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Original Research Article

Role of cerebro spinal fluid lactate as a diagnostic marker for differentiation from bacterial and aseptic meningitis

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ABSTRACT

Background: Meningitis is serious and a life-threatening condition among any age group associated with serious mortality and morbidity. CSF lactate may be a good marker to differentiate bacterial from other cause of meningitis. Objective of this study is to evaluate the efficiency of CSF lactate in differentiating bacterial/ pyogenic from non-pyogenic meningitis.
Methods: A one-year prospective study with all cases diagnosed as meningitis was enrolled and CSF analysis was done. Patients were grouped as bacteria, viral and tubercular meningitis based on clinical and CSF analysis. All cytological, biochemical and CSF lactate were estimated and compared with lactate to differentiate pyogenic from non-pyogenic meningitis. Statistical analysis was done using SPSS (Statistical Package for Social Sciences) version 20.
Results: A total of 120 cases with 74 males and 46 females, majority in 31-50 years age group were included. 59 pyogenic, 37 tubercular and 24 viral meningitis cases were diagnosed. Fever was common symptom (91.67%). Mean CSF protein was highest in pyogenic meningitis (271.1±142.28), 26 cases of tubercular meningitis demonstrated elevated levels of CSF lactate with a cut-off value of >2.1mmol/l (70.27%), five cases of viral meningitis (13.51%) and all 59 cases of pyogenic meningitis (100%).
Conclusions: This present study concludes that CSF lactate could be a reliable and valid marker in early differentiation of pyogenic from cases of nonpyogenic meningitis. Early detection may help in early decision on the type and institution of appropriate management could reduce the mortality and morbidity of meningitis.

Keywords: CSF analysis, CSF lactate, CSF protein, Meningitis

INTRODUCTION

Meningitis is serious and a life-threatening condition among any age group associated with serious mortality and morbidity. It is actually defined as acute inflammation of the protective membranes surrounding the brain and spinal cord known as meninges. The cause may be bacterial, viral and also fungal with different set of morbidity and severity. Differentiating bacterial from viral by clinical signs and symptoms is quite challenging to the clinicians. Bacterial meningitis is associated with severe mortality and post sequelae than viral and fungal meningitis. Prompt diagnosis and appropriate antibiotic therapy are required to reduce the mortality and morbidity. Any delay in diagnosis and appropriate therapy will worsen the prognosis. Hence early and rapid differentiation between bacterial and viral meningitis is essential in early initiation of therapy.[1]

CSF analysis is an important tool in diagnosis and differentiation from bacterial and viral meningitis. Conventional techniques of bacterial culture for identification of pathogen is gold standard but time consuming and not available in short time. However rapid detection methods like PCR are expensive and not available at basic set up in low income countries. Several biochemical and cytological variables are being used in differentiating from pyogenic, tubercular and viral

meningitis. However, there are several limitations of the above variables in differentiating bacterial from viral meningitis. Hence in this variability an acute reliable marker is necessary to mark this distinction.[2]

In recent years various studies have shown CSF lactate may be a good marker to differentiate bacterial from other cause of meningitis. Fe studies have differed saying that CSF lactate offers no additional information over other markers like CRP and procalcitonin. The above variables are never used as routine in diagnosis or differentiation of bacterial from viral meningitis.[3] Various studies have differed the reliability of CSF lactate in differentiating from bacterial and viral meningitis. CSF lactate can be elevated in other several disorders, such as subarachnoid haemorrhage, cerebral hypoxia, status epilepticus and inborn errors of metabolism. Hence validation of CSF lactate may complement the other CSF variables in differentiating from bacterial and other causes of meningitis.

Studies using lactate as a marker in differentiation of bacterial and viral are limited in Indian scenario. Hence the objective of the present study was to evaluate the efficiency of CSF lactate in differentiating bacterial/ pyogenic from non pyogenic meningitis.

