

CSF LACTATE IN MENINGITIS

Anjampakuthikal Aboobekar Haris¹, Rajeev Abraham², Jacob George³

¹Assistant Professor, Department of Neurology, Government Medical College, Kottayam, Kerala.

²Resident, Department of Medicine, Government Medical College, Kottayam, Kerala.

³Professor, Department of Neurology, Government Medical College, Kottayam, Kerala.

ABSTRACT

BACKGROUND

Meningitis is an infection within the subarachnoid space characterised by a CNS inflammatory reaction. It is a serious condition requiring immediate diagnosis and appropriate treatment to be started at the earliest to prevent mortality as well as irreversible neurological deficits. CSF lactate has been found useful in differentiating bacterial meningitis from viral meningitis in many studies in the western population, but studies in Indian population are limited.

The aim of the study is to study whether CSF lactate can be used to distinguish bacterial from viral meningitis and to study the levels of CSF lactate in tuberculosis meningitis.

MATERIALS AND METHODS

This was a descriptive study conducted in a tertiary care hospital. In this study, 78 cases of meningitis were selected. Cases are patients with bacterial, viral or tuberculosis meningitis admitted to the hospital under the Department of Medicine and Neurology. Cases are grouped into bacterial, viral and tuberculosis meningitis based on clinical picture, CSF analysis and imaging characteristics. CSF lactate estimation was done by dry chemistry method. Using appropriate statistical methods and SPSS software, CSF lactate levels were compared among these groups and analysed for any association with the final outcome.

RESULTS

The levels of CSF lactate in bacterial meningitis were higher than viral meningitis with a statistical significance of $p < 0.0001$. The sensitivity and specificity of CSF lactate > 35 mg/dL for bacterial meningitis in this study was 95% and 100% respectively and the positive predictive value was 100% and the negative predictive value was 96%. The mean CSF lactate values in bacterial, viral and tuberculosis meningitis were 124.40 ± 35.85 mg/dL, 24.34 ± 6.05 mg/dL and 50.13 ± 9.89 mg/dL, respectively.

CONCLUSION

CSF lactate level was significantly elevated in bacterial meningitis than tuberculosis or viral meningitis and can be used as a marker for differentiating bacterial from viral meningitis.

KEYWORDS

CSF Lactate, Meningitis.

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BACKGROUND

Meningitis is an inflammatory response of the leptomeninges or the pia-arachnoid and the underlying subarachnoid CSF produced by infections with bacteria, viruses, fungi, parasites and various noninfectious causes.¹ Differentiating acute bacterial and viral meningitis is not always easy. Combination of present CSF variables (proteins, glucose, leucocytes count and ratio of CSF/serum glucose) has been suggested effective in differentiating acute viral meningitis from bacterial meningitis. However, there are serious

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Corresponding Author:

Dr. Anjampakuthikal Aboobekar Haris,

*Assistant Professor, Department of Neurology,
Government Medical College, Kottayam, Kerala.*

E-mail: dr_aaharis@yahoo.com

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limitations of the above variables in diagnosing and differentiating bacterial and viral meningitis.² The CSF lactate concentration has been suggested as a useful parameter to differentiate bacterial from viral meningitis.³ Key goals of early management are to emergently distinguish between these conditions and identify the responsible pathogen and to initiate appropriate antimicrobial therapy.⁴ There are different methods to identify the onset of meningitis and to distinguish between different causative agents like CSF analysis and imaging modalities like Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) scan. CSF analysis includes Total Count (TC), Differential Count (DC), protein, sugar, Gram staining, culture and sensitivity, Acid-Fast Bacilli (AFB) staining, Adenosine Deaminase (ADA), etc. But, these variables have several limitations.⁵ Current microbiological investigations are highly specific, but less sensitive, so they are not much dependable in clinical decision making. So, many markers have been investigated like CSF C-reactive



protein, inflammatory cytokines, cortisol, lactate dehydrogenase, lactate, etc. However, a sensitive laboratory test, which is easy to perform and cost-effective is still required. CSF lactate has been found to be useful in differentiating bacterial meningitis from viral meningitis in many studies in the western population, but studies in Indian population are limited. Hence, CSF lactate is being investigated as it is relatively affordable to patients.

