

CSF lactate level: a useful diagnostic tool to differentiate acute bacterial and viral meningitis

Ali Hassan Abro, Ahmed Saheh Abdou, Abdulla M Ustadi, Ahmed Alhaj Saleh, Nadeem Javeed Younis, Wafa F Doleh
Infectious Disease Department, Rashid Hospital Dubai, United Arab Emirates.

Abstract

Objectives: To evaluate the potential role of CSF lactate level in the diagnosis of acute bacterial meningitis and in the differentiation between viral and bacterial meningitis.

Methods: This was a hospital based observational study, conducted at Infectious Diseases Unit, Rashid Hospital Dubai, United Arab Emirates, from July 2004 to June 2007. The patients with clinical diagnosis of acute bacterial meningitis and who had CSF Gram stain / culture positive, CSF analysis suggestive of bacterial meningitis with negative Gram stain and culture but blood culture positive for bacteria and patients with clinical diagnosis suggestive of viral meningitis supported by CSF chemical analysis with negative Gram stain and culture as well as negative blood culture for bacteria were included in the study. CT scan brain was done for all patients before lumbar puncture and CSF and blood samples were collected immediately after admission. CSF chemical analysis including lactate level was done on first spinal tap. The CSF lactate level was tested by Enzymatic Colorimetric method.

Results: A total 95 adult patients of acute meningitis (53 bacterial and 42 viral) fulfilled the inclusion criteria. Among 53 bacterial meningitis patients, *Neisseria meningitidis* were isolated in 29(54.7%), *Strept.Pneumoniae* in 18(33.96%), *Staph.Aureus* in 2(3.77%), *Klebsiell Pneumoniae* in 2(3.77%), *Strept.Agalactiae* in 1(1.8%) and *E.Coli* in 1(1.8%). All the patients with bacterial meningitis had CSF lactate >3.8 mmol/l except one, whereas none of the patients with viral meningitis had lactate level >3.8 mmol/l. The mean CSF lactate level in bacterial meningitis cases amounted to 16.51 ± 6.14 mmol/l, whereas it was significantly lower in viral group 2.36 ± 0.6 mmol/l, $p < .0001$.

Conclusion: CSF lactate level was significantly high in bacterial than viral meningitis and it can provide pertinent, rapid and reliable diagnostic information. Furthermore, CSF lactate level can also differentiate bacterial meningitis from viral one in a quick and better way (JPMA 59:508; 2009).

Introduction

Meningitis is a serious public health problem demanding early diagnosis, effective treatment, prevention and control. 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.¹ However, there are serious limitations of the above variables in diagnosing and differentiating bacterial and viral meningitis. The CSF lactate concentration is a useful parameter to differentiate bacterial from viral meningitis.² CSF lactate is produced by anaerobic metabolism and the level increases in any condition which causes decrease in oxygen supply to the brain and there is no correlation with serum lactate level.³ CSF lactate in bacterial meningitis originates from different sources. Bacterial pathogens themselves produce varying amounts of lactate; accounting for 10% of the total CSF lactate.⁴ Bacterial meningitis is associated with generalized brain

oedema, causing a reduction of global cerebral blood flow and inflammatory involvement of vasculature, with loss of autoregulatory mechanisms, vasospasm and thrombosis. This leads to cerebral ischaemia and consequently to glycolysis by means of anaerobic metabolism.⁵ In addition, cytokines that flood the brain in meningitis, reduce tissue oxygen uptake and cause a shift toward anaerobic metabolism, thus increasing lactate production. Cytokines also mediate invasion of neutrophils into the subarachnoid space, which may also contribute to the rise in CSF lactate level by glycolysis in bacterial meningitis.⁶ The CSF lactate level of 3.5 mmol/l or greater has been considered by the some authors superior to the other CSF tests to diagnose and differentiate bacterial and viral meningitis.⁷ However, the other investigators are of the opinion that the elevated CSF level is a non specific finding and occurs in number of diseases such as meningitis, hypoxic cerebral injury, subarachnoid haemorrhage and head injury.⁸ The purpose of this study was to report our findings with emphasis on CSF lactate level in adult population and to discuss the

usefulness of the test to differentiate bacterial from viral meningitis.

