MAK HILL Publications International Journal of Tropical Medicine

Research Article
doi: 10.36478/makijtm.2025.1.71.75

A Study of Lactate Dehydrogenase and Creatine Kinase in Cerebrospinal Fluid in Different Types of Meningitis

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ABSTRACT

Acute infections of the nervous system are among the most important problems in medicine because early recognition, efficient decision-making and rapid institution of therapy is lifesaving. Meningitis is causes by infectious and non-infectious etiologies. Infectious etiology can be bacterial, viral, fungal, protozoal organism. Bacterial meningitis is a life-threatening neurological condition and needs prompt parenteral antibiotics, compared to viral and aseptic meningitis which carries relatively better outcome. Many enzymes are known to be present in abundance in the nervous system. Meningitis disturbs the blood brain barrier (BBB) and is expected to cause rise in enzymatic activity. Enzymatic study (CSF LDH) is a better sensitive parameter in diagnosis of various types of meningitis when used along with conventional tests such as protein glucose and white cell count. Present study was aimed to study lactate dehydrogenase and creatine kinase in cerebrospinal fluid in different types of meningitis. 100 patients presenting with history, characteristic clinical signs and symptoms of meningitis are taken into the study. History was taken clinical examination was done and the relevant investigations are done in the selected patients. Mean CSF LDH and CK values are elevated from the baseline. The elevation of LDH was more in bacterial meningitis(267.9U/L) followed by cryptococcal(228.5U/L), tubercular(177.1U/L) and viral meningitis(124.8U/L). The elevation of CK was more in bacterial meningitis(90.3U/L) followed by cryptococcal (77.6U/L), tubercular(63.8U/L) and viral meningitis(50.1U/L) and this is statistically significant (P<0.001). There was a strong positive correlation between the serum and CSF level of CK and LDH .This is statistically significant (P<0.001) . Estimation of CSF LDH, CK will help in the diagnosis of meningitis along with other parameters like CSF cell count, glucose, proteins.

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Key Words
Meningitis, CSF, LDH, CK

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Received: 10 November 2024
Accepted: 16 December 2024
Published: 22 January 2025

Citation: K.S. Supritha, Akshay Biskop, Mahesh Koulagi, K. Kiran and Ahemer Siddiqui 2025. A Study of Lactate Dehydrogenase and Creatine Kinase in Cerebrospinal Fluid in Different Types of Meningitis. Int. J. Trop. Med., 20: 71-75, doi: 10.36478/makijtm. 2025.1.71.75

INTRODUCTION

Bacterial meningitis is the most common form of suppurative CNS infection, with an annual incidence in the United States of >2.5 cases/100,000 population[1]. The organisms most often responsible for community -acquired bacterial meningitis are Streptococcus pneumoniae (~50%), Neisseria meningitidis (~25%), group B streptococci (~15%) and Listeria monocytogenes (~10%)[2]. Haemophilus influenzae type b accounts for <10% of cases of bacterial meningitis in most series. N. meningitidis is the causative organism of recurring epidemics of meningitis every 8-12 years[2,3]. In 2016, nearly 0·6% of all-ages deaths and close to 3% of the total in children younger than 5 years were due to meningitis. The estimates indicate that, while most incident cases are now due to infections in the other meningitis category, meningococcal infections continue to be a major cause of meningitis mortality and most long-term disability is due to the after- effects of pneumococcal infection[4]. Infectious etiology can be bacterial, viral, fungal, protozoal organism. Bacterial meningitis is a life-threatening neurological condition and needs prompt parenteral antibiotics, compared to viral and aseptic meningitis which carries relatively better outcome. Many enzymes are known to be present in abundance in the nervous system. Meningitis disturbs the blood brain barrier (BBB) and is expected to cause rise in enzymatic activity. Enzymatic study (CSF LDH) is a better sensitive parameter in diagnosis of various types of meningitis when used along with conventional tests such as protein glucose and white cell count[4,5]. Present study was aimed to study lactate dehydrogenase and creatine kinase in cerebrospinal fluid in different types of meningitis.

