

## THE SENSITIVITY AND SPECIFICITY OF THE LDH LEVELS IN THE CEREBROSPINAL FLUID IN THE DIAGNOSIS OF BACTERIAL MENINGITIS IN CHILDREN

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### ABSTRACT

**Background:** Making a differential diagnosis between bacterial meningitis and aseptic meningitis is an important clinical problem. Standard routine analysis of CSF does not always provide rapid definitive information as for as causative agent is concerned. Therefore, there is a need for an additional test of CSF.

**Objective:** The study aims to determine the sensitivity and specificity of the LDH enzyme in CSF in the early diagnosis of bacterial meningitis. **Methods:** In a cross-sectional study design included 90 patients with a probability of meningitis aged between one day to 12 years. Complete blood cells (CBC), C-reactive protein (Crp) were measured. Lumbar puncture was done in all stable cases and CSF was collected in sterile bottles. Analysis of the sample done in Tishreen University Laboratory. CSF LDH was done.

**Results:** LDH levels were significantly high in bacterial meningitis and marginally raised in viral meningitis. The sensitivity of LDH enzyme in Cerebrospinal fluid in early diagnosis of bacterial meningitis was 97.22% and specificity was 86.20%. **Conclusion:** To conclude, LDH can be used alongside other routine tests to support the diagnosis of Meningitis and its differentiation from other types.

**KEYWORDS:** Meningitis, Lactate dehydrogenase, Cerebrospinalfluid.

### INTRODUCTION

Although the majority of meningitis in children is sterile and does not require specific treatment, about 5% of cases are bacterial and caused severe neurological sequelae especially when the diagnosis is delayed.<sup>[1]</sup> Distinguishing between aseptic and bacterial meningitis is difficult. Therefore, many recommendations of direct treatment with antibiotics in children with clinical evidence of acute meningitis until the results of cerebrospinal fluid (CSF) culture appear within (24-48) hours.<sup>[2]</sup>

These recommendations emphasize the use of antibiotics in children with sterile meningitis and the financial burdens.<sup>[3]</sup>

Clinical parameters, blood biomarkers (CRP, WBC), CSF test (protein, glucose levels, WBC and neutrophil count), Gram staining, and CSF bacterial antigen assay do not provide high sensitivity or specificity to distinguish between bacterial and sterile meningitis.<sup>[4]</sup> Therefore, the presence of new markers including LDH whose levels showed high sensitivity and accuracy to distinguish between bacterial and sterile infections.<sup>[5]</sup>

### MATERIAL AND METHODS

A cross-sectional analytic study included patients between 1day to 12 years with suspected meningitis who were admitted to the pediatric department at Tishreen University Hospital between September 2019 to August 2020.

On admission, detailed information was recorded including (age, sex, duration of illness, clinical symptoms) with a full clinical examination. Complete blood cells, C- reactive protein (Crp) were performed at the admission. A lumbar puncture of the CSF was conducted under sterile conditions and placed in three sterile dry tubes for a procedure (general count and formula for cells, titer of sugar and protein, titration LDH, and CSF culture).

Based on CSF examination (the gold standard) patients were divided into three groups (bacterial meningitis, sterile meningitis, and non- meningitis).

The patients were also divided into high LDH and normal values based on the LDH value higher than 70 units/l in infants and 40 units/l in younger children.<sup>[6]</sup>

All data were analyzed using the Statistical Package for Social Sciences (SPSS Version 20). Data were presented in simple measures of frequency, percentage, median, mean, standard deviation. Sensitivity (the percentage of people with a disease who have a positive test), specificity (the percentage of healthy people who have a negative test), positive predictive value (PPV) (the percentage of people with a positive test who have the disease) and negative predictive value (NPV) (the percentage of people with a negative test who do not have the disease) and the accuracy percentage were performed. Results were considered statistically significant with a p- value<5%.

This study was reviewed and approved by the ethical Committee of Tishreen University Hospital. Informed consent was obtained from the patient's parents.

