Original Article

Nepal Journal of Neuroscience 2025;22(1): 33-35

Laboratory analysis of CSF among patients admitted in Neurosciences department in a tertiary care hospital

Manisha Sharma[1], Beena Jha[2], Manisha Chapagain[3], CP Bhatt[4], Bidur KC[5]

[1,2,3,4,5] Kathmandu Medical College and Teaching Hospital, Sinamangal, Kathmandu, Nepal

Date of Submission: 15th January 2025 Date of Acceptance: 20th February 2025 Date of Publication: 15th May 2025

Abstract

Introduction: Cerebrospinal fluid evaluation is the single most important aspect of the laboratory diagnosis of meningitis. Analysis of the Cerebrospinal fluid abnormalities along with evaluation of biomarkers like Lactate dehydrogenase (LDH) and Adenosine deaminase (ADA) produced in bacterial, mycobacterial, and infections may greatly facilitate diagnosis and direct initial therapy.

Materials and Methods: A prospective, descriptive cross-sectional study was done in a tertiary care hospital from 15th August-15th November, 2024 after obtaining ethical clearance. 65 patients who met the inclusion criteria and consented to participate were included in the study. Cerebrospinal fluid was collected aseptically and processed for biochemical analysis including estimation of LDH and ADA, cytology, Gram's staining and culture using standard techniques. The data obtained were computed and analyzed using Statistical Package for Social Sciences 20.0 Version.

Results: Total of 65 patients were enrolled and their Cerebrospinal fluid was analyzed, among which, 19 were diagnosed as bacterial meningitis, 7 as tubercular meningitis and 39 as viral meningitis. CSF ADA was 23.91±15.37 U/L (Mean±SD) in the tubercular meningitis group. p value of ADA was significant in tubercular meningitis when a cut off value of 10 U/L was taken. The mean LDH value in bacterial meningitis was 234.26±155.45 U/L (Mean±SD). p-value of LDH in bacterial meningitis was significant.

Conclusions: CSF biomarkers such as lactate dehydrogenase and adenosine deaminase are simple, rapid and effective diagnostic tools in differentiating the etiology of meningitis. Elevated CSF LDH levels are indicative of bacterial meningitis, whereas significantly increased CSF ADA levels are characteristic of tuberculous meningitis (TBM).

Key words: Adenosine Deaminase, Bacterial Meningitis, Cerebrospinal Fluid, Tuberculous Meningitis

Introduction

Meningitis is defined as inflammation of the meninges and subarachnoid space.[1] The pathogens implicated in meningitis include bacteria, viruses, fungi and some parasites.[2] Rapid identification of the etiology of meningitis is utmost for the therapeutic management of the disease.

Bacterial meningitis (BM) has high mortality and morbidity globally, leading to 1.6 million years lived with disability yearly.[1] Direct examination of CSF or bacterial antigen detection in CSF is employed for immediate identification of BM; however, these have low sensitivity.[3] Currently, diagnosis of bacterial meningitis in developing countries is based on microscopical examination followed by culture of CSF. However, only 30-60% of the cases are positive for pyogenic meningitis in CSF culture.[4]

Adenosine deaminase (ADA) is an enzyme present in body cells and is involved in purine catabolism and the cell-mediated immune (CMI) response related to T-lymphocyte activation.[5] An increased CSF ADA level can be correlated with Tb and other bacterial infections which involve a cellular immune response.

Lactic dehydrogenase (LDH) is an intracellular enzyme released from damaged cells. CSF LDH level mirrors the amount of damage sustained by cells in the central nervous system.[6] Higher levels of CSF LDH are associated with bacterial meningitis.

Several CSF biomarkers have been used to differentiate acute BM, TBM and VM by various investigators since prompt and precise etiological diagnosis of meningitis remains a challenge. The objective of this study was to compare the differentiating ability of biomarkers (LDH, ADA) on the etiological diagnosis of meningitis.