METHODS

A hospital based one year prospective study was conducted at Narayana Medical College and hospital a tertiary care hospital of south India. The study was conducted by department of General medicine in association with department of emergency medicine for a period of one year from January 2018 to December 2018. The study was presented before the institutional ethical committee and was accepted. The study was conducted as per the guidelines of the committee. The study protocol was explained to all the participants and written informed consent was obtained from them. All the cases suspected with meningitis above 18 years of age irrespective of sex were admitted and clinically evaluated. Cases were examined for signs and symptoms of meningitis by a senior resident of the department and noted in a separate predesigned questionnaire sheet. The socio demographic data, history, age, gender, duration of signs and symptoms were recorded by interviewing the case or from the attendant of the case and noted in the questionnaire sheet. Neurological assessment of the cases for neck rigidity, kernig's sign or bridzinski's sign and any focal neurological inadequacy, cranial nerve palsies, hemiparesis and any signs of cerebral dysfunction which may include minor ailments like confusion, delirium or grave elements like diminishing level of sensorium and coma.

All the cases were clearly examined and appropriate haematological, radiological investigations were performed immediately upon admission. Patients with conditions which may cause elevated levels of lactate in CSF like brain hypoxia, seizures, brain trauma, recent CVA, subarachnoid haemorrhage and cases on immunosuppressive therapy, fungal meningitis and HIV were excluded from the study. Lumbar puncture was done under strict aseptic precautions and 10 ml of CSF collected and send to central laboratory for estimation of all biochemical parameters like sugars, protein, lactate, cell counts (Lymphocytes, neutrophils), Adenosine deaminase (ADA) levels. CSF lactate was estimated by enzymatic method using ABL 555 blood gas analyzer. The reference range in this study was 1.2-2.1mmol/L but ranges from 0.6-3.1mmol/L.[4] The results of the CSF analysis were noted and based on findings the cases were grouped as,

- Pyogenic meningitis: Neutrophilic pleocytosis (10-10000 cells/mm^3), protein >45mg/dl, sugar <40mg/dl.
- Nonpyogenic: Tubercular or Viral meningitis.

Tubercular

Lymphocytic pleocytosis (10-1000cells/mm^3). Protein >45mg/dl, sugars >2/3rd of blood sugar values, elevated ADA levels and demonstration of AFB on Zn staining.

Viral

Lymphocytic pleocytosis (25-500cells/mm^3), slightly elevated protein (20-80mg/dl), normal sugars and ADA levels without bacteria on staining.

Statistical analysis

Data were entered into the Microsoft Excel spreadsheet, and descriptive statistical analysis was done using SPSS (Statistical Package for Social Sciences) version 20. Results on continuous measurements were presented as mean and standard deviation. Results on categorical measurements were presented as percentages. Significance was assessed at 5% level of significance. The chi-square test was used to assess the significance of the study parameters on a categorical scale between the groups.

RESULTS

The present prospective study was conducted by department of General medicine and a total of 120 cases of meningitis which were diagnosed upon clinical evaluation were included in the study. The cases were grouped as pyogenic and non-pyogenic and viral and tubercular among the non-pyogenic group. With regard to sex distribution of cases, 74 (61.67%) were males and 46 (38.33%) were females. Majority of cases were in the age group of 31-50 years (31.67%) and mean age of all the cases in the study was 38.12±1.2 years, in the range of 20-74 years. Mean age of males in the study was 41.05±1.1 and female was 38.20±0.9 years (Figure 1). 120 cases of meningitis were diagnosed with 59 cases (49.16%) being pyogenic and 61 cases (50.83%) non-Pyogenic. Of the 61 cases of pyogenic meningitis, 37 cases (60.66%) were tubercular and 24 cases (39.34%) were aseptic /viral

meningitis. Majority of all the types of meningitis were observed in males. 61.01% of Pyogenic in males and 62.3% of non-Pyogenic among the males (Figure 2).

