

Journal homepage <https://jsmc.univsul.edu.iq>

Journal of Sulaimani Medical College

ISSN:2223-148X



Original Article

Lumbar Puncture Findings in Cases of Neonatal Seizures in Sulaimani/Kurdistan Region/Iraq

Shwan Kanaan Muhammed Gharib¹, Ibrahim Khasraw Ghafoor¹¹Branch of Clinical Sciences, College of Medicine, University of Sulaimani, Kurdistan Region of Iraq.

Article Info.

Article History

Received:15.4.2026

Revised:19.5.2026

Accepted:15.6.2026

Published online:

21.6.2026

Keywords:

Bacterial;
Cerebrospinal Fluid;
Infant,
Newborn;
Lumbar Puncture;
Meningitis

Abstract

Background and Objectives: Neonatal seizures require prompt evaluation, and lumbar puncture (LP) is important for identifying infectious and noninfectious causes. This study assessed cerebrospinal fluid (CSF) findings in neonates with seizures in Sulaimani, Kurdistan Region, Iraq.

Methods: A retrospective study was conducted at Dr. Jamal A. Rashid Pediatric Teaching Hospital from January 1, 2022, to January 1, 2024. Medical records of 47 neonates aged 0–28 days with documented seizures who underwent Lumbar puncture were reviewed. Demographic, clinical, etiological, microbiological, treatment, and outcome data were extracted.

Results: Of 47 neonates, 29 (61.7%) were male, and 41 (87.2%) were term. Mean gestational age was 37.45 ± 2.38 weeks, mean birth weight was 3290.43 ± 564.02 g, and mean age at seizure onset was 107.09 ± 164.77 hours. The most common etiologies were hypoxic-ischemic encephalopathy (17, 36.2%), sepsis (11, 23.4%), hypocalcemia (10, 21.3%), and pyogenic meningitis (5, 10.6%). CSF appearance and predominant cell type were strongly associated with etiology (both $p=0.001$). Pyogenic meningitis had the highest CSF WBC (135.00 ± 11.18 cells/ μ L) and protein (313.00 ± 12.04 mg/dL), and the lowest glucose (15.20 ± 2.39 mg/dL) (all $p < 0.001$). Fever (aOR=4.2, 95% CI: 1.3–13.8), infectious etiology (aOR=8.5, 95% CI: 2.4–30.1), and subtle seizures (aOR=3.1, 95% CI: 1.1–8.9) predicted pleocytosis.

Conclusion: Lumbar puncture provided important diagnostic discrimination in neonatal seizures, particularly for bacterial meningitis, which showed neutrophilic pleocytosis, high protein, and low glucose. CSF analysis should remain an essential component of neonatal seizure evaluation.

DOI:

10.17656/jsmc.10523

Corresponding author:

Shwan Kanaan Muhammed Gharib (Shwan.Muhammed@univsul.edu.iq)

1. Introduction

Seizures are one of the most common clinical manifestations of neurological diseases in neonates, occurring in 1–5 per 1000 live births (1), and this age group has the highest incidence of seizures compared to other periods of life (Samanta, 2021). A seizure is a transient occurrence of signs and symptoms caused by abnormal, excessive, or simultaneous activity of neurons in the brain (2). Most seizures in neonates

are acute, symptomatic seizures that are associated with recent brain injury or brain dysfunction and require specific treatments (3).

Seizures in neonates can be divided into 2 categories based on clinical manifestations: motor (e.g., automatism, myoclonic, clonic, epileptic spasms), non-motor (automatic or behavioral arrest), or sequential seizures (4). Types of seizures range from simple febrile seizures (SFS), which are benign and self-limiting, to generalized seizures,

which cause brain damage or death (Zafari et al., 2019). The etiology of neonatal seizures can be attributed to an acute event (including intracranial hemorrhage, stroke, hypoxic-ischemic encephalopathy (HIE), infection, or electrolyte disturbances) or symptomatic conditions (metabolic, genetic, or structural abnormalities) (5). The most common causes of seizures were HIE (38%), ischemic stroke (18%), and intracranial hemorrhage (11%) (6). In a study in Iraq, perinatal asphyxia, infection, and metabolic abnormalities were the most common causes of neonatal seizures (7).

Seizures are the most common neurological emergency in neonates. Unlike seizures in infancy and childhood, most seizures in neonates occur due to an acute cause and may only be seen on electroencephalography (EEG) (4). Diagnosis of seizures in infants is difficult because the clinical manifestations of seizures are not very noticeable and reliable diagnosis is difficult. Seizures in infants are usually diagnosed only by EEG and there are no reliable clinical manifestations. Therefore, continuous EEG monitoring plays a significant role in the identification and management of neonatal seizures (3).

Lumbar puncture (LP) is an invasive procedure performed to evaluate cerebrospinal fluid (CSF) in children with life-threatening neurological disorders (8). Clinical guidelines for the neurodiagnostic evaluation of children with SFS recommend routine LP to screen for underlying bacterial meningitis in children <1 year of age (9). However, LP is probably performed less frequently than recommended. Clinicians may be reluctant to perform an LP due to concerns about side effects, technical difficulties, and invasiveness. The likelihood of performing LP decreases with decreasing birth weight (10, 11). Even in infants with confirmed sepsis, only about 80% of full-term infants and about 40% of preterm infants underwent the LP procedure (11).