METHODS

A descriptive cross-sectional study was done in a tertiary care hospital from 15th August- 15th November, 2024. Ethical clearance was obtained from the Institutional Review

Access this article online

Website: https://www.nepjol.info/index.php/NJN

DOI: 10.3126/njn.v22i1.74070

HOW TO CITE
Sharma M, Jha B, Chapagain M, Bhatt CP, KC B. Laboratory analysis of CSF among patients admitted in Neurosciences department in a tertiary care hospital.NJNS. 2025;22(1):33-35

Address for correspondence:
Manisha Sharma
Kathmandu Medical College and Teaching Hospital
Sinamangal, Kathmandu, Nepal
Email: manishasharma84@yahoo.com

ISSN: 1813-1948 (Print), 1813-1956 (Online)

Committee with reference no. 12082024/07. Patients admitted to the Neurosciences department with a clinical diagnosis of meningitis, and providing written, informed consent for participation in the study were included in this study. Patients aged less than 14, from whom inadequate sample was collected, had hemorrhagic lumbar puncture or xanthochromic CSF were excluded from the study as hemolysis leads to elevated CSF LDH and ADA.

The demographic profile of the patient and clinical presentations were noted in a preformed proforma.

Sample size (n) was calculated with a prevalence of 8.2%7 using formula n = Z2 x p x q/e2

Hence, n = minimum number of sample size required= 59

After obtaining informed consent from patients meeting the inclusion criteria, a lumbar puncture was performed and CSF sample was immediately transported to the laboratory in 3 different vials.

A convenient sampling method was used and a total of 65 patients were enrolled in the study.

CSF samples collected from patients were further subjected to biochemical analysis, cytology and Gram's stain and culture using standard techniques. Bacterial meningitis was defined when CSF findings showed positive gram stain or culture reports, with neutrophilic predominance, CSF: serum glucose ratio < 0.4 and CSF protein concentration >45 mg/dl. The cases were categorized as tubercular meningitis when CSF AFB stain and mycobacterial culture were positive, CSF: serum glucose ratio < 0.4, had elevated WBCs in CSF with lymphocytic predominance along with greatly elevated CSF protein. Similarly, cases were labeled as viral meningitis when Gram, Z-N staining, and culture were negative, CSF: serum glucose ratio was low to normal, had mildly elevated WBCs in CSF with lymphocytic predominance along with normal to mildly elevated CSF protein.[8]

Further estimation of CSF ADA and LDH levels was done. A cutoff reference value of >10 U/L CSF ADA was considered significant as per standard guidelines.

The data obtained were computed and analyzed using Statistical Package for Social Sciences 20.0 Version using descriptive statistics (independent sample t-test, one-way ANOVA) with a 95% confidence interval. A p-value of <0.05 was considered statistically significant

Results

A total of 65 patients meeting the inclusion criteria were enrolled and their CSF sample was analyzed, among whom, 19 were diagnosed with pyogenic meningitis, 7 with tubercular meningitis and 39 with viral meningitis. (Table 1)

Table 1. Demographic profile of patients (n=65)

Study group	No. of patients	Age (years) (Mean±SD)	Gender (M:F)
Pyogenic meningitis	19	34±14.21	1.23:1
Tubercular meningitis	7	38.2±16.33	1.32:1
Viral meningitis	39	29.9±17.30	1.64:1

Table 2 presents the cerebrospinal fluid (CSF) levels of adenosine deaminase (ADA) and lactate dehydrogenase (LDH) in patients diagnosed with pyogenic, tuberculous, and viral meningitis. The analysis included 65 patients, and the results indicate significant differences among the three groups.

Patients with tuberculous meningitis (TBM) exhibited markedly elevated CSF ADA levels (Mean±SD: 23.91 ± 15.37 U/L), significantly higher than those observed in pyogenic meningitis (4.01 ± 2.02 U/L) and viral meningitis (2.19 ± 1.64 U/L).

Conversely, CSF LDH levels were highest in pyogenic meningitis (Mean±SD: 234.26 ± 155.45 U/L), significantly exceeding the levels seen in tuberculous meningitis (91.71 ± 39.31 U/L) and viral meningitis (26.27 ± 13.63 U/L).