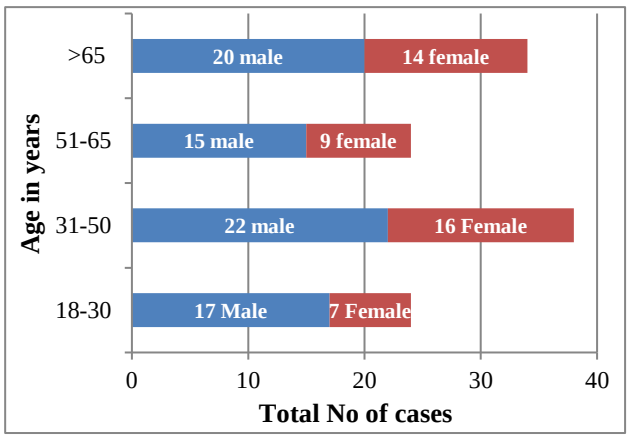

Figure 1: Age and sex distribution of cases in the study.

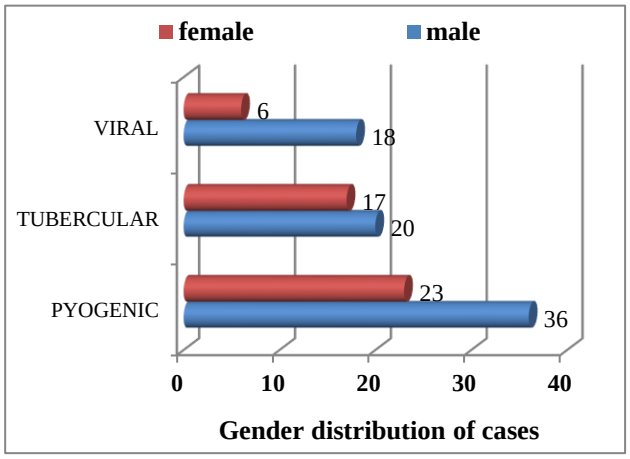

Figure 2: Types of meningitis and gender distribution in the study group.

Fever was the most common symptom (91.67%) followed by vomiting (75.83%), headache (70.83%) and altered sensorium in 61.67% of cases. Brudzinski's sign was observed in 70% of cases and neck stiffness in 63.33%, kernig's sign in 57.50% and nerve palsies in 21% of cases (Table 1).

Table 1: Signs and symptoms of cases in the study.

Clinical signs and symptoms		No	%
Symptoms	Fever	110	91.67
	Headache	85	70.83
	Vomiting	91	75.83
	Altered sensorium	74	61.67
Signs	Neck stiffness	76	63.33
	Kernig's sign	69	57.50
	Brudzinski's sign	84	70.00
	Cranial nerve palsy	21	17.50

Table 2 summarizes the findings of cytological parameters of different types of meningitis in this study. The mean total cell count was highest in cases of pyogenic meningitis with a mean of 841.84 and SD of 114.25 than viral and tubercular meningitis. However no statistical significance was associated with total count and types of meningitis. ('p' value -0.087) A clear neutrophil predominance was observed in all cases of pyogenic meningitis with a mean value of 78.21 and SD of 22.14 than among the cases of viral and tubercular meningitis. Lymphocytic predominance was observed in tubercular meningitis with mean of 75.2 and SD of 24.11 than viral and pyogenic meningitis. Both PMN and lymphocyte count had a clear statistical significance with 'p' value <0.001 in this study.

Table 3 explains the findings of biochemical parameters of CSF findings among different types of meningitis of the cases in this study. This study reveals that mean sugar levels are higher in viral (72.14±15.21) than pyogenic (41.1±22.48) and tubercular meningitis (47.21±12.48). Mean CSF protein was highest in pyogenic meningitis (271.1±142.28) than viral (95.21±43.28) and tubercular meningitis (194.25±211.24). In this study no statistical significance was associated with sugar and protein levels in CSF and types of meningitis. CSF sugar to blood sugar ratio was <0.4 in both pyogenic meningitis and tubercular meningitis and >0.6 in viral meningitis.

