epileptik ensefalopatiyaning klinik va immunologik xususiyatlari atroflicha o'rganilgan. Tadqiqot doirasida epileptik ensefalopatiyani erta tashxislash va uni epilepsiyaning boshqa shakllaridan differensial tashxis qilishga imkon beruvchi mezonlar ishlab chiqildi. Immunologik ko'rsatkichlar — interleykin-1 (IL-1), interleykin-10 (IL-10), o'sma nekroz omili alfa (TNF- $\alpha$ ) darajalari hamda ularning klinik belgilar bilan o'zaro bog'liqligi tahlil qilindi. Olingan natijalar asosida erta tashxislash va davolash samaradorligini oshirish bo'yicha ilmiy-amaliy tavsiyalar ishlab chiqildi.

**Kalit so'zlar:** epileptik ensefalopatiya, tutqanoq, West sindromi, Lennox-Gastaut sindromi, Ohtahara sindromi.

**Introduction.** Epilepsy is one of the most common disorders in child psychoneurology, as 70% of cases occur during early childhood and adolescence, reaching its peak in the first months of life [1]. The highest incidence is observed during the first year of life, with 120 cases per 100,000 population. By the age of 10, the incidence decreases to 40–50 per 100,000, and during adolescence it drops to 20 per 100,000 [2]. In 29% of cases, epilepsy manifests before the age of 3, with a prevalence ranging from 5 to 10 per 1,000 children [3,4]. Other studies report rates between 1.5 and 50 per 1,000, with an average of 15 per 1,000 [5]. It is also known that epilepsy and epileptic seizures are more frequently observed in males [6].

Early childhood epileptic encephalopathy (EE) is a severe pathological condition that significantly impairs neurological development. Patients present with frequent seizures, neurological deterioration, and a decline in cognitive and motor functions. Developing effective clinical and immunological criteria for early diagnosis is crucial to prevent the severe consequences of this condition. Furthermore, the study of immunological markers (IL-6, IL-10, TNF- $\alpha$ ) and their role

in disease progression increases the scientific relevance of this research.

**Objective of the study.** To investigate the clinical and immunological characteristics of early childhood epileptic encephalopathy and to analyze the course of the disease.

**Materials and Methods.** This study was conducted at the Neurology Department of the National Children's Medical Center. A total of 82 children aged 0 to 3 years with various forms of epilepsy were examined. Among them, epilepsy was diagnosed for the first time in 39 patients.

The patients were divided into the following groups:

- Group 1 (main group): 35 children (42.7%) diagnosed with epileptic encephalopathy.
- Group 2 (comparison group): 47 children (57.3%) with other forms of epilepsy, including focal epilepsy (35 patients, 42.7%) and generalized epilepsy (12 patients, 14.6%).
- Control group: 20 healthy volunteers.

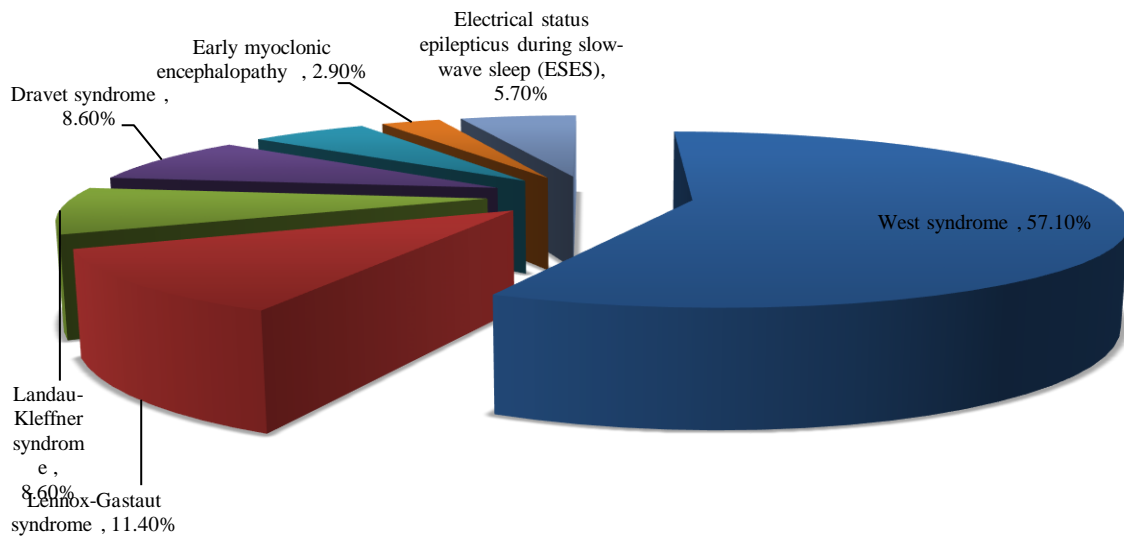
Clinical, neurological, and neuropsychological assessments were performed using the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley III). Instrumental diagnostic methods included electroencephalography (EEG) and magnetic resonance imaging (MRI). Immunological parameters were assessed by measuring serum levels of cytokines: interleukin-1 (IL-1), interleukin-10 (IL-10), and tumor necrosis factor-alpha (TNF- $\alpha$ ).