The difference between CSF ADA levels and CSF LDH levels were found to be statistically significant (P-value <0.01) between the pyogenic, tubercular and viral meningitis groups. (Table 2)

Table 2. Laboratory findings of CSF (n=65)

Lab parameter	CSF ADA (U/L) (Mean±SD)	CSF LDH (U/L) (Mean±SD)	P-value
Pyogenic meningitis	4.01±2.02	234.26±155.45	<0.01
Tubercular meningitis	23.91±15.37	91.71±39.31	
Viral meningitis	2.19±1.64	26.27±13.63	

Discussion

Early recognition of meningitis and its etiology is crucial for instituting appropriate therapeutical management. Many studies have highlighted the potential role of different biomarkers in initial diagnosis; however, there is no consensus on which to prioritize and its best utilization.

ADA activity in body fluids (pleural, peritoneal and CSF) has shown a potential to be a valuable marker for diagnosing extrapulmonary Tb.[9] ADA is an enzyme present in most body cells, playing a crucial role in purine catabolism and cell-mediated immune (CMI) response, through its involvement in T-lymphocyte activation.4 In a meta-analysis by Pormohammad A. et al., the sensitivity and specificity of CSF ADA for diagnosing TBM were reported to be 89 and 91%, respectively. [10]

This study showed CSF ADA levels (Mean±SD) in pyogenic meningitis, tubercular meningitis and viral meningitis to be 4.01±2.02, 23.91±15.37 and 2.19±1.64 U/L respectively (p <0.001). The cutoff value of 10 U/L was taken in this study. These findings align with previous researches which have reported ADA levels to be high in TBM compared to BM and VM with a mean value of ADA in TBM to be 16.46±6.24, 14.14 ±7.44 U/L.[9,11] These findings suggest that ADA is a useful biomarker for distinguishing TBM from other types of meningitis due to its association with the immune response to Mycobacterium tuberculosis.

LDH is an intracellular enzyme released upon cellular damage, the level of which indicates the extent of damage in the CNS.6 High levels of CSF LDH are associated with bacterial meningitis and viral meningoencephalitis.[12]

In our study, CSF LDH levels (Mean±SD) in pyogenic meningitis, tubercular meningitis and viral meningitis were 234.26±155.45, 91.71±39.31and 26.27±13.63 U/L respectively ($p< 0.001$). Other similar studies have revealed higher levels of CSF LDH to be associated with PM (271.4 ± 80.07, 94.1 U/L).[4,12] The elevated LDH levels in pyogenic meningitis likely reflect extensive tissue damage and neutrophilic inflammation.

CSF LDH levels for TBM cases were reported to be quite high in some of the studies (307.69± 61.57, 230.5 U/L) [4,13] while others reported it to be (119.9 U/L, 114.45±47.58 U/L) [12,14] , which albeit higher, is closer to the levels observed in our study (91.71±39.31U/L). The lower levels observed in our study could be attributable to lesser number of TBM cases in our study.

The CSF ADA and CSF LDH levels can be used in rapid screening for differentiation of various types of meningitis. However, it is essential to interpret these findings in conjunction with the patient's history and clinical presentation to ensure accurate diagnosis and effective treatment planning.

Conclusion

Our findings indicate that cerebrospinal fluid (CSF) lactate dehydrogenase (LDH) levels are significantly elevated in bacterial meningitis compared to aseptic meningitis. Similarly, CSF adenosine deaminase (ADA) levels show a marked increase in cases of tuberculous meningitis (TBM). These biomarkers offer a rapid and simple diagnostic tool that can significantly aid in the etiological diagnosis of meningitis.

