Section: General Medicine

Original Research Article

CLINICAL SIGNIFICANCE OF CSF LACTATE IN MENINGITIS

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Abstract

Background: Meningitis is an important CNS infection with serious mortality and morbidity, especially in developing countries, despite advanced antibiotic therapy and vaccines. This study aimed to differentiate between different types of meningitis using CSF lactate levels in clinical meningitis in the adult population. **Materials and Methods:** This cross-sectional study was conducted on 40 clinical meningitis patients admitted to GRH, Madurai, for six months from March 2021 to August 2021. Patients with clinically suspected meningitis aged > 12 years were included in the study. Relevant information was collected from all patients in the predesigned form. Basic investigations included a complete blood haemogram, renal function test, liver function test, serum electrolytes, CSF analysis, and imaging. **Result:** Among 40 patients, 20 were male and 20 were female, and most were 31-50 years old. In CSF analysis 55% had predominantly lymphocytes, and 45% had predominantly PMN. No significant differences were observed between the lactate scores for CSF sugar (p=0.5) and ADA levels (p=0.7). There was a significant difference in CSF protein levels between the lactate abnormalities (p= 0.03). The association of CSF Lactate level, sex, cytology, Gram stain, culture, sensitivity, and genexpert with meningitis was not statistically different. There were no significant differences between lactate for CSF sugar (p =0.5), protein (p=0.1) and ADA (p=0.9). **Conclusion:** This study revealed that CSF lactate levels were significantly higher in bacterial and tubercular meningitis than in viral meningitis and can provide rapid and reliable diagnostic information.

INTRODUCTION

Meningitis is severe inflammation of the meninges and protective membranes surrounding the brain and spinal cord. Various pathogens, including bacteria, viruses, and fungi, can cause infections. Bacterial meningitis is the most serious type and can be fatal if not treated promptly.[1,2] The symptoms of meningitis vary depending on the cause and severity of the infection. Common symptoms include fever, headache, stiff neck, nausea, and vomiting. In severe cases, meningitis can also lead to seizures, coma, and death.[1,2]

Early diagnosis and treatment are essential to improve the chances of survival and quality of life. Treatment typically involves antibiotics for bacterial meningitis, antiviral medications for viral meningitis, and antifungal medications for fungal meningitis. In some cases, corticosteroids may also be used to reduce inflammation.[3] Despite advancements in molecular technology, diagnosing meningitis remains a challenge. A combination of present CSF variables, such as proteins, glucose, leucocyte count, and CSF/serum glucose ratio, has been suggested to be effective in differentiating non-bacterial meningitis from bacterial meningitis. However, these variables have limitations in accurately diagnosing and differentiating bacterial and non-bacterial meningitis.[4]

CSF lactate concentration has been proposed as a useful parameter for differentiating bacteria from aseptic meningitis. CSF lactate levels in bacterial meningitis originate from various sources. Bacterial pathogens produce varying amounts of lactate, accounting for approximately 10% of total CSF lactate. Additionally, bacterial meningitis is associated with generalised brain oedema, causing a reduction in global cerebral blood flow and inflammatory involvement of the vasculature, with loss of autoregulatory mechanisms, vasospasm, and thrombosis. This leads to cerebral ischaemia and, consequently, glycolysis via anaerobic metabolism. Furthermore, cytokines that flood the brain in meningitis patients reduce tissue oxygen uptake and cause a shift toward anaerobic metabolism, thus increasing lactate production. Cytokines also mediate the invasion of neutrophils into the subarachnoid space, which may also contribute to the rise in CSF lactate level by glycolysis in bacterial meningitis.[5,6] This study aimed to differentiate between different types of meningitis using CSF lactate levels in clinical meningitis in the adult population.

MATERIALS AND METHODS

This cross-sectional study was conducted on 40 clinical meningitis patients admitted to GRH, Madurai, for six months from March 2021 to August 2021.

Inclusion Criteria

Patients with clinically suspected meningitis aged > 12 years were included in the study.

Exclusion Criteria

Patients with hypoxic ischaemic encephalopathy, recent stroke, brain trauma, subarachnoid haemorrhage, seizure disorder, immunosuppressive therapy, septic shock, cardiac failure, and renal failure were excluded.

Informed consent was obtained from all patients enrolled in the study. Relevant information was collected from all patients in the predesigned form.

Basic investigations included a complete blood haemogram, renal function, liver function, serum electrolytes, CSF analysis, and imaging. After neglecting all confounding factors, the data were analysed to compare the CSF lactate levels in bacterial, tuberculous, and viral meningitis.