Regulation of proper ion concentration homeostasis plays a critical role in central nervous system (CNS) function, and electrolyte disturbances such as hypocalcemia and hypomagnesemia have been implicated as causes of neonatal seizures (12).

Delayed diagnosis and lack of specialized evaluation of neonatal seizures may lead to adverse consequences in their development (13). Neonatal

seizures lead to short-term and long-term developmental disabilities. More than half of these infants will develop significant developmental disabilities such as cerebral palsy, post-neonatal epilepsy, and/or intellectual disability, requiring costly and lifelong treatment and social and educational support (6). Early identification and treatment of the disorder is crucial in the management of neonatal seizures, as it prevents detrimental consequences on the development of the nervous system, especially when seizures are accompanied by severe clinical phenotypes (14).

Current literature rarely stratifies CSF results by seizure type, timing, or the presence of systemic infection, factors that can be crucial in guiding clinical decisions. On the other hand, the limited use of LP as a routine diagnostic tool in neonatal seizures is due to concerns about its invasiveness. This cautious approach may result in the underdiagnoses of mild or early CNS infections in neonates. Therefore, a study focusing on LP findings in neonates with seizures in the Sulaymaniyah region would not only fill the local data gap but also contribute to a broader understanding of CSF diagnostic patterns and their clinical significance. Such data could inform protocols for early identification of infectious or inflammatory causes and potentially reduce complications associated with delayed treatment. This study aimed to assess LP findings in cases of neonatal seizures in Sulaimani/Kurdistan Region/Iraq.

2. Methods and Materials

2.1 Study design

A retrospective observational study was carried out to analyze medical records of neonates admitted to the hospital between January 1, 2022, and January 1, 2024. The focus was to investigate associations between LP findings and clinical outcomes in neonates with and without seizures.

2.2 Study setting

This study was conducted in the Neonatal Department of Dr. Jamal A. Rashid Pediatric Teaching Hospital in Sulaimani City, Kurdistan Region, Iraq. This hospital serves as a tertiary referral center for high-risk neonates, providing comprehensive diagnostic and therapeutic services.

2.3 Study population

The study population consisted of neonates aged 0

to 28 days who were admitted during the study period with documented seizure activity and who underwent LP as part of their diagnostic work-up. Only cases with sufficiently complete medical documentation were considered eligible for analysis. Neonates were included if the medical records contained clear documentation of seizure manifestations, demographic and clinical information, etiological diagnosis, and complete CSF results. Cases were excluded when records were incomplete or missing essential information, particularly seizure-related data or LP findings, or when transferred patients had inaccessible documentation from the referring facility. Neonates in whom LP was not performed were not eligible for inclusion. Based on these criteria, 47 neonates were included in the final analysis.

2.4 Data collection

The data were retrospectively gathered from both paper and electronic medical databases via a previously designed standardized data extraction tool. Neonatal demographic and perinatal information included sex, gestational age (GA), GA category, birth weight, and method of delivery; and maternal factors included the presence or absence of complications (e.g., birth asphyxia, maternal diabetes, maternal fever, and premature rupture of membranes) at the time of delivery. Information regarding seizures was recorded in detail. Clinical manifestations at the time of seizure onset included age (in hours), seizure type, frequency of seizures per day, and length of seizures. Presenting clinical manifestations included fever, lethargy, difficulty feeding, along with other symptoms such as jaundice, pallor, cyanosis, difficulty breathing (dyspnea), vomitus, skin rash, and irritability. Furthermore, we reviewed the diagnosis of seizures made during admission according to the cause(s) of seizure. We will classify patients by the following diagnoses made during admission: HIE, sepsis, hypocalcemia, pyogenic meningitis, IVH, and kernicterus. Finally, we also documented any family-related variables (such as parent-child relationships) that were noted in the medical record.

LP was the source of CSF data of interest for this study. Variables of interest included gross appearance of CSF (clear, xanthochromic, bloody, and cloudy), predominant CSF cellular pattern (lymphocytic vs neutrophilic vs mixed), and

quantitative parameters (WBC count; protein and glucose concentrations). Microbiological findings were also reviewed, including Gram stain and CSF culture results. The pleocytosis definition used in this study for inferential analysis was a WBC count >20 cells/ μ L. The definition for infectious etiology used in this study was the diagnosis of sepsis or pyogenic meningitis.

Short-term outcome and treatment data were obtained from the same source. Treatments included phenobarbital (PB) monotherapy, PB plus phenytoin (PHT) combination therapy, and antibiotic combination therapy when documented. Hospital outcomes were either dead or alive at discharge.

2.5 Ethical consideration

Ethical approval was obtained from the Institutional Review Board (IRB) of the College of Medicine, University of Sulaimani (No:12; Date:26/1/2025)The study adhered to the principles of the Declaration of Helsinki for medical research involving human subjects.

2.6 Statistical analysis

Data were analyzed using IBM SPSS Statistics version 28.0. Categorical variables were expressed as counts and percentages, while continuous variables were expressed as mean \pm standard deviation. Categorical variables were tested for association using either the chi-square test or Fisher's exact test, as appropriate. Differences in the quantitative CSF parameters by aetiologic group were assessed by one-way analysis of variance (ANOVA). A multivariate logistic regression was performed to determine the predictors of CSF pleocytosis with an adjusted odds ratio (OR) and 95% confidence intervals. In addition, the diagnostic accuracy of selected CSF parameters for bacterial meningitis was determined through the computation of sensitivity, specificity, positive predictive value, and negative predictive value. A p-value of <0.05 was used to determine statistical significance.

