



“STUDY OF BIOCHEMICAL PARAMETERS AND LDH LEVELS OF CSF IN CHILDREN WITH NEURO-INFECTIONS”

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ABSTRACT Aims And Objectives:

- Correlation between CSF biochemical parameters and LDH levels in children with neuro-infections

Methods: This is prospective observational hospital based study done during period of 2 years i.e. March 2021 – October 2022 in Hospitals attached to J.J.M Medical College, Bapuji Child Health Institute and C.G. Hospital, Davangere. All children undergoing lumbar puncture aged between 2 months to 18 years children who satisfied our inclusion criteria were included in our study. After detailed clinical and fundus examination, blood was drawn for estimation of blood sugar. Lumbar puncture was performed immediately were recorded as per pre-designed proforma and analysed. **Results:** 50 cases of various types of meningitis were studied with special reference to CSF analysis and LDH estimation. CSF LDH was significantly elevated in all types of meningitis. The highest titre of LDH was observed in pyogenic meningitis. LDH titres were marginally elevated in aseptic meningitis and intermediate values were observed in TBM. Significant rise in LDH activity was observed in fatal cases. **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

KEYWORDS : Pyogenic meningitis; Tuberculous meningitis; Aseptic meningitis; CSF; LDH.

INTRODUCTION

Meningitis refers to an inflammatory process of the leptomeninges and CSF within the subarachnoid space. 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.¹

So, the rapid diagnosis of bacterial meningitis is usually based on CSF examination though there are many test for rapid diagnoses of bacterial meningitis have been introduced, Enzymatic study (CSF-LDH) is a better sensitive parameter in diagnosis of various types of meningitis.²

Lactic dehydrogenase is present in most tissues and body fluids examined, including cerebrospinal fluid. Studies have shown that patients with an intracranial pathology such as malignancy or bacterial infection have increased CSF LDH activity compared to healthy subjects.

To see the Correlation of CSF-LDH in diagnosis of Neurological disorders such as meningitis, encephalitis, brain abscess, subarachnoid and intracranial haemorrhages, Guillain barre syndrome, leukaemia and lymphomas by doing lumbar puncture under aseptic precautions.

Examination of LDH 1/LDH 2 can be found as an adjunctive method to identify brain metastases and carcinomatous meningitis at the initial stage.

METHODOLOGY

Sources of data:

All children undergoing lumbar puncture aged between 2 months to 18 years admitted to the hospital attached to J.J.M. Medical College, Davangere.

- Bapuji Child Health Institute and Research Center, Davangere.
- Chigateri General Hospital, Davangere.

All cases of confirmed neurological disorder during a 2-year period from March 2021 to October 2022 will be considered for study.

Study Type: Prospective Observational hospital based study.

Study Period: March 2021 to October 2022.

Sample Size: 50 cases

Inclusion Criteria:

- Children with neuro-infections between 2 months to 18 years

Exclusion Criteria:

- Children with any contraindications for LP.
- LP for treatment – chemotherapy, anesthesia, radiography contrast media, antibiotic therapy.
- Already diagnosed case of neuro-infection.
- Patient <2 months and >18 years of age.
- Those patient who refused to be included in the study.
- Admitted for neurological disorders other than neuro-infections.

Methods of Collection of Data:

- Informed consent from all the patients was taken before undergoing the study.
- Purpose of the study was explained to the study subjects and their parents.
- A pre-structured proforma was used to record the relevant information from individual case selected for the study.
- Relevant investigation was conducted as per case like –
- CSF-LDH,
- CSF analysis
- CSF culture

LDH Estimation:

CSF - LDH. was estimated in the central lab with the help of calorimeter.

Method: CSF - LDH was done by optimized standard method using DR-LANGE LP 700 calorimeter. LDH was done using a kit from Boehringer Mannheim. Each kit contains 30 bottles of Buffer I substrate; 3ml in each bottle with NADH (30 reagent tablets) in another separate single bottle.

Statistical Analysis:

- Categorical data will be represented in the form of frequency and

percentage. Association between variables will be assessed with Chi Square Test.

- Quantitative data will be represented as Mean & Sd.
- P value of <0.05 will be considered statistically significant.
- Data was analyzed with IBM SPSS Version 22 for windows.

RESULTS

Table – 1: Comparison of partially treated from other cases of pyogenic meningitis

Type	Partially treated (n=5)	Other pyogenic meningitis (n=21)	Significance
Protein	135±42.3	115±40.1	0.331
Blood/CSF sugar	0.78±0.26	0.48±0.14	<0.001
Chloride	112±16.03	122±11.0	0.106
LDH	158±41	211±92.9	0.229
Cell count	191±230.62	110.9±360.3	0.260
Cell type	80% lymph	80% polym	-
Gram stain C/S/%	20%	55%	-

Table-1 shows the comparison of partially treated pyogenic meningitis with other cases of pyogenic meningitis. Protein was elevated, chloride was normal, whereas CSF sugar was normal and blood, CSF sugar ratio was 0.78±0.26 in 5 cases of partially treated pyogenic meningitis, compared to other cases of pyogenic meningitis (0.48±0.14). LDH levels were elevated (211±92.9) in other pyogenic meningitis, but the values were below the mean value of untreated group.