Statistical Analysis

The information collected regarding all selected cases was recorded in a Master Chart. Data analysis was performed using SPSS 16 software. Percentages, means, and standard deviation p-values were calculated using Student's t-test for raw data and the Chi-square test for consolidated data to test the significance of differences between variables. A 'p' value < 0.05 was taken to denote a significant relationship.

RESULTS

Among 40 patients, 20 were male and 20 were female, and most were 31-50 years old. In csf analysis 55% had predominantly lymphocytes and 45% had predominantly PMN. 5% were gram-negative diplococci, and 32.5% were gram-positive coccus.

25% were pneumococci, and 2.5% were staphylococci. In 30% MTB were detected and in 70% MTB were not detected. Most patients (45%) had bacterial meningitis, 30% had TB meningitis, and 25% had viral meningitis [Table 1].

No significant differences were observed between the lactate scores for CSF sugar (p=0.5) and ADA levels (p=0.7). There was a significant difference in CSF protein levels between lactate abnormalities (p= 0.03) [Table 2].

The association of lactate with cytology, gram stain, culture, sensitivity, and Genexpert implies no difference [Table 3].

The association of CSF Lactate, sex, cytology, gram stain, culture, sensitivity, and genexpert with meningitis was not statistically different [Table 4].

There were no significant differences between lactate for CSF sugar (p=0.5), protein (p=0.1) and ADA (p=0.9) [Table 5].

Table 1: Demographic data of the study

		Frequency	Percentage
Gender	Male	20	50
	Female	20	50
Age	14-20	4	10
	21-30	8	20
	31-40	12	30
	41-50	10	25
	51-60	6	15
CSF cytology	Predominantly lymphocytes	22	55
	Predominantly PMN	18	45
CSF gram stain	Gram-negative diplococci	2	5
	Gram-positive coccus	13	32.5
	Nil	25	62.5
CSF culture & sensitivity	No growth	29	72.5
	Pneumococcus	10	25
	Staphylococcus	1	2.5
CSF gene expert	MTB detected	12	30
	MTB not detected	28	70
Diagnosis	Bacterial meningitis	18	45
	TB meningitis	12	30
	Viral meningitis	10	25

Table 2: Comparison of CSF Lactate with sugar, protein and ADA

	Lactate score	Mean	Std. Deviation	P-value
CSF sugar (mg/dl)	Normal	47.5	14.976	0.557
	Abnormal	51.07	16.93	
CSF protein (mg/dl)	Normal	152.4	50.728	0.036
	Abnormal	113.03	49.067	
CSF ADA	Normal	5.35	7.242	0.709

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	Abnormal	6.41	7.848	

Table 3: Comparison of CSF lactate with various findings

		Normal	Abnormal	Total
Cytology	Predominantly lymphocytes	6	16	22
	Predominantly PMN	4	14	18
CSFGS	Nil	7	18	25
	Gram-negative diplococci	0	2	2
	Gram-positive coccus	3	10	13
Culture & Sensitivity	No growth	7	22	29
	Pneumococcus	3	7	10
	Staphylococcus	0	1	1
Genexpert	MTB not detected	7	21	28
	MTB detected	3	9	12

Table 4: Comparison of various findings with meningitis

		Bacterial Meningitis	Viral Meningitis	TB Meningitis	P-value
CSF Lactate	Normal	0	10	0	2
	Abnormal	18	0	12	
Sex	Male	11	6	3	0.1
	Female	7	4	9	
Cytology	Predominantly lymphocytes	8	6	8	0.5
	Predominantly PMN	10	4	4	
CSF gram stain	Nil	10	7	8	0.6
	Gram-negative diplococci	2	0	0	
	Gram-positive coccus	6	3	4	
Culture & Sensitivity	No growth	14	7	8	0.7
	Pneumococcus	3	3	4	
	Staphylococcus	1	0	0	
Genexpert	MTB not detected	12	7	9	0.9
	MTB detected	6	3	3	

Table 5: Comparison of CSF sugar, protein and ADA with meningitis

	Mean ± SD		
	CSF Sugar (mg/dl)	**CSF Protein (mg/dl)**	**CSF ADA**
Bacterial meningitis	48.78 ± 16.598	114.28 ± 49.147	6.58 ± 7.982
Viral meningitis	47.5 ± 14.976	152.4 ± 50.728	5.35 ± 7.242
TB meningitis	54.5 ± 17.563	111.17 ± 51.07	6.16 ± 7.988
Total	50.18 ± 16.35	122.88 ± 51.79	6.15 ± 7.624
P-value	0.55	0.112	0.924