**Results.** The distribution of epileptic encephalopathy syndromes in the main group was as follows:

- West syndrome — 20 patients (57.1%)
- Lennox–Gastaut syndrome — 4 patients (11.4%)
- Landau–Kleffner syndrome — 3 patients (8.6%)
- Dravet syndrome — 3 patients (8.6%)
- Ohtahara syndrome — 2 patients (5.7%)
- Electrical status epilepticus in slow-wave sleep (ESES) — 2 patients (5.7%)

- Early myoclonic encephalopathy — 1 patient (2.9%)

These data are illustrated in Figure 1.



**Figure 1. Analysis of various clinical syndromes of epileptic encephalopathy**

From the above figure, it can be seen that among all forms of epileptic encephalopathy in children, West syndrome shows the highest prevalence rate, accounting for 57.1% of cases.

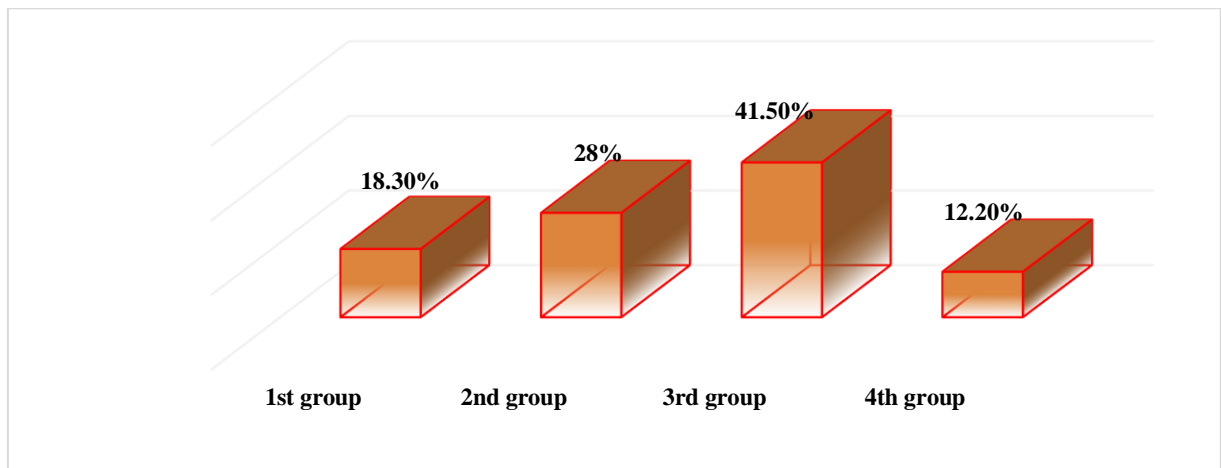
Age distribution of children. According to age indicators, the children were divided into four groups:

- Group 1: from birth to 6 months – 15 children (18.3%);
  - Group 2: from 6 to 12 months – 23 children (28%);
  - Group 3: from 12 to 24 months – 34 children (41.5%);
  - Group 4: from 24 to 36 months – 10 children (12.2%).

These results are presented in Figure 2.

A predominance of male children compared to females was observed. Boys accounted for 51 cases (62.1%), while girls represented 31 cases (37.9%). It should be noted that in the group of children with epileptic encephalopathy, boys constituted 19 cases (54.3%). Thus, the male-to-female ratio was 1,7:1.