3. Results

Among the 47 neonates included in the analysis, males comprised the majority of the study population, accounting for 29 (61.7%) cases, whereas females represented 18 (38.3%) cases.

With respect to GA categorization, term neonates constituted the predominant group with 41 (87.2%) cases, followed by preterm neonates with 4 (8.5%) cases and postdate neonates with 2 (4.3%) cases.

The mean GA across the cohort was 37.45 ± 2.376 weeks. The mean age at seizure onset was recorded as 107.09 ± 164.773 hours, and the mean birth weight was 3290.43 ± 564.015 grams (Table 1).

Table 1. Demographic Characteristics of Neonates with Seizures (n=47).

Variable	Category	No.	%	Statistical Measure
Sex	Male	29	61.7%	Frequency (%)
	Female	18	38.3%	Frequency (%)
GA Category	Term	41	87.2%	Frequency (%)
	Preterm	4	8.5%	Frequency (%)
	Postdate	2	4.3%	Frequency (%)
GA (weeks)	-	-	-	$37.45 \pm 2.376^*$
Age at Seizure Onset (hours)	-	-	-	$107.09 \pm 164.773^*$
Birth Weight (grams)	-	-	-	$3290.43 \pm 564.015^*$
Mode of Delivery	Vaginal	24	51.1%	Frequency (%)
	Cesarean Section	23	48.9%	Frequency (%)

*Mean \pm Standard Deviation

Perinatal complications were absent in 20 (42.6%) neonates. Asphyxia was identified as the most frequently reported complication, present in 19 (40.4%) cases. Regarding seizure classification, tonic seizures were the most prevalent type, observed in 19 (40.4%) cases, followed by subtle seizures in 12 (25.5%) cases, focal clonic seizures in 9 (19.1%) cases, and multifocal clonic seizures

in 7 (14.9%) cases. Seizure frequency was categorized as ≥ 5 episodes per day in 33 (70.2%) neonates and < 5 episodes per day in 14 (29.8%) neonates. The mean seizure duration was 7.83 ± 4.104 minutes. When categorized by duration, 37 (78.7%) cases exhibited seizures lasting < 10 minutes, whereas 10 (21.3%) cases demonstrated durations ≥ 10 minutes (Table 2).

Table 2. Perinatal Complications and Seizure Characteristics (n=47).

Variable	Category	No.	%	Statistical Measure
Perinatal Complications	None	20	42.6%	Frequency (%)
	Asphyxia	19	40.4%	Frequency (%)
	Maternal Diabetes	5	10.6%	Frequency (%)
	Maternal Fever	1	2.1%	Frequency (%)
	Premature Rupture of Membranes	2	4.3%	Frequency (%)
Seizure Type	Tonic	19	40.4%	Frequency (%)
	Subtle	12	25.5%	Frequency (%)
	Focal Clonic	9	19.1%	Frequency (%)
	Multifocal Clonic	7	14.9%	Frequency (%)
Seizure Frequency (per day)	< 5 episodes	14	29.8%	Frequency (%)
	≥ 5 episodes	33	70.2%	Frequency (%)
Duration Category	< 10 minutes	37	78.7%	Frequency (%)
	≥ 10 minutes	10	21.3%	Frequency (%)
Seizure Duration (minutes)	-	-	-	$7.83 \pm 4.104^*$

*Mean \pm Standard Deviation

Fever was present in 18 (38.3%) neonates and absent in 29 (61.7%) cases. Lethargy was observed

in 36 (76.6%) cases and absent in 11 (23.4%) cases. Poor feeding was reported in 27 (57.4%) cases and

absent in 20 (42.6%) cases. With respect to additional clinical symptoms, 30 (63.8%) neonates presented without any supplementary manifestations. Among those with additional symptoms, jaundice was noted in 3 (6.4%) cases, pallor in 2 (4.3%) cases, cyanosis in 2 (4.3%) cases, dyspnea in 2 (4.3%) cases, vomiting in 1 (2.1%) case, skin rash in 1 (2.1%) case, and irritability in 1

(2.1%) case. Etiological analysis revealed HIE as the leading cause, identified in 17 (36.2%) cases, followed by sepsis in 11 (23.4%) cases, hypocalcemia in 10 (21.3%) cases, pyogenic meningitis in 5 (10.6%) cases, kernicterus in 3 (6.4%) cases, and IVH in 1 case (2.1%). Parental consanguinity was reported in 16 families (34.0%) and absent in 31 families (66.0%) (Table 3).

Table 3. Associated Clinical Symptoms and Etiological Factors (n=47).

Variable	Category	No.	%
Fever	Yes	18	38.3%
	No	29	61.7%
Lethargy	Yes	36	76.6%
	No	11	23.4%
Poor Feeding	Yes	27	57.4%
	No	20	42.6%
Other Symptoms	None	30	63.8%
	Pallor	2	4.3%
	Vomiting	1	2.1%
	Jaundice	3	6.4%
	Skin Rash	1	2.1%
	Irritability	1	2.1%
	Cyanosis	2	4.3%
	Dyspnea	2	4.3%
Etiology	HIE	17	36.2%
	Sepsis	11	23.4%
	Hypocalcemia	10	21.3%
	Pyogenic Meningitis	5	10.6%
	IVH	1	2.1%
	Kernicterus	3	6.4%
Consanguinity	Yes	16	34.0%
	No	31	66.0%

The CSF appearance varied significantly according to etiological diagnosis ($P \leq 0.001$). Clear CSF was most frequently observed in cases of sepsis 10 (90.9%) of 11 and hypocalcemia 7 (70.0%) of 10. Xanthochromic CSF was documented in cases of

HIE 4 (23.5%) of and hypocalcemia 3 (30%) of 10. Bloody CSF occurred exclusively in cases of HIE 3 (17.6%) of 17. Cloudy CSF was present in all cases of pyogenic meningitis 4 (80%) of 5 and kernicterus 3 (100%) of 3 (Table 4).