DISCUSSION

Accurate initial diagnosis is the key to the management of acute meningitis, as bacterial meningitis is a frequent and life-threatening disease associated with serious morbidity and mortality. Currently, techniques for diagnosing or discriminating bacteria from viral meningitis are limited. The CSF Gram stain may be negative or inconclusive because of the low number of pathogens present in the CSF or because therapy has been instituted. CSF cultures mostly require days for growth and can be negative in partially treated patients. The interpretation of CSF glucose levels is not always accurate. Glucose concentrations in the CSF depend upon serum glucose levels: patients with hypoglycaemia have reduced glucose levels in the CSF, whereas hyperglycaemia patients have higher concentrations even when bacterial meningitis is present. A panel of newer and rapid diagnostic methods, including CSF lactate, are currently available to help in the diagnosis of meningitis, and estimation of CSF lactate has recently been used as a good diagnostic test in the early diagnosis of bacterial meningitis, as well as separating this entity from aseptic/viral meningitis.

In our study, of 40 patients, 20 were males and 20 were females. 30% of meningitis patients belonged to the 31-40 years of age group. Clinical, laboratory, and microbiological confirmation of meningitis was found in 62.5% of patients whose CSF cytology was acellular. Gram stain was useful in isolating 8 cases of bacterial meningitis, i.e., 37.5% of patients had microbiological confirmation of bacterial meningitis. 11 cases were culture positive; 10 cases had S. pneumoniae, and 1 had Staphylococcus aureus, suggesting 61.11% of bacterial meningitis were identified by cultures among the 18 cases.

Among the 40 patients with meningitis studied, age and sex were not significantly correlated with CSF lactate levels. In a study by Asuti et al., the mean patient age was 33±11 years.[7] Our study's mean age was 37.17 years, with equal sex distribution. Baker RC et al. and Viallon et al. have found high CSF pleocytosis with neutrophil predominance in bacterial meningitis compared to viral meningitis.[8,9] In our study, 55.55% of patients had neutrophilic pleocytosis, and 44.44% had relatively significant lymphocytic pleocytosis.

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In our study, the mean sugar level was lower in bacterial (36.38 mg%) and tubercular meningitis (49.5 mg%) than in those with viral meningitis (57.9 mg%). A study by Abro AH et al. showed similar findings with mean CSF sugar 26.5 ± 21.6 and 67 ± 18.96 mg/dl in bacterial and viral meningitis, respectively. The mean CSF protein level was higher in pyogenic and tubercular meningitis than in viral meningitis.[10]

Robert L et al., in their study, could not find CSF lactate as a reliable marker compared to other biochemical investigations like sugar, protein, cell count and typing.[11] In our study, the mean CSF lactate level was significantly higher in patients with pyogenic and tubercular meningitis than in those with viral meningitis ($p<0.001$). However, mean CSF lactate was very high (62.33mg /dL) in bacterial meningitis compared to tubercular (35.2mg/dL) and viral meningitis (19.50 mg/dL). A study by Abro AH et al. showed mean CSF lactate was 134.77±55.23 mg/dL and 21.44±5.32 mg/dL in bacterial meningitis and viral meningitis, respectively.10 Smith et al. and Genton B et al. reported similar findings.[12,13]

In the present study, CSF lactate levels were high in all patients with pyogenic meningitis. Further evaluation suggested no correlation between the mean CSF lactate value and gram stain/culture results, except for CSF protein. In the present investigation using a higher cut-off value of 43mg /dL, CSF lactate helped differentiate pyogenic meningitis from tubercular meningitis (p-value <0.001). The present study confirms previous studies, such as Asuti et al. and Jereb et al., that CSF lactate levels are increased more in bacterial meningitis than in tubercular and viral meningitis and are directly correlated with the diagnosis.[7,14]

CONCLUSION

This study revealed that CSF lactate levels were significantly higher in bacterial and tubercular meningitis than in viral meningitis and can provide rapid and reliable diagnostic information. In addition to its cost-effectiveness, CSF lactate levels can rapidly and better differentiate bacterial meningitis from tubercular and viral meningitis. This also suggests that CSF lactate can be included in the diagnostic workup, even in patients with suspected meningitis.

Limitations

This study was conducted at a single-centre tertiary care hospital. Our study had a small sample size, was a cross-sectional observational study, the follow-up details were not evaluated, and this was not compared to the normal population. Our study did not include other types of meningitis owing to fungal and parasitic aetiologies.

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