MATERIALS AND METHODS

This is a descriptive study conducted in Medicine and Neurology Departments of Government Medical College, Kottayam, Kerala, India. All suspected cases of meningitis having clinical features of fever, headache and signs of meningeal irritation were assessed with detailed history, general and neurological examination followed by computed tomography of brain and CSF study after obtaining consent. Patients were evaluated according to the proforma and cases were divided into bacterial, viral and tuberculous meningitis groups based on the following criteria.

Bacterial Meningitis³

Acute onset symptoms with any of the following- Fever, headache or neck stiffness and CSF showing-

1. Neutrophilic pleocytosis (10-10,000 cells/mm³).
2. Raised protein (>45 mg/dL).
3. Low sugar (<40 mg/dL or less than 40% of the blood glucose concentration). With Gram stain positivity.

Viral Meningitis⁶

- Lymphocytic pleocytosis (25-1000 cells/mm³).
- Protein 20-80 mg/dL.
- Normal sugar (>40 mg/dL).

Tuberculous Meningitis⁷

Insidious onset symptoms with any of the following- Fever, headache or neck stiffness and CSF showing-

- Lymphocytic pleocytosis (10-1000 cells/mm³).
- Protein >45 mg/dL.
- Sugar <40 mg/dL or less than 40% of the blood glucose concentration.
- High ADA (>10).
- With positive AFB staining.
- Neuroimaging- Normal or meningeal enhancement, basal exudates or tuberculoma.

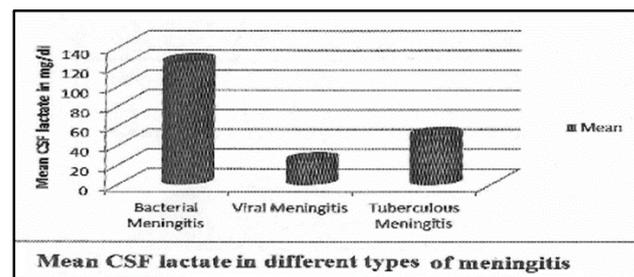
Final outcome was defined as whether the patient died during the hospital stay (expired) or was cured and discharged from the hospital (recovered). Then, CSF lactate levels were analysed for any association using statistical methods. Fresh sample of CSF collected in sterile CSF vials by lumbar puncture were subjected for CSF lactate estimation by dry chemistry method. The normal reference range was chosen as provided by the laboratory. Data was entered in Microsoft (MS) Excel and analysed using Statistical Package for Social Sciences or SPSS version 22. Descriptive statistical analysis has been carried out in this study. Results of continuous measurements are presented

on Mean ± SD and results on categorical measurements are presented in number or percentage. Significance of association will be analysed by calculating p value and a p value of <0.05 is taken as significant. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated to know the diagnostic performance of lactate in relation to the types of meningitis.

RESULTS

A total of 78 patients fulfilled inclusion criteria for meningitis. Most number of cases studied were tubercular followed viral and bacterial meningitis with a percentage distribution of 42%, 32%, 26%, respectively. Among different groups, 60% of viral meningitis, 51% of tubercular and 45% of bacterial meningitis were female. Among the total cases, most of the cases occurred in the younger age groups mainly 18-30 years and 31-45 age groups. Most of the TB meningitis occurred in older age groups. Fever, headache and altered sensorium were the most common presenting symptoms and majority of patients had signs of meningeal irritation.

In bacterial meningitis, majority of cases had CSF total counts of >1000, while in tubercular and viral meningitis. Majority had a count of <500. All cases of bacterial meningitis had predominance of neutrophils (>50%) and more than half had neutrophils greater than 80% of the total cell count, while both viral and tuberculous meningitis had predominant lymphocytes. The mean value of CSF lactate in bacterial meningitis group were significantly higher than viral meningitis (124.40 ± 35.85 mg/dL vs. 24.34 ± 6.05 mg/dL). In TB meningitis group, also CSF lactate was moderately elevated (50.13 ± 9.89 mg/dL).