Clinical characteristics



**Figure 2. Distribution of the examined children by age group**

The clinical characteristics included the following criteria: identification of etiological factors, description of seizure semiology, assessment of the evolutionary dynamics of epileptic seizures, evaluation of psychomotor developmental delay, and comparison of disease onset with other clinical presentations. In addition, in the main group, such factors as the course of pregnancy in the mother and the condition of the child during the neonatal period were also considered. These data are summarized in Table 1.

**Table 1.**

**Distribution of anamnestic indicators in the main group of children**

Indicators	Yes		No	
	abs	%	abs	%
Presence of miscarriage risk	15	42.8	20	57.2
Family history of epilepsy	2	5.7	33	94.3
Consanguineous marriages	3	8.6	32	91.4
Neonatal seizures	5	14.3	30	85.7
Depression	17	48.6	18	51.4
Severe gestosis	7	20	28	80

The analysis of this table indicates that in children with epileptic

encephalopathy, the prevalence of risk factors such as threatened miscarriage, severe gestosis, and neonatal depression was significantly higher.

The etiological factors contributing to the development of early childhood epileptic encephalopathy were diverse, with prenatal factors playing the leading role. Among them, congenital malformations of the central nervous system (CNS) were predominant, including pachygyria, lissencephaly, and focal cortical dysplasia (FCD).

**Table 2.**

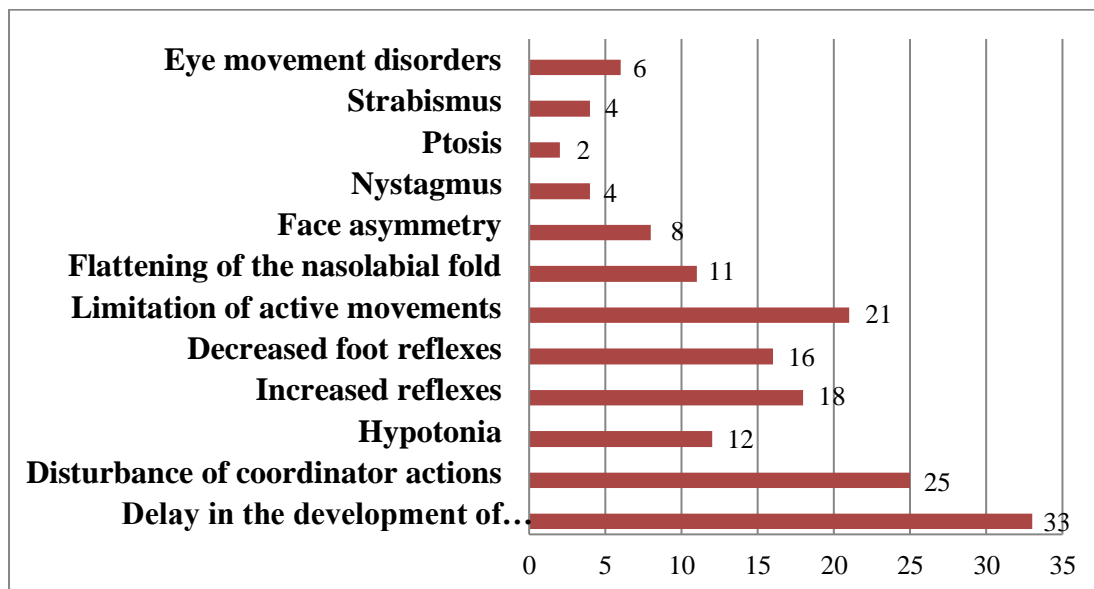
**Frequency of etiological factors in the occurrence of epileptic encephalopathy in early childhood**

Etiological factors	Children		Etiological factors	Children	
	abs	(%)		abs	(%)
Congenital malformations of the CNS	8	22.8	Organic brain changes	6	17.1
Neurocutaneous syndromes	1	2.9	Hypoxic-ischemic encephalopathy	7	20
Tuberous sclerosis complex	4	11.4	Consequences of intrauterine infections	6	17.1
Chromosomal aberrations	1	2.9	Consequences of neuroinfections	3	8.6
Metabolic disorders	2	5.7	Acute cerebrovascular complications	1	2.9
Aicardi syndrome	1	2.9	Congenital tumor	1	2.9

According to the analysis of Table 2, the main etiological factors were prenatal conditions, which accounted for 59.4% of cases.

