

# Diagnostic significance of lactate dehydrogenase activity in cerebrospinal fluid in childhood meningitis

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## Abstract

**Background:** Meningitis is one of the important causes of morbidity and mortality in children. For a better outcome, a precise and reliable diagnosis is essential at its early stage. There remains a significant group of patients in whom the initial diagnosis is often in doubt because of overlapping symptoms and signs even after routine CSF analysis. **Aims and Objectives:** 1) To study the role of routine CSF analysis in early diagnosis of meningitis. 2) To study the utility of CSF Lactate Dehydrogenase level to diagnose meningitis in children. 3) To evaluate the diagnostic significance of Lactate Dehydrogenase (LDH) activity in CSF in different types of meningitis. **Methods:** This study was a hospital based prospective study which included children aged between 1 month to 18 years with clinical suspicion of meningitis. Total of 103 cases were studied, according to criteria cases were divided into pyogenic meningitis (n=16), tubercular meningitis (n=4), viral meningitis (n=52), 31 cases of febrile seizures were taken as control. CSF LDH was estimated by continuous spectrophotometric method using A25 bio system auto analyser and correlated with different types of meningitis. **Results:** In our study, highest mean CSF cell count of 890.31 cells/mm<sup>3</sup> was observed in pyogenic meningitis cases followed by 116 cells/mm<sup>3</sup> in TB meningitis. Pyogenic meningitis cases had low CSF sugar with mean of 40.56 mg/dl. CSF Protein was highest in pyogenic meningitis with mean protein of 143.49 mg/dl. The highest titre of CSF LDH was observed in pyogenic meningitis with mean CSF LDH of 547.75 IU/L (p<0.0001) followed by 139 IU/L in TB meningitis (p<0.0001) and only marginal elevation in CSF LDH was noted in Viral meningitis (p<0.0001). CSF LDH were significantly elevated in all the cases of meningitis in CSF as compared to control group. **Conclusion:** The estimation of CSF-LDH activity is cost effective and rapid diagnostic assay with high sensitivity and specificity that can be used on regular basis along with other investigation to diagnose meningitis in children and also to differentiate between the pyogenic, tubercular and viral meningitis. **Keywords:** Meningitis, CSF analysis, Lumbar puncture, Cerebrospinal fluid, Lactate dehydrogenase

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## INTRODUCTION

Meningitis is an inflammatory process of the leptomeninges and CSF within the subarachnoid space, usually caused by an infection<sup>1</sup>. Despite the advances in

diagnosis and treatment of infectious diseases, meningitis is still an important cause of mortality and morbidity, specially in the pediatric population<sup>2</sup>. Pyogenic meningitis is a major pediatric problem all over the world, especially in developing countries like India. Antibiotics have reduced the mortality from almost 100% to 8-30%. Early and reliable diagnosis is the key to successful outcome<sup>2</sup>. Therefore it is important to distinguish Bacterial Meningitis from aseptic meningitis during the acute phase of the disease, when clinical symptoms are often similar. The CSF variables like total cell count, glucose, protein levels, CSF/serum glucose ratio are effective in differentiating bacterial meningitis from viral meningitis. The gold standard for the diagnosis of any infection is the demonstration or isolation of the causative agent. Unfortunately, the yield of microorganisms on Gram stain

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depends on factors like the number of organisms present, prior use of antibiotics, technique of preparing the slide and the observer's skill. The CSF culture is time consuming and in many places is not available. The CSF culture is also affected by prior use of antibiotics, defect in transport and storage of CSF specimen which can give false negative results<sup>3</sup>. A precise and reliable etiological diagnosis remains a challenge and often a thorough cerebrospinal fluid examination may not give a diagnosis. In cases of meningitis there is disruption of the blood brain barrier (BBB) leading to rise in enzymatic activity<sup>4</sup>. The CSF LDH is around 1/10th of the serum LDH level .CSF level of LDH was found to be elevated in patients with meningitis in some studies . CSF LDH value will not be altered with a short period of antibiotic therapy as it needs complete eradication of microorganisms<sup>4,5</sup>. In this regard the present study was taken to evaluate the diagnostic significance of CSF Lactate dehydrogenase in cases of meningitis in children and its utility to differentiate between types of meningitis