Table 2: Analysis of cytological parameters of CSF among cases in the study.

CSF parameters	Type of Meningitis	Number of cases	Mean	SD	Range	p-value
Total Count (cells/mm3)	Tubercular	37	143.21	65.01	21-248	0.087
	Viral	24	128.44	98.1	22-435	
	Pyogenic	59	841.84	114.25	44-2687	
PMN	Tubercular	37	39.08	30.1	02- 98	<0.001
	Viral	24	32.47	19.21	04-78	
	Pyogenic	59	78.21	22.14	21-102	
Lymphocytes	Tubercular	37	75.2	24.11	11-114	<0.001
	Viral	24	69.12	19.11	34- 99	
	Pyogenic	59	26	11.24	5-78	

Table 3: Analysis of biochemical parameters of CSF among cases in the study.

CSF parameters	Type of meningitis	Number of cases	Mean	SD	Range	p' value
Sugar(mg/dl)	Tubercular	37	47.21	12.48	22.1-42.15	0.004
	Viral	24	72.14	15.21	41.2-124.24	
	Pyogenic	59	41.1	22.48	10.24-142.1	
Protein(mg/dl)	Tubercular	37	194.25	211.24	47-279	0.024
	Viral	24	95.21	43.28	72-240	
	Pyogenic	59	271.1	142.28	78-847	
Lactate(mmol/l)	Tubercular	37	5.1	1.54	2.1-6.8	<0.001
	Viral	24	2.1	0.85	1-4.1	
	Pyogenic	59	12.58	3.58	3.1-15.8	
CSF sugar/Blood sugar ratio	Tubercular	37	0.0324	0.0724	0.24-0.48	<0.001
	Viral	24	0.071	0.1241	0.47-0.87	
	Pyogenic	59	0.2528	0.1214	0.076-0.048	

Lactate levels of the CSF were elevated than normal in both pyogenic and tubercular than viral, however the mean CSF lactate was higher (12.58 mmol/l) in pyogenic than tubercular (5.1 mmol/l). A clear statistical significance was observed in CSF sugar/blood glucose ratio and CSF lactate levels in this study with 'p' value <0.001.

In this study, 26 cases of tubercular meningitis demonstrated elevated levels of CSF lactate with a cut-off value of >2.1 mmol/l (70.27%), five cases of viral meningitis (13.51%) and all 59 cases of pyogenic meningitis (100%). A clear statistical significance was observed with regard to CSF lactate levels and types of meningitis in this study. This study revealed that of the total 120 cases, 90 cases (75%) had elevated levels of lactate (>2.1 mmol/L) (Table 4).

Table 4: Analysis of CSF lactate (mmol/L) in different group of meningitis.

Type of meningitis	Lactate		Total	p' value
	≤2.1	>2.1		
Tubercular	11	26	37	<0.001
Viral	19	5	24	
Pyogenic	0	59	59	
Total	30 (25%)	90 (75%)	120	

Table 5: Comparison of CSF lactate between tubercular and pyogenic meningitis with cut off of 5mmol/L.

Type of meningitis	CSF lactate		Total	p' value
	<=5	>5		
Tubercular	1	25	26	<0.001
Pyogenic	4	55	59	
Total	5	80	85	

When the cut off value for CSF lactate was raised to 5mmol/l, and compared with tubercular and pyogenic meningitis, this study revealed that 25 cases of tubercular meningitis and 55 cases of pyogenic meningitis had elevated levels of CSF lactate (>5 mmol/l). A clear statistical significance was observed with levels of CSF lactate and type of meningitis in this study (Table 5).