**Table 2: Comparison of the CSF results between studied groups.**

Diagnose	CSF analyses				
	Cells (cell/mm3)	Neutrophils (%)	Lymphocyte (%)	Protein (mg/dl)	Glucose (mg/dl)
Group A	136.55±84.10	76.47±19.35	24.69±20.48	116.83±57.65	40.00±19.91
Group B	51.72±68.43	13.60±20.48	92.16±17.57	40.80±19.76	43.32±10.63
Group C	2.21±4.25	6±2	86.00±32.62	21.00±10.51	60.55±16.94
p-value	0.00001	0.00004	0.001	0.00006	0.0006

The frequency of high LDH in CSF was 51.1%. overall, 40 patients were from group A, 6 from group B and none of them from group C. The mean value of LDH in patients from group A was 19.22 ± 107.24 compared to 25.34 ± 46.12 in patients from group B, while the mean value was 16.17 ± 29.80 in patients from group C with a statistically significant difference between groups in

**Table 3: Sensitivity, specificity, PPV, NPV, and accuracy of LDH elevation in the diagnosis of aseptic and bacterial meningitis.**

Diagnose	Sensitivity	specificity	PPV	NPV	accuracy
Bacterial meningitis	97.2%	86.20%	89.7%	96.1%	92.30%
Aspect meningitis	24%	95%	85.7%	56%	55.6%

## RESULTS

The current study was carried out on 90 patients aged between 1day to 12 years with suspected meningitis who were admitted to the pediatric department at Tishreen University Hospital between September 2019 to August 2020. The median age of the study patients was 7 years. **Table 1** showed the characteristics of the study group.

The clinical symptoms of the study varied between, fever which was the most common 90 patients (100%), vomiting 45 patients (50%), consciousness 20 patients (22.2%), headache 48 patients (53.3%), and photophobia 10 patients (11.1%).

Depending on the gold standard (CSF analysis and the culture), the patients were divided into 3 groups (group A: bacterial meningitis 40[44.4%], group B: aspect meningitis 25[27.8%], group C: non- meningitis 25[27.8%])

**Table 1: The characteristics of the study group.**

Variables	Total neonates	P-value
<b>Gender</b>		
Male, n (%)	43(47.8)	0.6
Female, n (%)	47(52.2)	
<b>age</b>		
>5 year, n (%)	32 (36.7)	0.004
≤ 5 year, n (%)	58 (63.60)	

**Table 2** comprised the results of CSF in the 3 groups with a statistically significant differences in the CSF results.

terms of LDH values (p- value = 0.0001).

**Table 3** demonstrated the sensitivity, specificity, positive and negative predictive value, and accuracy of LDH elevation in the diagnosis of aseptic and bacterial meningitis.

## DISCUSSION AND CONCLUSION

The current study supports the importance of CSF LDH in differentiating between the types of meningitis. 51.1% of patients had high LDH with an increase in the value of LDH in bacterial meningitis patients. The sensitivity of the LDH in CSF was greater in diagnosing bacterial meningitis.

Meningitis is a serious disease with side effects that may lead to neurological sequelae. The Delayed diagnosis is associated with the use of antibiotics that confusing diagnosis (alter cell counts, protein, and sugar in CSF).<sup>[7]</sup>

Sinha M and Sharma M noted an elevated level of LDH in the CSF with purulent meningitis that is consistent with the result of our current study. It may be explained by blood-brain barrier disorder that enables plasma LDH to reach the CSF, and the production of LDH by inflammatory tissues, leukocytes, or exogenous bacterial sources.<sup>[8,9]</sup> Also Banik. A conducted in his study a significant elevation of CSF LDH in patients with purulent and tuberculous meningitis compared with viral meningitis, which is similar to our study which found a significant rise in purulent meningitis compared with aseptic meningitis.<sup>[10]</sup>

Sensitivity and specificity ratios varied in international studies, reaching the lowest in verkaria study in India in 2015 with a sensitivity of 52.5% and specificity of 87.5%, and the highest in Donald's study in 1986 with a sensitivity of 86.3% and specificity of 93.2% compared to our study with a sensitivity of 97% and specificity of 86%. This is explained by the different reference values, the gold standard used in the classification and diagnosis of meningitis. The study relied on the examination of CSF as a goldstandard for diagnosis, while most studies used PCR in addition to examining CSF in the diagnosis.<sup>[11,12,13]</sup>

The present study found that CSF LDH is elevated in all types of meningitis with a significant elevation in bacterial meningitis, making it a high-accuracy and specific choice in diagnosing bacterial meningitis in children. CSF LDH can be used in conjunction with other routine tests to support the diagnosis of meningitis and differentiate it from other types.

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