When analyzing the neurological status, the following general neurological signs are observed: sleep disturbance, severe headache, dizziness, rapid fatigue; focal neurological signs: signs of BMN damage, unilateral hyperreflexia of tendon reflexes,

anisotonia, presence of pathological reflexes, dysmetria were observed (Fig. 3).



**Figure 3. Neurological changes in children in epileptic encephalopathy.**

Significant differences were observed in the characteristics of epileptic seizures between the main and comparison groups, while no seizures were recorded in the control group. In the main group, the most frequent type of seizure was epileptic spasms, detected in 23 cases (65.8%). Other types included:

- Generalized tonic–clonic seizures — 3 cases (8.6%)
- Myoclonic seizures — 3 cases (8.6%)
- Polymorphic seizures — 2 cases (5.7%)
- Absence seizures — 2 cases (5.7%)
- Focal seizures — 1 case (2.8%)
- Non-convulsive variants — 1 case (2.8%)

In the comparison group, the distribution differed substantially:

- Generalized tonic–clonic seizures were most common, recorded in 22 patients (46.8%)
- Polymorphic seizures — 8 cases (17%)
- Focal seizures — 11 cases (23.4%)
- Infantile spasms — only 3 cases (6.4%) (a marked difference compared to the main group)
- Absence seizures — 2 cases (4.3%)

- Myoclonic seizures — 1 case (2.1%)

#### Immunological findings

To evaluate immunological parameters in the studied groups, cytokine profiling was performed. In particular, the serum levels of IL-1 $\beta$ , IL-6, IL-10, and TNF- $\alpha$  were measured, and significant differences were observed in children with epileptic encephalopathy (EE).

The results demonstrated that IL-1 $\beta$ , IL-6, and TNF- $\alpha$  levels were markedly elevated in EE patients, while IL-10 concentrations were reduced. This indicates enhanced inflammatory activity along with suppressed anti-inflammatory immune responses. Compared with the control group, all parameters showed statistically significant differences ( $p < 0.01$ ).

- In Group 1, the mean IL-1 $\beta$  level was  $28.4 \pm 4.7$  pg/ml, significantly higher than in Group 2 ( $19.1 \pm 3.2$  pg/ml) and the control group ( $10.6 \pm 2.4$  pg/ml) ( $p < 0.05$ ).
- The IL-10 level in Group 1 was  $6.2 \pm 1.1$  pg/ml, indicating weakened anti-inflammatory defense mechanisms.

From a biological perspective, IL-1 $\beta$  is secreted by astroglia and microglia, disrupting neuronal activity and inducing synaptic imbalance that triggers epileptic seizures. IL-6 promotes later stages of inflammation and contributes to blood–brain barrier impairment. TNF- $\alpha$  exhibits proapoptotic and proconvulsive properties, and its elevated concentration increases neuronal death in epileptogenic zones. Reduced IL-10 reflects deepened immune imbalance and weakened antiepileptic immune defense, since IL-10 normally suppresses the activity of IL-1 $\beta$  and TNF- $\alpha$ .

#### **Conclusion.**

1. Epileptic encephalopathies in children aged 0–3 years predominantly manifest as severe clinical forms, most commonly West syndrome (57.1%). The disease is more frequent in boys (male-to-female ratio 1.7:1) and is characterized by profound psychomotor developmental delay, epileptic spasms, and refractory seizures. Paraclinical examinations revealed hypsarrhythmia, burst-suppression patterns, brain atrophy, and ventriculomegaly.

2. Immunological investigations showed that children with EE had significantly elevated pro-inflammatory cytokines (IL-1 $\beta$ , IL-6, TNF- $\alpha$ ), while IL-10 levels were reduced. This confirms the presence of active neuroinflammatory processes in the central nervous system and weakened anticonvulsive immune protection. IL-1 $\beta$  and TNF- $\alpha$  correlated positively with seizure severity, whereas IL-10 correlated negatively ( $r=+0.51$  and  $r=-0.60$ ).

3. Integration of clinical, EEG, MRI, and immunological data can serve as an effective approach for early diagnosis of EE, detection of refractory forms, prognosis, and the development of personalized therapy. Cytokine profiling, in particular, may be applied in clinical practice as a diagnostic and prognostic biomarker.

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