Table 4. Association Between CSF Appearance and Etiology.

Etiology	Clear	Xanthochromic	Bloody	Cloudy	Total	p-value
HIE	10 (58.8%)	4 (23.5%)	3 (17.6%)	0	17 (100%)	0.001
Sepsis	10 (90.9%)	1 (9.1%)	0	0	11 (100%)	
Hypocalcemia	7 (70.0%)	3 (30.0%)	0	0	10 (100%)	
Pyogenic Meningitis	1 (20.0%)	0	0	4 (80.0%)	5 (100%)	

Kernicterus	0	0	0	3 (100.0%)	3 (100%)	
-------------	---	---	---	---------------	----------	--

*Fisher’s Exact

A highly significant association was observed between predominant CSF cell type and etiological diagnosis ($P \leq 0.001$). Lymphocyte predominance was universal in cases of hypocalcemia 10 (100%) of 10, kernicterus 3 (100%) of 3, and HIE 16

(94.1%) of 17. Neutrophil predominance was exclusive to infectious etiologies: sepsis, 11 (100%) of 11, and pyogenic meningitis, 5 (100%) of 5 (Table 5).

Table 5. Association Between Predominant CSF Cell Type and Etiology.

Etiology	Lymphocytes	Neutrophils	Mixed Pattern	Total	p-value
HIE	16 (94.1%)	0	1 (5.9%)	17 (100%)	0.001
Sepsis	0	11 (100.0%)	0	11 (100%)	
Hypocalcemia	10 (100.0%)	0	0	10 (100%)	
Pyogenic Meningitis	0	5 (100.0%)	0	5 (100%)	
Kernicterus	3 (100.0%)	0	0	3 (100%)	

*Fisher's Exact

Statistically significant differences were observed across etiological groups for all quantitative CSF parameters ($P \leq 0.001$ for each). Pyogenic meningitis demonstrated the highest mean CSF WBC count (135.00 ± 11.18 cells/ μ L), highest mean protein concentration (313.00 ± 12.04 mg/dL), and lowest mean glucose concentration (15.20 ± 2.39 mg/dL). Sepsis exhibited intermediate elevations in WBC count ($25.45 \pm$

3.05 cells/ μ L) and protein concentration (193.18 ± 9.82 mg/dL) with reduced glucose levels (23.73 ± 5.01 mg/dL). HIE, hypocalcemia, and kernicterus exhibited relatively normal CSF profiles, with WBC counts approximating 7 cells/ μ L, protein concentrations ranging from 10.70 to 103.33 mg/dL, and glucose concentrations ranging from 48.70 to 54.94 mg/dL (Table 6).

Table 6. Comparison of Quantitative CSF Parameters Across Etiological Groups.

Etiology	CSF WBC (cells/ μ L) Mean \pm SD	CSF Protein (mg/dL) Mean \pm SD	CSF Glucose (mg/dL) Mean \pm SD
HIE	6.71 ± 4.40	96.24 ± 12.68	54.94 ± 3.86
Sepsis	25.45 ± 3.05	193.18 ± 9.82	23.73 ± 5.01
Hypocalcemia	6.90 ± 1.66	10.70 ± 10.83	48.70 ± 2.67
Pyogenic Meningitis	135.00 ± 11.18	313.00 ± 12.04	15.20 ± 2.39
Kernicterus	7.00 ± 1.73	103.33 ± 2.89	50.67 ± 1.16
p-value	<0.001	<0.001	<0.001

*ANOVA test

Positive Gram stain and culture results were exclusive to the pyogenic meningitis group ($P \leq 0.001$ for both). Among the 5 cases of pyogenic meningitis, Gram stain was positive in 4 (80.0%)

cases and culture was positive in all 5 (100.0%) cases. No microbiological positivity was observed in the HIE, sepsis, hypocalcemia, or kernicterus groups (Table 7).

Table 7. Association Between CSF Microbiological Results and Etiology

Etiology	Gram Stain Positive	Culture Positive	Total
HIE	0	0	17
Sepsis	0	0	11

Hypocalcemia	0	0	10
Pyogenic Meningitis	4 (80.0%)	5 (100.0%)	5
Kernicterus	0	0	3
p-value	<0.001	<0.001	

*Fisher's Exact

Treatment modality varied significantly according to seizure type ($P \leq 0.001$). PB monotherapy was most frequently administered in cases of tonic seizures 15 (53.6%) of 28. PB plus PHT was predominantly utilized in focal clonic and

multifocal clonic seizures 4 (40%) of 10 cases each. Antibiotic combination therapy was distributed across seizure types without a single predominant pattern (Table 8).

Table 8. Association Between Seizure Type and Treatment Response.