Patients and Methods

This hospital based study was conducted from July 2004 to June 2007 in the Infectious Diseases Unit of Rashid Hospital Dubai, UAE. Rashid Hospital is one of the biggest tertiary hospitals of Dubai accredited by Joint Commission International (JCI). A separate proforma was filled for each case entered into the study. The demographics and data about clinical features and laboratory results of the cases were entered in each proforma separately. CT scan brain was done for all (95) patients before the lumbar puncture. The CSF analysis was done on the first spinal tap and it included lactate, protein, glucose, cell count, Gram's stain and culture. CSF lactate level was done by Enzymatic Colorimetric method by Hitachi 912 machines, 1.6-2.4 mmol/L was taken as reference range as standardized by Roche in adults. Other laboratory investigations including liver function test (LFTs), full blood count (FBC), blood sugar, blood culture, coagulation profile and urea electrolytes were also done for all patients. CSF viral profile was performed in a few patients.

The inclusion criteria were: Patients with clinical diagnosis of meningitis and CSF Gram's staining and/or culture positive for bacteria. Patients with clinical and CSF chemical analysis findings suggestive of bacterial meningitis with negative Gram's staining and culture but blood culture positive for bacteria. Patients with clinical diagnosis of suspected viral meningitis. The diagnosis of viral meningitis was established by clinical and laboratory criterion, including appropriate history and physical examination and it was defined as a positive result on viral culture, serological testing or PCR. If viral meningitis was not proven, the criteria for probable viral meningitis were clear CSF with inflammatory reaction, negative CSF Gram stain and culture, negative blood culture for bacteria and favourable evolution of the disease without antibiotic treatment.⁹

Exclusion criteria were: Patients who received antibiotics before presenting to the hospital, clinically suspected and CSF changes suggestive of bacterial meningitis but CSF Gram's staining, culture and blood culture negative and these patients were treated for bacterial meningitis. Patients with suspected or confirmed Tuberculosis and fungal meningitis. Patients with concomitant illness such as HIV/on immunosuppressive therapy, Conditions which can contribute in elevation of CSF lactate such as recent stroke, brain hypoxia/ anoxia, brain trauma and seizures.

The patients with bacterial meningitis received empirically Ceftriaxone 2gm BD, Vancomycin 1gm BD and

Dexamethasone 10mg QID and antibiotic continued or changed according to report of culture and sensitivity. Dexamethasone was continued for four days in Streptococci Pneumoniae meningitis. Patients with Streptococci Pneumoniae received antibiotic for 10-14 days whereas patients with Meningococci were given antibiotic for 7-10 days. Majority of the viral meningitis patients were treated symptomatically, however, a small number of confirmed or suspected cases of varicella-zoster or herpes simplex viruses received Acyclovir for 7-10 days. Data was analyzed by SAS Enterprise Guide 4.1. Statal analyses included descriptive statistics, bivariate analysis i.e., t-test, chi-square and Analysis of Variance (ANOVA). A p value of <.05 was taken as significant for all statistical analysis.

Results

A total of 95 (53 bacterial and 42 viral) patients fulfilled the inclusion criteria. The mean age of the patients under study was 34 ± 11.5 years range 15-70 years and there was male predominance, males 80 (84.21%) vs females 15 (15.78%). Majority of the patients were expatriates who visited or lived in the UAE. Out of 95 patients; 48 (50.1%) were Indian, 15 (15.7%) UAE nationals, 9 (9.47%) Bangladeshi, 7 (7.36%) Pakistani and 16 (16.84%) were other nationals. Fever, headache and altered sensorium were the most common presenting symptoms and majority of the patients had positive signs of meningeal irritation. Among 53 confirmed bacterial meningitis patients; Meningococci were isolated in 29 (54.7%), Strep.Pneumoniae in 18 (33.96%), Staph.Aureus in 2 (3.77%), Klebsiella Pneumoniae in 2 (3.77%), Strept. Agalactiae in 1 (1.8%) and E.Coli in 1 (1.8%) (Figure-1). The CSF Gram's staining and/or culture was positive in 49 (92.45%) and negative in 4 (7.54%) but blood culture was positive in these patients.