References

1. Van de Beek D, Brouwer M, Hasbun R, Koedel U, Whitney CG, Wijdicks E. Community-acquired bacterial meningitis. Nat Rev Dis Primers. 2016 Nov 3;2:16074. https://doi.org/10.1038/nrdp.2016.74
2. Koskiniemi M, Rantalaiho T, Piiparinen H, Röyttä M, Vaheri A. Infections of the central nervous system of suspected viral origin: A collaborative study from Finland. J Neurovirol. 2001;7(5):400-408. https://doi.org/10.1080/135502801753170255
3. Viallon A, Desseigne N, Marjollet O, Birynczyk A, Belin M, Guyomarch S, Borg J, Pozetto B, Bertrand JC, Zeni F. Meningitis in adult patients with a negative direct cerebrospinal fluid examination: value of cytochemical markers for differential diagnosis. Crit Care. 2011;15(3):R136. https://doi.org/10.1186/cc10254
4. Dash PC, Patro D. Role of CSF CK, LDH, GGTP Enzyme Levels in Diagnostic and Prognostic Evaluation of Meningitis. Journal of Clinical and Diagnostic Research: JCDR. 2014 Jul;8(7):MC19-22. https://doi.org/10.7860/JCDR/2014/.4615
5. Song J, Kim SH, Jung YR, Choe J, Kang CI, Min JH. 10-Year Retrospective Review of the Etiologies for Meningitis With Elevated Adenosine Deaminase in Cerebrospinal Fluid: Etiologies Other Than TB. Front Cell Infect Microbiol. 2022 Jul 5;12:858724. https://doi.org/10.3389/fcimb.2022.858724
6. Jakka SR, Veena S, Atmakuri RM, Eisenhut M. Characteristic abnormalities in cerebrospinal fluid biochemistry in children with cerebral malaria compared to viral encephalitis. Cerebrospinal Fluid Res. 2006 Jun 9;3:8. https://doi.org/10.1186/1743-8454-3-8
7. Sharma S, Acharya J, Caugant D, Thapa J, Bajracharya M, Kayastha M, Sharma S, Chalise B, Karn R, Banjara M, Ghimire P, Singh A. Meningococcal meningitis: A multicentric hospital-based study in Kathmandu, Nepal. Open Microbiol J. 2019;13:27-33. http://dx.doi.org/10.2174/1874285801913010273
8. Hrishi AP, Sethuraman M. Cerebrospinal Fluid (CSF) Analysis and Interpretation in Neurocritical Care for Acute Neurological Conditions. Indian J Crit Care Med. 2019 Jun;23(Suppl 2): S115-S119. https://doi.org/10.5005/jp-journals-10071-23187
9. Chander A, Shrestha CD. Cerebrospinal fluid adenosine deaminase levels as a diagnostic marker in tuberculous meningitis in adult Nepalese patients. Asian Pac J Trop Dis. 2013 Feb;3(1):16–9. https://doi.org/10.1016/S2222-1808(13)60004-3
10. Pormohammad A, Riahi SM, Nasiri MJ, Fallah F, Aghazadeh M, Doustdar F, Pouriran R. Diagnostic test accuracy of adenosine deaminase for tuberculous meningitis: A systematic review and meta-analysis. J Infect. 2017 Jun;74(6):545-554. https://doi.org/10.1016/j.jinf.2017.02.012
11. Belagavi AC, Shalini M. Cerebrospinal fluid C reactive protein and adenosine deaminase in meningitis in adults. J Assoc Physicians India. 2011 Sep;59:557-60. PMID: 22334968.
12. Anita SP, Legha R, Manu PS. The role of CSF LDH estimation is to differentiate different types of meningitis. JSCMR. 2017;05: 32056-70. https://dx.doi.org/10.18535/jmscr/v5i12.128
13. Lee SA, Kim SW, Chang HH, Jung H, Kim Y, Hwang S, Kim S, Park HK, Lee JM. A new scoring system for the differential diagnosis between tuberculous meningitis and viral meningitis. J Korean Med Sci. 2018 Jun;33(31):e201. https://doi.org/10.3346/jkms.2018.33.e201
14. Jalees SS, Hussain ST. Adenosine deaminase and lactate dehydrogenase levels in serum and cerebrospinal fluid of patients with tuberculous meningitis. Int J Clin Biochem Res. 2020;7(3):411-415. https://doi.org/10.18231/j.ijcbr.2020.088