Table – 2: Comparison of partially treated pyogenic meningitis and TBM

Type	Partially treated pyogenic meningitis (n=5)	TBM (n=1)	p-value
Protein	135±42.3	231	<0.001
Blood/CSF Sugar	0.78±0.26	0.50	<0.001
Chloride	112±16.03	95	<0.001
LDH	158±41	141	<0.001
Cell count	191±23.62	152	<0.001
Cell type	80% lymph	80% lymph	-

Table-2 shows comparison of partially treated pyogenic meningitis with cases of TBM (Group-IV). Elevation of protein persists but was not as high as in cases of TBM. Chloride levels were low in TBM. Whereas it was normal in cases of partially treated pyogenic meningitis. Blood, CSF sugar ratio was 0.78±0.26 in cases of partially treated group. Cell count was not altered but the type of cells were lymphocytes in both the groups. The study found statistically significant difference between the two diagnoses in terms of all parameters.

Table –3: Mean LDH in patients died and comparison with survivors

Cases	Pyogenic meningitis (n=2/26)	Tuberculous meningitis (n=1/7)	Aseptic meningitis (n=4/17)
Died	211.78	101	40.03
Recovered	201.12	92.34	44.72
p-value	<0.001	<0.001	<0.001

Table-3 shows the mean LDH values in patients who died and patients who recovered in various groups. There was statistically significant difference in the LDH values in these two groups. (pyogenic meningitis and tubercular meningitis)

DISCUSSION

CSF analysis showed raised CSF pressure in 53% cases and in all cases CSF was clear. The mean CSF values in proven neuroinfection were protein 135±42.3, chloride 112±16.03, sugar 0.78±0.26.

Comparing our study and study by Sathpathy *et al.*,¹ CSF sugar and chloride were normal in both groups, but a slightly high value of protein was observed in Sathpathy *et al.*, study. Cell counts were 191±23.62 cells/cu.mm and majority of the cells were lymphocytes. Cell count as high as 1000 cells/cu.mm was observed by some authors. A marginal increase in LDH activity was observed by Jain *et al.*,² and Sathpathy *et al.*¹ But Agarwal *et al.*,³ showed normal LDH activity in aseptic meningitis.

To know the specificity and sensitivity of LDH some values were taken as the cut off point. To diagnose meningitis from non meningitis group, 52 IU/L (2 SD above normal mean LDH levels) was taken as the cut off point. When 52 IU/L was taken as the cut off point, LDH estimation has got sensitivity of 74.1%, specificity of 92%, positive predictive value of 96.9%, negative predictive value of 51.1% and an overall accuracy of 51.1% to diagnose meningitis. In different types of meningitis when LDH levels of 52 IU/L was taken as the cut off point, pyogenic meningitis and TBM has a diagnostic sensitivity of 100% and specificity of 92%, whereas in aseptic meningitis the sensitivity was 12% and specificity was only 8%.

To differentiate pyogenic meningitis from tuberculous meningitis, 140 IU (2 SD above the mean for tuberculous meningitis cases) was taken as the cut off point. When 140 IU/L was taken as the cut off point, LDH estimation has got sensitivity of 80%, specificity of 100%, positive predictive value of 100%, negative predictive value of 87.5% and an over all accuracy of 91.71% to differentiate pyogenic from tuberculous meningitis. Agarwal *et al.*,³ and Jain *et al.*,² have also observed the usefulness of LDH in differentiating pyogenic from tuberculous meningitis. But these observations were questioned by Dave *et al.*,⁴ and Nand *et al.*⁵

Correlation between LDH activity and cytological and biochemical parameters were observed by many authors. Jain *et al.*,² and Gupta *et al.*,⁶ found a linear relationship between rise in LDH activity and cell count, where as Sathpathy *et al.*,¹ found rise in LDH activity when pus cells were present in the CSF. Khanna *et al.*,⁸ and Jain *et al.*,² also observed linear relation between LDH activity and other biochemical parameters like protein and chloride levels.

In this study, even though LDH activity was high in few cases with high CSF cell count, there was no steady correlation between increase in cell count and rise in LDH activity. Comparing other biochemical parameters with LDH activity, no steady correlation was found.

Nand *et al.*,⁵ observed, a subsequent rise or sustained high values of LDH in patients who deteriorated clinically even after appropriate treatment. In our study, repeat CSF assessment was not done in any case. Dave *et al.*,⁴ and Nand *et al.*,⁵ studied LDH activity in CSF and serum and observed that rise in LDH activity in CSF was more consistent than the serum LDH activity in meningitis.

CSF was analysed in all the cases of tuberculous meningitis, pressure was increased in 28% cases and it was clear in 86% cases and opalescent in 15% cases. Cob web was formed in 75% cases. In a study by Upadyaya *et al.*,⁹ CSF was turbid in 50% cases and cob web was formed in 15% cases of tuberculous meningitis.

Bohr *et al.*,¹⁰ have shown that with prior antibiotic treatment, the culture positivity reduces from 64 to 38% and Gram stain positivity from 54 to 34%. In this study, LDH activity was reduced compared to other pyogenic meningitis group, but LDH levels were well above, when compared with aseptic meningitis and tuberculous meningitis. Jain *et al.*,² have shown 60% decline in LDH activity in treated cases within 3-5 days. High LDH activity can persists even after treatment in cases of diffuse brain damage.⁵

To conclude, even though LDH activity is used as supportive evidence of meningeal inflammation, this test can be used in difficult situations where diagnosis of meningitis or differentiation of pyogenic from tuberculous meningitis is difficult.

CONCLUSION

To conclude, a diligent attempt to identify and culture organisms, cannot be overlooked, and still remains the best test. Even though LDH activity is used as a supportive evidence of meningitis, this test can be used in difficult situations to diagnose meningitis or differentiate pyogenic meningitis from TBM.

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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