DISCUSSION

Meningitis is considered one of the serious and grave clinical conditions associated with morbidity and mortality in any age group. Differentiating the type of meningitis, bacterial, viral and tubercular is essential and a key point in management. The protocol depends on type of meningitis and its early diagnosis which is corner stone in successful recovery of the case. Gram staining and culture and sensitivity are less sensitive, time consuming and is associated with financial concern. Hence the necessity of a safe and reliable marker in differentiating pyogenic from non pyogenic meningitis is essential at this moment. Studies and literature stating CSF lactate along with other biochemical and cytological variables is of help in differentiation.

This study presently focused the reliability and validity of CSF lactate as a marker to differentiate pyogenic and non-pyogenic cases of meningitis. In this study, males (61.67%) outnumbered the females (38.33%) with most common age group of 31-50 years. Similar findings were reported in the study of van de Beek et al, with 75% of males and 25% females.[5] Mean age of the male was higher than the female in this study which is similar to many studies universally, but the noted feature of the study was mean age of all the cases was 38.12±11.2 years which is less than many studies conducted in the west and few studies in India.[6,7] In this study, almost equal distribution of pyogenic and non-pyogenic case distribution was observed with 59 pyogenic and 24 viral and 37 of tubercular meningitis.

Fever (91%) was most common symptom followed by vomiting, headache, and altered sensorium. Signs of meningeal irritation were observed in 20% of the cases only. Nerve palsies was identified in 21% of cases. However these were not specific in differentiating

pyogenic from non-pyogenic cases of meningitis. Few studies in the west reported higher incidence of nerve palsies with 30-40% in their studies but this is quite variable depending upon the associated co-morbidities and age selection of cases in the study.[8]

This study revealed that mean total cell count was highest in cases of pyogenic meningitis with a mean of 841.84 and SD of 114.25 than viral and tubercular meningitis which is similarly reported in the study of Ranbeer Kumar Singh et al. Pyogenic meningitis showed neutrophil (PMN) predominance whereas non-pyogenic group showed lymphocyte predominance which was similar to findings of Ranbeer Kumar Singh et al, and was associated with significant statistical association in this study.[9] However, Negrini et al, have reported that most of the patients with aseptic meningitis had neutrophil predominant pleocytosis.[10] This study reveals that mean sugar levels are higher in viral (72.14 ±15.21) and mean CSF protein was highest in pyogenic meningitis (271.1±142.28).Similar findings were reported in the study of Huy et al, who reported that mean sugar levels in viral meningitis was 78.01±12.41 and mean CSF protein was 285.1±122.28 in his study and was statistically significant.[11] CSF sugar to blood sugar ratio was <0.4 in both pyogenic meningitis and tubercular meningitis and >0.6 in viral meningitis and the ratio of CSF sugar to blood sugar is a better parameter in this study which was similar to the findings of Viallon A et al.[12]

In present study the mean CSF lactate was higher (12.58mmol/l) in pyogenic than tubercular (5.1mmol/l) and a clear statistical association was observed. Mean CSF lactate was very high in pyogenic meningitis compared to tubercular. Findings of this study were on par with the findings of many studies in the west and few studies from India.[13,14] In the present study, CSF lactate was high in all cases of pyogenic meningitis. In this study mean CSF lactate was able to differentiate Tubercular meningitis from viral/aseptic meningitis.

In the present investigation using a higher cut off value of 5mmol/L, CSF lactate helped in differentiating pyogenic meningitis from tubercular meningitis (p-value <0.001). Finidngs of iur study were on par with the findings of Leen W et al, who observed the findings in 200 cases of meningitis.[15] This present study reveals the direct correlation of the mean CSF lactate level (12.58mmol/l) value with mean CSF sugar to blood sugar ratio (0.25) in the pyogenic meningitis group. The magnitude of CSF lactate level may also provide a clue in predicting poor outcome and may also determine likely prognosis which requires further evaluation and studies.