MATERIALS AND METHODS

Present study was single-center, prospective, observational study, conducted in department of General Medicine, Karnataka Institute of Medical Sciences, Hubballi, India. Study duration was of 2 years (July 2020 to June 2022). Study was approved by institutional ethical committee.

Inclusion Criteria:

- Patients age above 18 years, admitted with signs and symptoms of meningitis, willing to participate in present study.

Exclusion Criteria:

- Liver disorder-Chronic liver disease, alcoholic liver disease, malignancy, hepatitis, etc.
- Cardiac disease-IHD, CAD, myocarditis etc
- Hematological abnormalities-hemolysis, malignancies.
- Cerebrovascular diseases, ICSOL, brain abscess, Guillain Barre syndrome, subarachanoid hemorrhage, malignancies of CNS.
- Haemorrhagic lumbar puncture.
- Patients suffering from renal diseases.

Study was explained to participants in local language and written informed consent was taken. Patients presenting with history, characteristic clinical signs and symptoms of meningitis are taken into the study and the following investigations will be done in the selected patients. (Complete hemogram, Blood urea, Serum creatinine, Liver function tests, CSF analysis-cell type, cell count, glucose, protein, chloride, Gram stain, ZN stain, culture and sensitivity, LDH, CK, ADA, CB-NAAT, GRBS. Fundoscopy. Serum electrolyte, Electrocardiography, CT brain, Blood culture, Serum CK, LDH, 2D-ECHO, Chest X ray PA view and MRI brain (when needed). Data was collected and compiled using Microsoft Excel, analyzed using SPSS 23.0 version. Statistical analysis was done using descriptive statistics.

RESULTS AND DISCUSSIONS

For the study, a total 100 patients were included. Majority were from age group 41-60 years (46%), followed by 20-40 years (36%), >60 years (11%) and <20 years (7%). In gender distribution, 60 (60%) were males and rest 40 (40%) were females. 28(28%) patients had diabetes mellitus and 30(30%) had hypertension. Past history of pulmonary TB was present in 7(7%) patients and 15 (15%) were HIV seropositive. Out of 100 patients, 28(28%) patients reported consumption of alcohol, 34 (34%) were smokers and 13(13%) had both habits.

Table 1: General Characteristics

Characteristics	No. of subjects	Percentage
Age group (in years)		
≤20	7	7.0
21-40	36	36.0
41-60	46	46.0
>60	11	11.0
Gender		
Male	60	60.0
Female	40	40.0
Comorbidities		
Diabetes mellitus	28	28.0%
Hypertension	30	30.0%
Pulmonary TB	7	7.0%
HIV	15	15.0%
Habits		
Alcohol	28	28.0
Smoking	34	34.0
Alcohol and Smoking	13	13.0

Out of total 100 patients, altered sensorium was the most common presentation reported by all 100(100%), followed by vomiting in 90(90%) patients, 88 (88%) reported fever, 87 (87%) had reported headache, Seizure was present in 7(%) patients and History regarding focal deficit was present in 5 (5%) patients. Regarding signs, neck rigidity was the most common presentation found in all 100(100%) patients, Kernig's sign was present in 32(32%) patients and Brudzinski sign was positive in 33 (33%) patients.

Table 2: Clinical Features

	No. of subjects	Percentage
Symptoms		
Fever	88	88.0
Head ache	87	87.0
Altered sensorium	100	100.0
Seizure	7	7.0
Vomiting	90	90.0
Focal deficit	5	5.0
Signs		
Neck rigidity	100	100.0
Kernig's sign	32	32.0
Brudzinski sign	33	33.0

The most common diagnosis was bacterial meningitis (42%), followed by viral meningitis (28%), TB meningitis (22%) patients and cryptococcal meningitis in 8 (8%) patients.