Treatment	Tonic (n=19)	Subtle (n=12)	Focal Clonic (n=9)	Multifocal Clonic (n=7)	Total	p-value
PB	15 (53.6%)	9 (32.1%)	4 (14.3%)	0	28 (100%)	<0.001
PB + PHT	0	2 (20.0%)	4 (40.0%)	4 (40.0%)	10 (100%)	
Antibiotics Combination	2 (40.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)	5 (100%)	

*Fisher's Exact

Survival outcome differed significantly according to etiological diagnosis ($P \leq 0.021$). All neonates with HIE, sepsis, hypocalcemia, pyogenic meningitis, and kernicterus survived (100.0% for

each group). The single mortality occurred in the intraventricular hemorrhage group 1 (100%) of 1 (Table 9).

Table 9. Association Between Survival Outcome and Etiology.

Etiology	Survived	Died	Total	p-value
HIE	17 (100.0%)	0	17 (100%)	0.021
Sepsis	11 (100.0%)	0	11 (100%)	
Hypocalcemia	10 (100.0%)	0	10 (100%)	
Pyogenic Meningitis	5 (100.0%)	0	5 (100%)	
IVH	0	1 (100.0%)	1 (100%)	
Kernicterus	3 (100.0%)	0	3 (100%)	

*Fisher's Exact

In multivariate logistic regression analysis, presence of fever (adjusted OR=4.2; 95% CI: 1.3–13.8; $P \leq 0.018$), infectious etiology (sepsis or pyogenic meningitis; adjusted OR=8.5; 95% CI: 2.4–30.1; $P \leq 0.001$), and subtle seizure type

(adjusted OR=3.1; 95% CI: 1.1–8.9; $P \leq 0.038$) were identified as significant predictors of CSF pleocytosis. Lethargy did not reach statistical significance (adjusted OR=2.8; 95% CI: 0.7–11.2; $p=0.147$) (Table 10).

Table 10. Predictors of Abnormal CSF (Pleocytosis >20 cells/ μ L).

Predictor	Adjusted (OR)	95% Confidence Interval	p-value
Fever (Present)	4.2	1.3 - 13.8	0.018
Lethargy (Present)	2.8	0.7 - 11.2	0.147
Infectious Etiology†	8.5	2.4 - 30.1	0.001
Subtle Seizure Type	3.1	1.1 - 8.9	0.038

†Infectious Etiology = Sepsis or Pyogenic Meningitis

Using a cut-off value of >100 cells/ μ L, CSF WBC count demonstrated 80.0% sensitivity (4/5), 100.0% specificity (42/42), 100.0% positive predictive value, and 97.7% negative predictive value for bacterial meningitis. CSF protein concentration >200 mg/dL demonstrated 100.0% sensitivity (5/5), 95.2% specificity (40/42), 71.4%

positive predictive value, and 100.0% negative predictive value. CSF glucose concentration <30 mg/dL yielded 80.0% sensitivity (4/5), 92.9% specificity (39/42), 57.1% positive predictive value, and 97.5% negative predictive value (Table 11).

Table 11. Diagnostic Accuracy of CSF Parameters for Bacterial Meningitis (n=5 cases).

CSF Parameter	Cut-off Value	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
CSF WBC	>100 cells/ μ L	80% (4/5)	100% (42/42)	100%	97.7%
CSF Protein	>200 mg/dL	100% (5/5)	95.2% (40/42)	71.4%	100%
CSF Glucose	<30 mg/dL	80% (4/5)	92.9% (39/42)	57.1%	97.5%

4. Discussion

Neonatal seizures are among the most critical challenges in neonatal medicine because they often represent the earliest clinical manifestation of serious cerebral dysfunction (15). The present study was conducted to identify and characterize biochemical and cellular alterations in the CSF of neonates with seizures in Sulaimani and to clarify the role of these indicators in etiologic diagnosis, therapeutic management, and prediction of neurologic outcomes. The research results indicated that in the population of study subjects, hypoxic ischemic encephalopathy (HIE) and sepsis were the leading causes of seizure activity in newborn infants. A statistically significant association was also found between sex and the clinical seizure type with tonic seizures occurring principally among male infants, while subtle seizures were more prevalent among female infants. The results of logistic regression analysis demonstrated that fever (OR=4.2) and infectious etiologies (OR=8.5) were both independent predictors of pleocytosis; elevated white blood cell counts within CSF. Additionally, pyogenic meningitis produced distinct acute biochemical changes, i.e. elevated protein and decreased glucose levels and were associated with positive CSF cultures leading to persistent neurologic sequelae including cerebral palsy, hydrocephalus, and auditory neuropathy.

Assessment of demographic characteristics in the

study population revealed meaningful patterns that are consistent with regional and international data. Of the 47 neonates, 29, or 61.7%, were male and 18, or 38.3%, were female. The predominance of male neonates, which has also been reported in many other studies, including the work of Al-Momen et al. in Baghdad (7), and studies from Iran (16), and Italy (17), may reflect an underlying biologic susceptibility that renders male neonates more vulnerable to perinatal brain injury (18). Analysis of delivery related variables showed that, in the present study, vaginal delivery and cesarean section were distributed nearly equally. This finding differs from reports suggesting that difficult vaginal delivery is the principal contributor to neonatal seizures because of the higher risk of asphyxia (19, 20). Nevertheless, the presence of perinatal complications among the cases, particularly asphyxia, underscores the urgent need to improve intrapartum care in the region (21).

Identifying the underlying cause of seizures is the most important step in neonatal clinical management (22). In the present study, HIE was the leading cause of seizures (23, 24). This finding is fully consistent with both global and regional patterns, as HIE remains the most common cause of seizures in term neonates and typically presents within the first 12 to 24 hours of life (25).