### MATERIAL AND METHODS

The present study was carried out in the Department of Pediatrics, Mahadevappa Rampure Medical College, Kalaburagi. Patient's attenders were informed about the purpose of the study and written consent was before start of the study. Ethical clearance was obtained by the ethical

clearance committee of the institution. The study included clinical evaluation and CSF analysis of the children presenting with clinical suspicion of meningitis admitted to Pediatrics wards during the period from December 2017 to June 2019 .

#### Inclusion criteria :

All Children aged between 1month to 18 years with clinical suspicion of meningitis admitted in pediatric ward .

#### Exclusion criteria :

- 1)Those with documented parenteral antibiotic intake prior to admission
- 2)Children with history of hemolytic anemia ,liver disorders, muscles diseases , malignancy
- 3)Traumatic tap during Lumbar Puncture

#### Statistical data analysis:

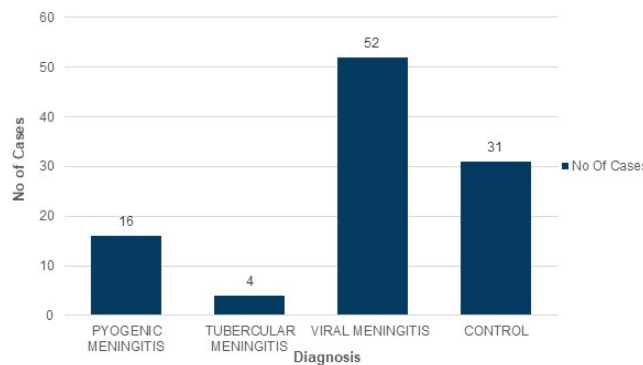
Statistical data was analyzed by using IBM SPSS 20.0 version software was used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc. For qualitative data analysis chi-square test was applied for quantitative data analysis t test and ANOVA tests were applied for statistical significance.. If P-value was less than 0.05 was considered as statistical significant for the study Sensitivity, Specificity, PPV, NPV, Accuracy was computed in the study to find the relationship of LDH levels with various types of meningitis.

### OBSERVATIONS AND RESULTS

Table 1: Diagnosis wise distribution of cases

Diagnosis	No. of cases	Percentage(%)
PYOGENIC MENINGITIS (PM)	16	15.5
TUBERCULAR MENINGITIS (TBM)	4	3.9
VIRAL MENINGITIS (VM)	52	50.5
CONTROL (C)	31	30.1
<b>TOTAL</b>	<b>103</b>	<b>100.0</b>

A Total of 103 cases were studied : among them 16 cases(15.5%) were Pyogenic meningitis 4 cases (3.9%) were Tubercular meningitis , 52 cases (50.5%) were Viral meningitis and 31 cases (30.1%)which were diagnosed as Febrile Seizures and were taken as control group for this study . Following data is presented in Table 1 and graphically depicted in Graph 1



Graph 1

**Table 2:** CSF analysis in different type of meningitis

DIAGNOSIS	CSF total cell count Mean ± SD	Polymorphs Mean ± SD	Lymphocytes Mean ± SD	Sugar mg/dl Mean ± SD	Protein mg/dl Mean ± SD
PM	890.31 ± 163.3	79.37±8.5	21.02 ± 12.73	40.56 ± 26.55	143.49 ± 78.81
TBM	116.0 ± 40.20	23.75±12.5	76.3 ± 20.6	53.00 ± 23.35	65.51± 27.19
VM	81.02 ± 52.16	16.69±2.5	83.31 ± 33.2	67.95 ± 17.06	107.78 ± 67.50
CONTROLS	6.77 ± 4.67	00	05	84.97 ± 86.87	28.11 ± 18.75
ANOVA test	F = 7.812	F=26.681	F=70.48	F = 2.82	F = 17.789
P-value and Significance	P = 0.001 VHS	P = 0.0001 VHS	P = 0.001 VHS	P = 0.042 S	P = 0.0001 VHS