Table 3: Distribution of Etiology of Meningitis

Diagnosis	No. of subjects	Percentage
Bacterial meningitis	42	42.0
Tubercular meningitis	22	22.0
Viral meningitis	28	28.0
Cryptococcal meningitis	8	8.0

Serum LDH levels was highest in bacterial meningitis (325.1U/L) followed by Cryptococcal Meningitis (271.5 U/L), tubercular meningitis (230.8) and lowest in viral meningitis (146.6 U/L) and this difference was statistically significant (P<0.001). Serum CK levels was highest in bacterial meningitis (170.6 U/L) followed by cryptococcal meningitis (122.3 U/L), tubercular meningitis (122.7 U/L) and lowest in viral meningitis (81.8 U/L) and this difference was statistically significant (P<0.001). Mean cell count was highest in bacterial meningitis (441.0 cells/cmm) followed by TB meningitis (335.5cells/cmm), viral meningitis (177.1 cells/) and lowest in cryptococcal meningitis (102.8 cells/cmm). The difference in mean cell count was significant (P<0.001). Neutrophil count was raised in bacterial meningitis (81.2%) followed by cryptococcal meningitis (48.3%), viral meningitis (44.2%) and lowest in TB meningitis (19.5%) and this difference was statistically significant (P<0.001). Lymphocyte count was highest in TB meningitis (80.5%) followed by viral meningitis (55.8%), cryptococcal meningitis (51.8%) and lowest in bacterial meningitis (18.8%) and this difference was statistically significant (P<0.001). CSF protein levels was highest in bacterial meningitis (162.4 mg/dl) followed by tubercular meningitis (135.0 mg/dl), cryptococcal meningitis (117.9 mg/dl) and lowest in viral meningitis (106 mg/dl) and this difference was statistically significant (P<0.001). CSF glucose levels was lowest in bacterial meningitis (41.3mg/dl), followed by tubercular meningitis (69.0 mg/dl), viral meningitis (78.2mg/dl) and highest in cryptococcal meningitis (80mg/dl)., this difference was statistically significant (P<0.001). CSF LDH levels was highest in bacterial meningitis (267.9 U/L) followed by cryptococcal meningitis (228.5 U/L), Tubercular (177.1 U/L) and viral meningitis (124.8 U/L) and this difference was statistically significant (P<0.001). CSF CK levels was highest in bacterial meningitis (90.3) followed by cryptococcal meningitis (77.6 U/L), Tubercular meningitis (63.8 U/L) and lowest in viral meningitis (50.1 U/L) this difference was statistically significant (P=0.001). CSF ADA (21.5 U/L) levels increased multiple folds in TB meningitis compared to other causes. In CSF culture and sensitivity, 11.9% with bacterial meningitis had growth of streptococcal pneumonia. Patients with other types of meningitis did not show growth of streptococcal pneumonia. In the present study, 45.5% with TB meningitis were CBNAAT positive. Patients with other types of meningitis did not show positive result in CBNAAT. All eight patients (100%) with cryptococcal meningitis were positive for cryptococcal antigen.

The present study is a prospective observational study with a sample size of 100 patients, conducted to study the level of LDH and CK enzyme level in CSF, its elevation from the baseline in different meningitis. The present study includes a sample size of 100 which is not comparable with the other studies. Purna Chandra[1] study includes 44 patient, M Sharma[6] includes 25 patients, Manish K Sinha[7] included 160 patients, Ankur Banik[8] included 50 patients, Abhishek Jha[9] included 150 patients in their respective studies In the present study 42% (n=42) of the cases are Bacterial meningitis which is comparable with Manish K Sinha[7] 39% (n=46) and Abhishek Jha[9] 33.3(n=50). In the present study 22% (n=22) of the cases are Tubercular meningitis which is nearly comparable with Abhishek Jha[9] 33.3%(n=50), M Sharma[6] 40%(n=10). In the present study 28% (n=28) of the cases are viral meningitis which is comparable with Manish K Sinha[7] 20%(n=24), In the present study 8%(n=8) cases are cryptococcal meningitis which is not comparable with any other study. In the present study 60% (n=60) of the patients were males which is comparable with other studies Abhishek Jha[9] with 60%(n=30) male patients, M Sharma[6] with 64% (n=16) male patients and Purna Chandra[1] study with 65% (n=29) male patients. In the present study 40% (n=60) of the patients were females which is comparable with other studies, Abhishek Jha[9] with 40% (n=20) female patients, M Sharma[6] with 36% (n=9) female patients and Purna Chandra[1] study with 35% (n=15) female patients. In the present study neck rigidity is present in 100% (n=100) of the patients which is comparable with the Purna Chandra[1] study 100% (n=44) and Abhishek Jha[9] study 100%(n=50). Headache is seen in 87% of the patients which is