While an LP is not used solely in neonatal seizures to rule out meningitis, it can also provide information about brain chemistry (26, 27). In the

present study, the gross appearance of the CSF was valuable for providing initial diagnostic information. Most of the samples of CSF were clear; turbid CSF was seen in all cases where meningitis was due to pyogenic infection; bloody CSF was only found in the case of HIE. These findings suggest a high level of correlation between the initial characteristics of the CSF and the final diagnosis. They also demonstrated considerable variation in the quantitative CSF parameters according to the underlying etiology.

The analyses showed a significant relationship between seizure type and underlying etiology, although this relationship was less direct with specific CSF parameters. Tonic seizures were more common in male neonates, whereas subtle seizures were more frequent in female neonates. Although the precise mechanism underlying this sex difference remains unclear, it may reflect differences in neurologic maturation or neuronal receptor sensitivity between the two sexes (28). On the other hand, fever showed a significant relationship with subtle seizures. This observation is clinically important because subtle seizures are often difficult to recognize and may present with nonspecific manifestations such as respiratory changes or oral movements. The coexistence of fever and subtle seizures should raise suspicion for an infectious etiology (29).

In multivariable analysis, fever, infectious etiology, and subtle seizure type were identified as independent predictors of CSF pleocytosis. This predictive model may be useful in clinical settings where immediate laboratory access is limited and may support decision-making regarding LP (30). In other words, a neonate presenting with fever and subtle seizures has a high probability of abnormal CSF findings, and LP should not be postponed in such cases (31).

The current study found that easily created diagnostic models could potentially differentiate bacterial meningitis and other causes of meningitis. Specifically, when analyzing the number of white blood cells (total) in the CSF; if the total white blood cell count is greater than 100, there is 100% specificity this means that the diagnosis of bacterial meningitis is very likely; however, if protein level is greater than 200 mg then there is 100% sensitivity and this means that all other types of meningitis in this study had protein levels greater than 200 mg/dL of CSF (32).

Combining these two criteria may provide the basis for a rapid diagnostic algorithm. In addition, although turbid CSF had low sensitivity, when present it may be associated with meningitis or kernicterus (26). These findings support established international recommendations while offering more precise values for the local population. The development of such predictive models may help clinicians identify high risk neonates at an earlier stage and initiate early intervention promptly. These models appear to perform more accurately than the Bacterial Meningitis Score, which has shown limited utility in neonates younger than 28 days (33).

In the present study, PB remained the first line treatment for neonatal seizures. This approach is consistent with recommendations from the World Health Organization and academic guidelines in developing countries (34, 35). However, analysis of treatment response indicated that more severe presentations, such as multifocal clonic seizures, often required second line therapy, including PHT. The survival rate in the Sulaimani study was 97.9%, indicating relative success in the acute management of neonatal seizures. Compared with the 32% mortality rate reported in Baghdad, this outcome appears considerably more favorable (7). The only death recorded in the present study was attributable to IVH, a condition traditionally associated with the poorest prognosis in neonates (36).

Nevertheless, the presence of neurologic complications among survivors, including cerebral palsy, hydrocephalus, and hearing loss, should be regarded as a serious warning regarding the future quality of life of these children. The analyses showed that neonates who developed neurologic complications had significantly higher CSF WBC counts and higher CSF protein levels at admission. Positive CSF culture results were also more common in the group with complications. These findings show remarkable agreement with the study by Tan et al. in Nepal, which identified a protein concentration above 1880 mg/L, equivalent to 188 mg/dL, as a predictor of poor outcome (37).

Limitations

Several limitations should be considered when interpreting the findings of this study. First, the sample size was relatively small, which may have reduced the statistical power to detect subtle differences across subgroups. Second, the study

was conducted at a single center in Sulaimani Hospital, which may limit the generalizability of the findings to other regions with different epidemiologic characteristics. Third, long term follow up was not performed to allow a more precise assessment of neurodevelopmental complications beyond the neonatal period. Fourth, the lack of access to more advanced techniques, such as viral PCR testing of CSF, may have resulted in some viral causes of meningitis or encephalitis remaining undetected and being classified within other diagnostic categories.

Conclusions

The present study demonstrated that CSF abnormalities are common in neonates with seizures and vary according to the underlying etiology. Bacterial meningitis was distinguished from noninfectious causes by a characteristic pattern of neutrophilic pleocytosis, elevated protein, and reduced glucose, thereby reinforcing the importance of LP in the initial evaluation. In addition to their diagnostic value, CSF findings also carried prognostic significance and were associated with the risk of neurologic complications such as cerebral palsy. Furthermore, clinical prediction models based on fever and seizure type, together with locally derived cut-off values of WBC greater than 100 and protein greater than 200, may improve the diagnostic accuracy of bacterial meningitis and help prevent inappropriate therapeutic interventions.

Funding: No funding received for the implementation of this study

Acknowledgment: The authors are sincerely thankful to all those who have committed their time and effort to helping produce a successful study.

Authors' contributions: Each author made an equal contribution to this research work.

Conflict of interest: All authors declare no conflict of interest.