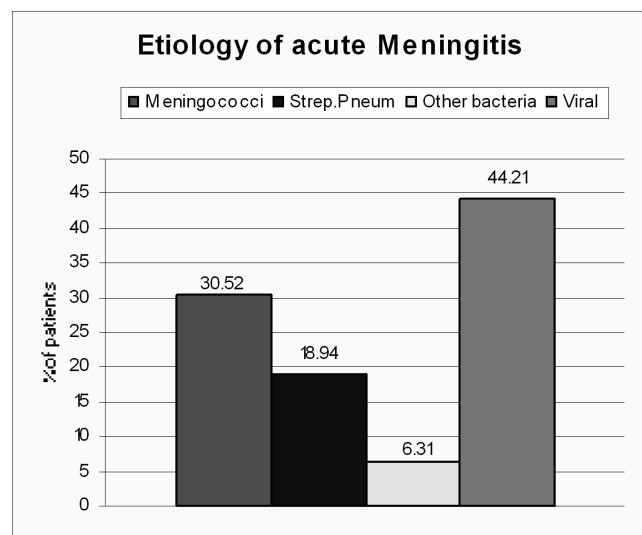


Figure-1: Etiological distribution of 95 patients with acute meningitis.

Overall blood culture was negative in 38 (71.6%) but positive in 15 (28.3%) patients. There were 42 patients who fulfilled the criteria for viral meningitis. The CSF viral studies were done for 12 patients who revealed herpes simplex virus in 3, varicella -zoster virus in 2, enterovirus in 2 and adenovirus in one patient.

The CSF analysis showed, all patients with bacterial meningitis had lactate level more than 3.8 mmol/L except one patient who had CSF lactate 1.6 mmol/L, whereas of patients with viral meningitis, none had CSF lactate ≥ 3.8 mmol/l (Table). In comparison to viral meningitis, bacterial

Table: CSF lactate level (Mean±SD) in acute Bacterial and Viral Meningitis.

Etiology	No. of cases	Lactate-Mean±SD	(Range-mmol/l)
Nisseria Meningitides	29	17.03 ± 7.9	(1.6-35.5)
Strepto. Pneumoniae	18	17.02 ± 6.8	(9.1-29)
Staph. Aureus	2	7.6	(7.2-8)
Klebseilla Pneumoniae	2	14.5	(8.2-20.8)
Strepto. Agalactiae	1	15.9	
E.Choli	1	14.7	
Viral	42	2.36 ± 0.6	(1.6-3.7)

CSF Lactate Ref.range:1.6-2.4 mmol/L.

cases had significantly high CSF lactate level, with mean lactate level of 16.51 ± 6.1 mmol/l (range 1.6-35.5) versus 2.36 ± 0.6 mmol/l (range 1.6-3.7); $p < .0001$ (Figure-2). The CSF proteins and cell count (predominantly polymorphs)

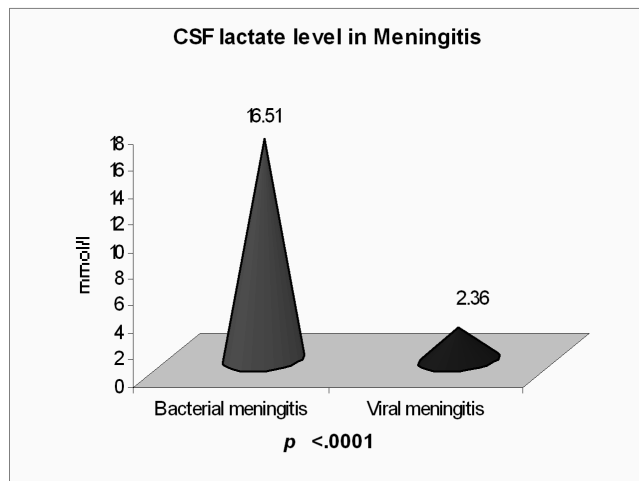


Figure-2: CSF Lactate level in bacterial versus viral meningitis.