CONCLUSION

This present study concludes that CSF lactate could be a reliable and valid marker in early differentiation of pyogenic from cases of non-pyogenic meningitis. Early detection may help in early decision on the type and institution of appropriate management could reduce the mortality and morbidity of meningitis. Associated with CSF blood/CSF sugar ratio is also a helpful and supportive marker in differentiating viral, tubercular and pyogenic meningitis.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Tavares WM, Machado AG, Matushita H, Plese JP. CSF markers for diagnosis of bacterial meningitis in neurosurgical postoperative patients. Arquiv Neur Psiquiat. 2006 Sep;64(3A):592-5.
2. Kleine TO, Zwerenz P, Zöfel P, Shiratori K. New and old diagnostic markers of meningitis in cerebrospinal fluid (CSF). Brain Res Bull. 2003 Aug 15;61(3):287-97.
3. Scarborough M, Thwaites GE. The diagnosis and management of acute bacterial meningitis in resource-poor settings. Lancet Neurol. 2008 Jul 1;7(7):637-48.
4. Holbrook I, Beetham R, Cruickshank A, Egner W, Fahie-Wilson M, Keir G, et al. National audit of cerebrospinal fluid testing. Ann Clini Biochem. 2007 Sep 1;44(5):443-8.
5. Van de Beek D, De Gans J, Spanjaard L, Weisfelt M, Reitsma JB, Vermeulen M. Clinical features and prognostic factors in adults with bacterial meningitis. New Engl J Medi. 2004 Oct 28;351(18):1849-59.
6. Heyderman RS, Lambert HP, O'Sullivan I, Stuart JM, Taylor BL, Wall RA. Early management of suspected bacterial meningitis and meningococcal septicaemia in adults. J Infect. 2003 Feb 1;46(2):75-7.
7. Asuti S, Jagadish G, Narayan A. Estimation of CSF lactate as a diagnostic marker to differentiate pyogenic meningitis from nonpyogenic meningitis. Indian J Neurosci. 2019;5(3):106-12.
8. Chavanet P, Schaller C, Levy C, Flores-Cordero J, Arens M, Piroth L, et al. Performance of a predictive rule to distinguish bacterial and viral meningitis. J Infect. 2007 Apr 1;54(4):328-36.
9. Kumar Singh R, Usmani F, Haque SS, Tanweeruddin M, Singh BK. Estimation of Lactate Dehydrogenase Activity in cerebrospinal fluid in different types of meningitis. Int J Adv Biolog Biomed Res. 2017;5(1):48-51.
10. Negrini B, Kelleher KJ, Wald ER. Cerebrospinal fluid findings in aseptic versus bacterial meningitis. Pediatrics. 2000 Feb 1;105(2):316-9.
11. Huy NT, Thao NT, Diep DT, Kikuchi M, Zamora J, Hirayama K. Cerebrospinal fluid lactate concentration to distinguish bacterial from aseptic meningitis: a systemic review and meta-analysis. Crit Care. 2010 Dec 1;14(6):R240.
12. Viallon A, Desseigne N, Marjollet O, Birynczyk A, Belin M, Guyomarch S, et al. Meningitis in adult

patients with a negative direct cerebrospinal fluid examination: value of cytochemical markers for differential diagnosis. Crit Care. 2011 Jun 1;15(3):R136.
13. Ray P, Badarou-Acossi G, Viallon A, Boutoille D, Arthaud M, Trystram D, et al. Accuracy of the cerebrospinal fluid results to differentiate bacterial from non-bacterial meningitis, in case of negative gram-stained smear. Am J Emerg Medi. 2007 Feb 1;25(2):179-84.
14. Mandal BK, Dunbar EM, Hooper J, Parker L. How useful is cerebrospinal fluid lactate estimation in differential diagnosis of meningitis?. J Infect. 1983 May 1;6(3):231-7.
15. Leen WG, Willemsen MA, Wevers RA, Verbeek MM. Cerebrospinal fluid glucose and lactate: age-specific reference values and implications for clinical practice. PloS One. 2012;7(8).

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