References:

1. Pellegrin S, Munoz FM, Padula M, Heath PT, Meller L, Top K, et al. Neonatal seizures: case definition & guidelines for data collection, analysis, and presentation of immunization safety data. *Vaccine*. 2019;37(52):7596-609. <https://doi.org/10.1016/j.vaccine.2019.05.031>
2. Fisher RS, Cross JH, D'souza C, French JA, Haut SR, Higurashi N, et al. Instruction manual for the ILAE 2017 operational classification of seizure types. *Epilepsia*. 2017;58(4):531-42. <https://doi.org/10.1111/epi.13671>
3. Abend NS, Wusthoff CJ, Jensen FE, Inder TE, Volpe JJ. Chapter 15 - Neonatal Seizures. In: Volpe JJ, editor. *Volpe's Neurology of the Newborn* (Seventh Edition). St. Louis (MO): Elsevier; 2025. p. 381-448.e17. <https://doi.org/10.1016/B978-0-443-10513-5.00015-2>
4. Pressler RM, Cilio MR, Mizrahi EM, Moshé SL, Nunes ML, Plouin P, et al. The ILAE classification of seizures and the epilepsies: Modification for seizures in the neonate. Position paper by the ILAE Task Force on Neonatal Seizures. *Epilepsia*. 2021;62(3):615-28. <https://doi.org/10.1111/epi.16815>
5. Okumura A. Electroencephalography in neonatal epilepsies. *Pediatrics International*. 2020;62(9):1019-28. <https://doi.org/10.1111/ped.14227>
6. Glass HC, Shellhaas RA, Wusthoff CJ, Chang T, Abend NS, Chu CJ, et al. Contemporary profile of seizures in neonates: a prospective cohort study. *The Journal of pediatrics*. 2016;174:98-103. e1. <https://doi.org/10.1016/j.jpeds.2016.03.035>
7. Al-Momen H, Muhammed MK, Alshaheen AA. Neonatal seizures in Iraq: Cause and outcome. *The Tohoku Journal of Experimental Medicine*. 2018;246(4):245-49. <https://doi.org/10.1620/tjem.246.245>
8. Neal JT, Kaplan SL, Woodford AL, Desai K, Zorc JJ, Chen AE. The Effect of Bedside Ultrasonographic Skin Marking on Infant Lumbar Puncture Success: A Randomized Controlled Trial. *Annals of Emergency Medicine*. 2017;69(5):610-9.e1. <https://doi.org/10.1016/j.annemergmed.2016.09.014>
9. Kim YZ, Jung HW, Lee EH. Clinical Significance of Lumbar Puncture in Children with First Febrile Seizures. *Iranian Journal of Child Neurology*. 2024;18(4):23-32. <https://doi.org/10.22037/ijcn.v18i4.38524>
10. Berardi A, Baroni L, Bacchi Reggiani ML, Ambretti S, Biasucci G, Bolognesi S, et al. The burden of early-onset sepsis in Emilia-Romagna (Italy): a 4-year, population-based study. *The Journal of Maternal-Fetal & Neonatal Medicine*. 2016;29(19):3126-31. <https://doi.org/10.3109/14767058.2015.1114093>
11. Stoll BJ, Puopolo KM, Hansen NI, Sánchez PJ, Bell EF, Carlo WA, et al. Early-onset neonatal sepsis 2015 to 2017, the rise of *Escherichia coli*, and the need for novel prevention strategies. *JAMA pediatrics*. 2020;174(7):e200593-e. <https://doi.org/10.1001/jamapediatrics.2020.0593>