Table 4: Serum Parameters in Meningitis

Parameter	Bacterial meningitis		Tubercular meningitis		Viral meningitis		Cryptococcal meningitis		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	P-value
Serum LDH	325.1	23.7	230.8	32.1	146.6	61.5	271.5	14.1	<0.001
Serum CK	170.6	15.7	122.7	19.8	81.8	10.1	122.3	21.3	<0.001
Cell count (cells/cmm)	441.0	66.6	335.5	46.9	177.1	20.6	102.8	31.0	<0.001
Neutrophils (%)	81.2	7.3	19.5	6.1	44.2	4.6	48.3	7.8	<0.001
Lymphocytes(%)	18.8	7.3	80.5	6.1	55.8	4.6	51.8	7.8	<0.001

Table 5: CSF parameters in Meningitis

Parameter	Bacterial meningitis		Tubercular meningitis		Viral meningitis		Cryptococcal meningitis		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	P-value
CSF protein	162.4	23.1	135.0	16.0	106.1	9.8	117.9	12.3	<0.001
CSF Glucose	41.3	8.1	69.0	10.1	78.2	11.9	80.3	16.4	<0.001
CSF LDH	267.9	16.5	177.1	20.1	124.8	18.8	228.5	20.8	<0.001
CSF CK	90.3	8.4	63.8	11.5	50.1	7.1	77.6	15.6	0.001
CSF ADA	3.3	1.5	21.5	4.9	3.1	1.6	2.8	1.5	<0.001

Table 6: CSF Culture and Sensitivity in Meningitis

CSF C and S	Bacterial meningitis		Tubercular meningitis		Viral meningitis		Cryptococcal meningitis		
	N	%	N	%	N	%	n	%	P-value
Streptococcal pneumonia	5	11.9	0	0.0	0	0.0	0	0.0	
No growth	37	88.1	22	100.0	28	100.0	8	100.0	0.064

Table 7: CSF CBNAAT in Meningitis

CBNAAT	Bacterial meningitis		Tubercular meningitis		Viral meningitis		Cryptococcal meningitis		
	N	%	N	%	N	%	N	%	P-value
Yes	0	0.0	10	45.5	0	0.0	0	0.0	<0.001
No	42	100.0	12	54.5	28	100.0	8	100.0	

Table 8: CSF Cryptococcal Antigen in Meningitis

Cryptococcal antigen	Bacterial meningitis		Tubercular meningitis		Viral meningitis		Cryptococcal meningitis		
	N	%	N	%	n	%	n	%	P-value
Yes	0	0.0	0	0.0	0	0.0	8	100.0	<0.001
No	42	100.0	22	100.0	28	100.0	0	0.0	