Graph 1

Type of meningitis	Mean ± SD of CSF lactate in mg/dl
Bacterial Meningitis	124.40±35.85
Viral Meningitis	24.34±6.05
Tuberculous Meningitis	50.13±9.89
Mean ± SD of CSF lactate in different types of meningitis	

Table 1

Lactate* Type of Meningitis	Between Groups	Combined	Mean Square	F	Sig.
			58946.772	155.561	0.0001
		Within Groups	378.931		
ANOVA Table of CSF Lactate and type of meningitis					

Table 2

DISCUSSION

An immediate and accurate diagnosis is the most important factor in the decision making and treatment of acute meningitis since bacterial meningitis is a serious condition associated with significant mortality and morbidity in the form of permanent neurological deficits.⁸ Gram stain of CSF is less reliable since bacteria are usually present only in low quantity. Culture and sensitivity is also not very sensitive and is also time consuming. So, many other markers have been investigated by many to find a reliable one that can differentiate bacterial from viral meningitis in quick and accurate way.⁹ CSF lactate has been studied by many investigators in this respect. The present study was conducted in 78 patients with meningitis admitted to Government Medical College Hospital, Kottayam. Patients with conditions in exclusion criteria were excluded from the study in order to obtain a group of patients without any other factors contributing to the elevation of CSF lactate values. In our study, CSF lactate has been found to be a sensitive indicator in differentiating bacterial from viral meningitis. All cases with bacterial meningitis were correctly identified except one, when the cutoff value of CSF lactate was taken as 35.0 mg/dL. The mean CSF lactate levels of bacterial meningitis were significantly higher than that of viral meningitis. The mean level of CSF lactate in bacterial meningitis group was 124.40 ± 35.85 mg/dL while that in viral meningitis group were 24.34 ± 6.05 mg/dL and the association was statistically significant with p value of <0.0001 . The sensitivity and specificity of CSF lactate in diagnosing bacterial meningitis in this study was 95% and 100%, respectively. The positive predictive value was 100% and the negative predictive value was 96%. This study showed comparable result with respect to the following studies. In a retrospective study of 78 cases of adult meningitis by Genton B et al in Vaudois University Hospital, Switzerland, the CSF lactate was determined in patients with bacterial and viral meningitis. The median CSF lactate level among the 25 bacterial cases amounted to 13.6 mmol/L (range- 3.5-24.5) or 122.4 mg/dL (range- 31.5-220.5), whereas it remained low in the 28 viral cases- 2.7 mmol/L (range- 1.4-4.2) or 24.3 mg/dL (range- 12.6-24.5) and the differences were highly significant.¹⁰ In comparison with the other routine tests in CSF, lactate showed the highest sensitivity, specificity and predictive values. Alain Viallon et al, de Saint-Etienne University Hospital, France, showed that most highly discriminative parameters for the differential diagnosis of bacterial meningitis proved to be CSF lactate with a sensitivity of 94%, a specificity of 92%, a negative predictive value of 99%, a positive predictive value of 82% at a diagnostic cutoff level of 3.8 mmol/L, (Area Under the Curve (AUC), 0.96; 95% Confidence Interval (CI), 0.95 to 1).⁹ In this study, a high CSF lactate value was found to be associated with adverse outcome with a p value less than 0.00021 and is highly significant and the results are similar to that observed by Ali Hassan Abro et al,^{11,12} Klein et al and Robert et al also reported that the CSF lactate level has higher reliability than the other CSF tests in diagnosing and differentiating bacterial meningitis from viral meningitis.^{2,13}

The mean CSF lactate value in tuberculous meningitis group was 50.13 ± 9.89 mg/dL. With a significant p value, Lok Ming Tang studied lactate levels in the cerebrospinal fluid (CSF) in 21 patients with culture-proved Tuberculous Meningitis (TBM). All patients showed uniformly high lactate level (>3.9 mmol/L),¹⁴ neither the clinical stage of TBM nor the prognosis was related to the CSF lactate concentration.

CONCLUSION

1. CSF lactate level is markedly elevated in bacterial meningitis than viral meningitis and it can be used to distinguish bacterial meningitis from viral meningitis.
2. The mean CSF lactate level in tuberculosis meningitis was moderately elevated.

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