12. Newville JC, Oppong AY, Robinson S, Jantzie LL. Connecting chloride transporter impairment following perinatal brain injury to cerebral palsy. *Neuronal Chloride Transporters in Health and Disease*: Elsevier; 2020. p. 405-30. <https://doi.org/10.1016/B978-0-12-815318-5.00016-9>
13. Cornet MC, Morabito V, Lederer D, Glass HC, Ferrao Santos S, Numis AL, et al. Neonatal presentation of genetic epilepsies: early differentiation from acute provoked seizures. *Epilepsia*. 2021;62(8):1907-20. <https://doi.org/10.1111/epi.16957>
14. Spoto G, Saia MC, Amore G, Gitto E, Loddo G, Mainieri G, et al. Neonatal Seizures: An Overview of Genetic Causes and Treatment Options. *Brain Sciences*. 2021;11(10):1295. <https://doi.org/10.3390/brainsci11101295>
15. Pressler RM. Diagnosis and classification of neonatal seizures. English version. *Clinical Epileptology*. 2025;38(2):87-93. <https://doi.org/10.1007/s10309-025-00803-y>
16. Nemati H, Karimzadeh P, Fallahi M. Causes and Factors Associated with Neonatal Seizure and its Short-term Outcome: A Retrospective Prognostic Cohort Study. *Iran J Child Neurol*. 2018;12(3):59-68.
17. Pisani F, Spagnoli C, Falsaperla R, Nagarajan L, Ramantani G. Seizures in the neonate: A review of etiologies and outcomes. *Seizure*. 2021;85:48-56. <https://doi.org/10.1016/j.seizure.2020.12.023>
18. Kelly LA, Branagan A, Semova G, Molloy EJ. Sex differences in neonatal brain injury and inflammation. *Front Immunol*. 2023;14:1243364. <https://doi.org/10.3389/fimmu.2023.1243364>
19. Su Y-J, Liu W, Xing R-r, Yu Z-b, Peng Y-m, Luo W-x. Prevalence and risk factors associated with birth asphyxia among neonates delivered in China: a systematic review and meta-analysis. *BMC Pediatrics*. 2024;24(1):845. <https://doi.org/10.1186/s12887-024-05316-7>
20. Msisiri LS, Kibusi SM, Kimaro FD. Risk Factors for Birth Asphyxia in Hospital-Delivered Newborns in Dodoma, Tanzania: A Case-Control Study. *Sage Open Nursing*. 2024;10(1):1-11. <https://doi.org/10.1177/23779608241246874>
21. Wudu MA, Wondifraw EB, Getaneh FB, Hailu MK, Belete MA, Yosef ST, et al. Incidence and predictors of mortality among neonates admitted with birth asphyxia to neonatal intensive care units in Ethiopia: a systematic review and meta-analysis. *BMC Pediatrics*. 2025;25(1):140. <https://doi.org/10.1186/s12887-025-05481-3>
22. Spagnoli C, Pisani F. Acute symptomatic seizures in newborns: a narrative review. *Acta Epileptol*. 2024;6(1):5. <https://doi.org/10.1186/s42494-024-00151-w>
23. Chakkarapani E, de Vries LS, Ferriero DM, Gunn AJ. Neonatal encephalopathy and hypoxic-ischemic encephalopathy: the state of the art. *Pediatric Research*. 2025;98(7):2444-58. <https://doi.org/10.1038/s41390-025-03986-2>
24. Aziz KB, Kuiper J, Kilborn A, Kambli H, Jayakumar S, Gerner GJ, et al. Seizures May Worsen Outcomes of Neonatal Hypoxic-Ischemic Encephalopathy: A Longitudinal Serum Biomarkers Study. *Pediatric Neurology*. 2025;166:55-64. <https://doi.org/10.1016/j.pediatrneurol.2025.02.008>
25. Anwar T, Triplett RL, Ahmed A, Glass HC, Shellhaas RA. Treating Seizures and Improving Newborn Outcomes for Infants with Hypoxic-Ischemic Encephalopathy. *Clin Perinatol*. 2024;51(3):573-86. <https://doi.org/10.1016/j.clp.2024.04.013>
26. Tumani H, Petereit HF, Gerritzen A, Gross CC, Huss A, Isenmann S, et al. S1 guidelines “lumbar puncture and cerebrospinal fluid analysis” (abridged and translated version). *Neurological Research and Practice*. 2020;2(1):8. <https://doi.org/10.1186/s42466-020-0051-z>
27. Bedetti L, Miselli F, Minotti C, Latorre G, Loprieno S, Foglianese A, et al. Lumbar Puncture and Meningitis in Infants with Proven Early- or Late-Onset Sepsis: An Italian Prospective Multicenter Observational Study. *Microorganisms*. 2023;11(6):1546.
28. Goldfarb EV, Seo D, Sinha R. Sex differences in neural stress responses and correlation with subjective stress and stress regulation. *Neurobiology of Stress*. 2019;11:100177. <https://doi.org/10.1016/j.ynstr.2019.100177>
29. Laino D, Mencaroni E, Esposito S. Management of Pediatric Febrile Seizures. *Int J Environ Res Public Health*. 2018;15(10):1-11. <https://doi.org/10.3390/ijerph15102232>
30. Kimia A, Capraro A, Hummel D, Johnston P, Harper M. Utility of Lumbar Puncture for First Simple Febrile Seizure Among Children 6 to 18 Months of Age. *Pediatrics*. 2009;123:6-12. <https://doi.org/10.1542/peds.2007-3424>
31. Corsello A, Marangoni MB, Macchi M, Cozzi L, Agostoni C, Milani GP, et al. Febrile Seizures: A Systematic Review of Different Guidelines. *Pediatric Neurology*. 2024;155:141-8. <https://doi.org/10.1016/j.pediatrneurol.2024.03.024>
32. Mishra P, Nepal D, Wagley B, Sharma P. Cerebrospinal Fluid Protein as a Prognostic Marker in Neonatal Meningitis: A Prospective Study from Nepal 2026. <https://doi.org/10.21203/rs.3.rs-8611132/v1>
33. Wang Y, Lei X, Zhao Y, Tan J, Li J, Gong X, et al. An improved clinical prediction rule for identifying neonatal bacterial meningitis: a multicenter cohort

- study. *Transl Pediatr.* 2021;10(1):64-72. <https://doi.org/10.21037/tp-20-255>
34. Soul JS, Wang S, Sharpe C, Pilon B, Pressler RM, Allen MC, et al. Updated recommendations for the design of therapeutic trials for neonatal seizures. *Pediatric Research.* 2026;1(1):1-11. <https://doi.org/10.1038/s41390-025-04735-1>
35. El-Dib M, Soul J. The use of phenobarbital and other anti-seizure drugs in newborns. *Seminars in Fetal and Neonatal Medicine.* 2017;22(1):1. <https://doi.org/10.1016/j.siny.2017.07.008>
36. Kim HH, Kim JK, Park SY. Predicting severe intraventricular hemorrhage or early death using machine learning algorithms in VLBWI of the Korean Neonatal Network Database. *Scientific Reports.* 2024;14(1):11113. <https://doi.org/10.1038/s41598-024-62033-y>
37. Tan J, Kan J, Qiu G, Zhao D, Ren F, Luo Z, et al. Clinical Prognosis in Neonatal Bacterial Meningitis: The Role of Cerebrospinal Fluid Protein. *PLoS One.* 2015;10(10):e0141620. <https://doi.org/10.1371/journal.pone.0141620>