Table no 2 shows our study observed highest mean CSF total count in cases with pyogenic meningitis with a mean of 890.31 ± 163.3, followed by tubercular meningitis 116.0 ± 40.20 whereas mean cell count in viral meningitis cases were 81.02 ± 52.16. Pyogenic meningitis had a predominantly neutrophilic lymphocytosis picture while TBM and viral meningitis showed predominance of lymphocytes. Pyogenic meningitis group had the lowest mean CSF sugar of 40.56 ± 26.55 and highest CSF mean protein of 143.49 ± 78.81.

**Table 3:** Comparison among study group and control group with mean LDH levels

Diagnosis	No. of cases	CSF LDH levels (iu/dl)		Comparison with Control t - test value , P-value
		Min-max	Mean ± SD	
PM	16	106--1200	547.75 ± 331.1	t = 8.997 P = 0.001, VHS
TBM	4	92--182	136.0 ± 42.04	t = 16.15 P = 0.001, VHS
VM	52	33--172	69.9 ± 34.79	t = 9.16 P = 0.042, S
CONTROL	31	10--31	17.35 ± 5.69	----
Total	103	10--1200	130.88 ± 222.16	----
ANOVA test P-value and sig.			F = 65.08 P = 0.0001 VHS	

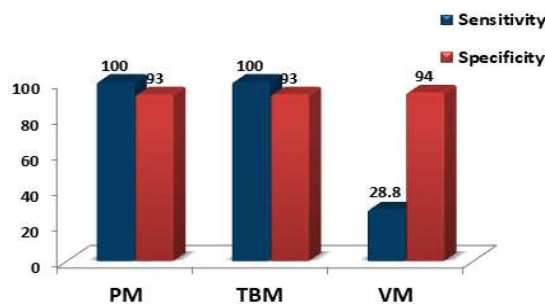
Table no 3 shows the highest Mean CSF LDH level of 547.75 ± 331.1 IU/L was observed in pyogenic meningitis cases and minimum and maximum values seen were 106 to 1200 respectively. With a Mean CSF LDH level of 136.0 ± 42.04 IU/L in TB meningitis showed significant elevation whereas viral meningitis group showed only marginal elevation of CSF LDH (69.9 ± 34.79).

**Table 4:** Sensitivity, Specificity, PPV, NPV and Accuracy of elevated LDH levels for diagnosing the PM, TBM and VM when compared to control group

Diagnosis	Sensitivity	Specificity	PPV	NPV	Accuracy	P-value
PM	100.0	93.0	92.0	100.0	97.4	0.001
TBM	100.0	93.0	91.0	100.0	97.6	0.001
VM	28.8	94.0	86.7	58.0	65.0	0.042

**Table no 04** shows accuracy of elevated LDH levels in diagnosing the PM, TBM and VM when compared to control group

Elevated LDH levels in Pyogenic Meningitis with 100% sensitivity, 93% specificity and Predictive value of positive test of 92% and the Predictive value of Negative test of 100 % in present study, while in Viral meningitis elevated LDH showed a relatively low sensitivity of 28.8% and specificity of 94%.