comparable with Purna Chandra[1] study 81%. Seizure 7% (n=7) and focal deficit 5% (n=5) are the least common presentation in this study which is comparable with Purna Chandra[1] study and Abhishek Jha[9] study. In the present study mean serum LDH in bacterial meningitis is 325.1 U/L which is comparable with Abhishek Jha[9] (351.9 U/L) and Purna Chandra *et al.* study (393.8U/L). In the present study mean serum LDH in Tubercular meningitis is 230.8 U/L which is comparable with M Sharma[6] (196.8 U/L). In the present study mean serum CK in bacterial meningitis is 170.6 U/L which is not comparable with Purna Chandra[1] study (267.9U/L) , M Sharma[6] study (261 U/L) and Abhishek Jha[9] study (66.5 U/L) Mean serum CK in tubercular meningitis is 122.7U/L which is nearly comparable with M Sharma[6] study with mean value of 196.8U/L. In the present study mean CSF protein in bacterial meningitis is 162.4 mg/dl and in tubercular meningitis is 135 mg/dl, which is nearly comparable with the study conducted by Manish K Sinha[6] mean CSF protein values of 138.4mg/dl and 170.6mg/dl in bacterial and tubercular meningitis respectively. Mean CSF glucose in Tubercular meningitis is 69 mg/dl and, which is nearly comparable with the studies conducted by Manish K Sinha[6] mean CSF glucose values of 39.4 mg/dl. In the present study mean CSF LDH in bacterial meningitis is 267.9 U/L which is comparable with the studies conducted by M Sharma[6] (260.3 U/L), Purna Chandra[1] (271.4 U/L) and Ankur Banik[8] (280.9 U/L). Mean CSF LDH in Tubercular meningitis is 177.1 U/L which is comparable with the studies conducted by M Sharma[6] (190.4 U/L), Ankur Banik[8] (192.1 U/L) and Purna Chandra[1] (199.7 U/L). Mean CSF LDH in Viral meningitis is 124.8 U/L which is not comparable with the studies conducted by M Sharma[6] (49.5 U/L). Mean CSF LDH in Cryptococcal meningitis is 228.5 U/L which is not comparable with other studies. In present study mean CSF CK in bacterial meningitis is 90.3 U/L which is comparable with the studies conducted by Ankur Banik[8] (88.76 U/L) and Purna Chandra[1] (87.1 U/L). Mean CSF CK in tubercular meningitis is 63.8 U/L which is comparable with the studies conducted by Purna Chandra[1] (51.8 U/L) and Ankur Banik[8] (50.9 U/L). Mean CSF CK in Viral meningitis is 50.1 U/L which is comparable with the study conducted by Ankur Banik[8] (39.6U/L). Mean CSF CK in Cryptococcal meningitis is 77.6 U/L which is not comparable with the studies. There was a strong positive correlation between serum and CSF levels of CK and this was statistically significant.

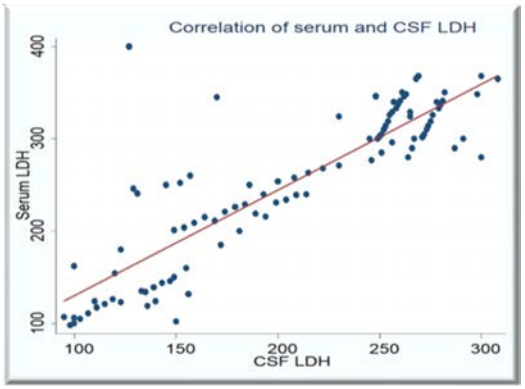

Fig. 1: Correlation of Serum and CSF LDH Levels

There was a strong positive correlation between serum and CSF levels of CK and this was statistically significant.

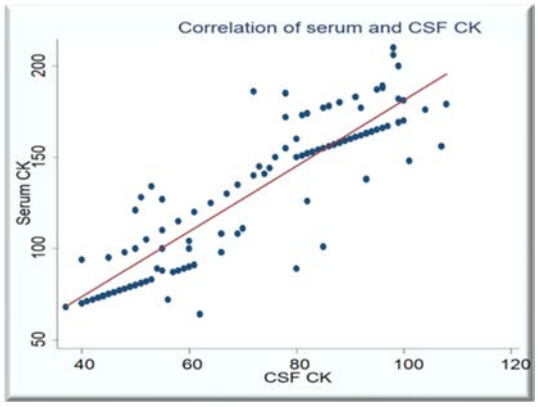

Fig. 2: Correlation of Serum and CSF CK Levels

Limitations of present study were small sample size, hospital based study, CSF LDH and CK levels were not compared with the prognosis and mortality. CSF LDH and CK iso enzyme estimation was not done. No control group. Long term follow up was not done.

CONCLUSION

Enzymes LDH, CK, are detectable in CSF in patients with meningitis. Estimation of these LDH, CK will help in the diagnosis of meningitis along with other parameters like CSF cell count, glucose, proteins. The present study showed the elevation of the CSF LDH level from the baseline. CSF LDH levels are more in bacterial meningitis followed by cryptococcal, tubercular and viral meningitis. The present study showed the elevation of the CSF CK level from the baseline. CSF CK levels are more in bacterial meningitis followed by cryptococcal, tubercular and viral meningitis. There was strong positive correlation between serum and CSF level of LDH and CK.

Conflict of Interest: None to declare.

Source of Funding: Nil.

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