were high in bacterial meningitis, whereas, CSF glucose was high in viral meningitis. The hospital stay was longer in bacterial than viral meningitis cases (9.52 ± 3.4 vs 6.82 ± 2.7 days), $p < .0001$. Mortality rate was also noticed higher in bacterial group as compared to viral one, 4 (7.54%) vs 1 (2.38%). The patients who died had higher CSF lactate

(average 19.4 mmol/l) than patients who were discharged healthy.

Discussion

Accurate initial diagnosis is the corner stone for therapeutic decision making of acute meningitis as bacterial meningitis is a common and serious disease associated with significant morbidity and mortality.¹⁰ Presently used techniques have serious limitation to diagnose or differentiate bacterial from viral meningitis. The CSF Gram stain can be negative or misleading because of the either small number of organisms present in the CSF or therapy has been instituted. Cultures often require a day or so for growth, and may also be negative in partially treated cases. Interpretation of glucose is difficult. Glucose concentrations in CSF depend on those in serum: patients with hypoglycaemia have low glucose in CSF, where as hyperglycaemia patients have high concentrations even when bacterial meningitis is present. A number of new, rapid methods including CSF lactate are becoming available to aid in the diagnosis of meningitis and measurement of CSF lactate has been recently advocated as a useful diagnostic test in establishing an early diagnosis of bacterial meningitis, as well as being of some value in separating this entity from aseptic/viral meningitis.¹¹

In this study, CSF lactate was shown to be a sensitive indicator of untreated bacterial meningitis. All patients with untreated bacterial meningitis had elevated levels of lactate in CSF except in one. Lactate was elevated in patients with meningitis caused by both Gram positive and Gram negative cocci and bacilli. In comparison to viral meningitis CSF lactate was significantly high in bacterial than viral meningitis (mean 16.51 ± 6.1 vs 2.36 ± 0.6 mmol/L), an observation which also has been reported by the earlier investigators.¹² Smith et al have reported, CSF lactate as a useful tool in the early diagnosis of bacterial meningitis with high sensitivity (92%) and specificity (99%) as well as in differentiating bacterial from viral meningitis.¹³ Genton B et al have endorsed the idea that the measurement of the CSF lactate is worth performing when meningitis is suspected, as it appeared to be the best way of distinguishing bacterial from non bacterial meningitis and it has highest sensitivity, specificity and predictive value.¹⁴ Klein et al have also reported that the CSF lactate level has higher reliability than the other CSF tests in diagnosing and differentiating bacterial meningitis from viral meningitis.¹⁵ However, Robert et al¹⁶ in their study suggested that the lactate level in the cerebrospinal fluid did not provide unequivocal evidence of bacterial infection and did not gave assistance to any greater degree than the standard parameters of leukocyte count, protein and glucose contents

in the differential diagnosis of bacterial meningitis from that of any other etiology.

The level of CSF lactate has been considered to be an important prognostic factor to predict the outcome of bacterial meningitis and perhaps the most interesting data obtained from this study was the level of CSF lactate. The mean lactate level in the CSF of our patients with bacterial meningitis was 16.51 ± 6.1 mmol/L which is a quite high value than reported by the other investigators such as by Imuekehme et al.¹⁷ It was also noticed that the patients who died had higher CSF lactate level (avg. 19.4 mmol/L) than those who were discharged with or without sequellae, an observation which is also reported by the other investigators.¹⁸

Conclusion

This study showed that the CSF lactate level was significantly high in bacterial than viral meningitis and can provide pertinent, rapid and reliable diagnostic information. Furthermore, CSF lactate level can also differentiate bacterial meningitis from viral meningitis in a quick and better way. However, it has also been suggested that CSF lactate determination should not replace the conventional tests for meningitis.

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