## DISCUSSION

This Hospital based prospective study included 103 children with clinical suspicion of meningitis to study the CSF analysis with special reference to CSF LDH estimation. In our study, we noted a male preponderance among cases comprising 63.1%. Pyogenic meningitis was common in < 1 year age group, whereas Viral meningitis and Tubercular meningitis were common in >5 year age group. This correlated with that reported by Kumar *et al*<sup>6</sup> and Parul N Vekaria *et al*<sup>7</sup>. 62.1% of the cases in study group belonged to Rural area and 48.5% of the cases were reported during the months of June to November. 40.8% of the children were incompletely immunized / unimmunized in the study group. Fever was the most consistent presenting complaint (100%) followed by convulsions (86.4%) Headache (65%), vomiting (51%) which were more common among the study group while Altered sensorium and neck pain was seen in 46% and 51% respectively. 10% of the study group had cranial nerve palsy while Kerning's sign and Brudzinski's sign was positive in 38% and 32 % of the cases respectively indicative of low sensitivity in children as comparable to observations made by Thomas KE *et al*<sup>8</sup>. Motor weakness was seen in 24.3% of the cases in study group. Etiologically Viral meningitis was the commonest type with 50.1% of the study group, followed by Pyogenic meningitis (15.5%). CSF pleocytosis was observed in all types of meningitis, highest cell count was observed in pyogenic meningitis cases with a mean CSF cell count of 890.31cells/mm<sup>3</sup> and Viral meningitis with a mean cell count of 81.02cells/mm<sup>3</sup>. Cell typing was helpful in differentiating types of meningitis with Neutrophilic leukocytosis observed in pyogenic meningitis and Lymphocytic leukocytosis observed in TB meningitis and Viral meningitis. In Pyogenic meningitis all cases had low CSF sugar with a mean of 40.56mg/dl. The mean CSF /serum glucose ratio is 0.24 in pyogenic meningitis. In TBM mean CSF sugar was 53mg/dl and in viral meningitis mean CSF sugar was 67mg/dl. CSF Protein was found to be highest in pyogenic meningitis with mean protein of 143.49mg/dl followed by viral meningitis (107.78 mg/dl) which correlated with observations in studies by Manish K S *et al*<sup>9</sup> and Singh RK *et al*<sup>10</sup>. Neuroimaging showed abnormality in 23.4% of the cases in study group, highest were in the pyogenic meningitis group (36.5%). CSF LDH was significantly elevated in all type of meningitis. The highest titre of CSF LDH was observed in pyogenic meningitis with mean CSF LDH of 547.75 IU/L. Only a marginal elevation in CSF LDH was noted in Viral meningitis (69.9 IU/L) whereas an intermediate values were observed in TB meningitis (139 IU/L). The LDH

activity in CSF in Pyogenic meningitis was significantly elevated ( $p < 0.0001$ ) compared to TB meningitis and Viral meningitis group, these observations were consistent with studies by M Sharma *et al*<sup>4</sup>, Manish K S *et al*<sup>9</sup>, Singh RK *et al*<sup>10</sup>, Jha A *et al*<sup>11</sup> Borgaonkar *et al*<sup>12</sup>, Purna Chandra Dash *et al*<sup>13</sup> who also observed significant elevation of CSF LDH levels.

**TABLE NO 05 : Comparative Analysis Of CSF LDH Levels In Pyogenic Meningitis With Other Studies**

STUDY	YEAR	Mean CSF LDH level in Pyogenic Meningitis
PRESENT STUDY	2019	547.75 ± 331.1
Purna Chandra Dash <i>et al</i>	2014	371.6 ± 39.5
M Sharma <i>et al</i> <sup>4</sup>	2006	260.30 ± 110.96
Manish K S <i>et al</i> <sup>9</sup>	2010	247.65
Jha A <i>et al</i> <sup>11</sup>	2017	211.48 ± 28.86

We noted a linear correlation between CSF LDH activity and CSF pleocytosis. LDH is a zinc-containing enzyme released in various neurological conditions, increase in their CSF levels is due to increased permeability of membranes and disruption of blood brain barrier. Hence elevated LDH activity reflects the extent of brain injury<sup>14,15</sup>. In the present study the enzymatic activity was significantly elevated in CSF in cases of Pyogenic meningitis and Tubercular meningitis as compared to control subjects.

## CONCLUSION

The measurement of CSF Lactate Dehydrogenase(LDH) concentration is a simple, rapid, inexpensive assay. In our study it was helpful in diagnosing meningitis and showed high specificity and sensitivity and it was helpful in differentiating pyogenic meningitis from non bacterial meningitis. The estimation of CSF LDH can be advocated in establishing an early diagnosis of meningitis and can aid the clinician in identifying the type of meningitis and to administer appropriate antimicrobials early which improves the overall outcome of the patient.

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