

Cerebrospinal Fluid Bioprofiling

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ABSTRACT

Introduction: Meningitis is one of the most serious health issues. The World Health Organization (WHO) defines as inflammation of the meninges, the covering of brain, and spinal cord. Most common cause is by infection. It is always reported with very aggressive and devastating outcome on health and continues to cause significant morbidity and mortality worldwide. The current study is focused on bioprofiling of cerebrospinal fluid (CSF) which can be aided for early diagnosis of meningitis and helpful for differentiating meningitis from nonmeningitis for deciding treatment regimen by the treating clinician.

Objective: To study the biochemical parameters in meningitis patients and compare CSF bioprofile.

Materials and methods: It is an observational analytical study with a total of 60 subjects aged between 18 and 60 years, conducted in Father Muller Medical College Hospital, Mangaluru, for a duration of 3 months, after obtaining clearance from the institutional ethics committee. The samples sent for the analysis to the clinical biochemistry laboratory were collected and the same were used for the study after obtaining the informed consent from the patient. The traumatic samples and systemic disorder patient samples were excluded from the study. The parameters analyzed were: CSF C-reactive protein (CRP), CSF electrolytes, CSF aspartate transaminase (AST), and CSF lactate dehydrogenase (LDH) apart from the routine CSF protein and glucose in both group I (meningitis) and group II (nonmeningitis).

Results: The statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 23, with the significance value of 0.05. The mean of the CSF CRP was 2.0 ± 1.12 in group I compared with group II 0.09 ± 0.15 ; CSF AST was 17.42 ± 6.24 , 5.1 ± 3.8 in groups I and II respectively; and CSF LDH was 211.1 ± 49.0 , 23.71 ± 10.29 in groups I and II respectively, with p-value < 0.001 (highly significant).

Conclusion: The CSF CRP was found to be increased in patients with meningitis compared with the negative CSF, and the significant increase in the CSF AST and LDH; this knowledge can help to aid the routine CSF protein and glucose to differentiate the meningitis before the result of the culture is reported for deciding the treatment regimen.

Keywords: Aspartate transaminase, Cerebrospinal fluid, Cerebrospinal fluid C-reactive protein, Cerebrospinal fluid lactate dehydrogenase.

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INTRODUCTION

Meningitis is one of the most serious health issues and incident among the children is always alarming.¹ The WHO defines it as: "Meningitis is inflammation of the meninges, the covering of the brain and spinal cord." It is most often caused by infection (bacterial, viral, or fungal), but can also be produced by chemical irritation, subarachnoid hemorrhage, cancer, and other conditions.² Apart from the infection, it has always been reported with very aggressive and devastating outcome on health. Despite the effectiveness of current antibiotics and treatment, meningitis continues to cause significant morbidity and mortality worldwide. The case fatality rate for adult was approximately 25% and transient or permanent neurological morbidity occurred in 21 to 28% of survivors.³ The early diagnosis and treatment play a very crucial role in the outcome of patient.⁴ The signs and symptoms the person presents with meningitis include fever, malaise, vomiting, and petechial rashes in some cases. Among the younger children, the signs of meningeal irritation like neck stiffness, Kernig's sign, and Brudzinski's sign can be seen. Moreover, inability to feed, vomiting, drowsiness, and convulsion can even be observed in younger patients.⁵

The diagnostic criteria conventionally used to identify the meningitis include: CSF biochemical analysis, Gram stain and culture. By the biochemical analysis of the CSF, it is helpful for treating meningitis earliest when culture reports are negative. Hence, the current study is focused on the Bioprofiling of CSF which can be reported at the earliest and aiding for early diagnosis of meningitis and helpful for differentiating between bacterial and viral meningitis for deciding the treatment regimen by the treating clinician.

OBJECTIVES

- To study the biochemical parameters in patients diagnosed with meningitis.
- To compare the CSF bioprofile with the nonmeningitis patients.

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MATERIALS AND METHODS

This is an observational analytic study, conducted at the Central Biochemistry Laboratory, Medical College Hospital Laboratory. A total of 60 subjects were included in the current study, for a duration of 3 months. Inclusion criteria: age group between 18 and 60 years; male/female patients diagnosed with meningitis were included in the study. Exclusion criteria: traumatic sample, systemic disorders like liver disease, multiple sclerosis, and amyloidosis. The CSF and blood samples were collected from the clinical biochemistry laboratory and stored in deep freezer for the purpose of study. Study subjects were divided into cases (positive for meningitis) and control (negative for meningitis) based on the clinical diagnosis.

The other information regarding the patient was accessed from Hospital Information System (HIS). The collected CSF sample was analyzed for the following parameters in COBAS-6000 autoanalyzer: CSF CRP (immunoturbidometric method); CSF sodium, potassium, chloride (ISE, Indirect method); CSF AST (kinetic, enzymatic method), and CSF LDH (kinetic, lactate to pyruvate method).

Statistics: The result was analyzed by student t-test for the significant difference between the groups, with the significant level alpha as less than 0.05, Pearson's correlation to evaluate the strength of association between the variables, and statistical software SPSS version 23 was used for analysis. The sample size was calculated by using the SamplePower 3-SPSS software for minimum 80% power and significance of less than 0.05 for the study.

RESULTS

The results of the variables included in the study were analyzed. The study population was divided into cases diagnosed with the meningitis, and controls who were negative for the meningitis. The demographic details of the cases and controls are given in Table 1. The student t-test is used to compare the mean in cases and controls to find the significance in CSF samples (Table 2) and in serum samples (Table 3). Correlation of CSF variables is shown in Table 4.

DISCUSSION

The patients were treated as viral and bacterial meningitis based on the WHO criteria after analyzing the CSF sample

Table 1: Descriptive data of the individuals included in study

		Cases	Controls
Participants	N (%)	28 (59.6)	19 (40.4)
Gender	Male n (%)	17 (68.0)	8 (32.0)
	Female n (%)	11 (50.0)	11 (50.0)
Age	Mean ± SE	26.82 ± 3.96	35.11 ± 6.69

The table includes the demographic details of the cases included in the study; SE: Standard error

Table 2: The t-test results of CSF variables to compare the means

	Meningitis	Mean ± SD	p-value	Significance
CSF protein	Present	353.47 ± 449.47	0.005	HS
	Absent	45.29 ± 19.26		
CSF CRP	Present	2.0 ± 1.12	0.000	HS
	Absent	0.09 ± 0.15		
CSF sodium	Present	140 ± 6.3	0.626	NS
	Absent	138.8 ± 7.91		
CSF chloride	Present	115.05 ± 7.88	0.534	NS
	Absent	117.41 ± 6.37		
CSF potassium	Present	4.33 ± 1.9	0.113	NS
	Absent	2.82 ± 0.24		
CSF AST	Present	17.42 ± 6.24	0.000	HS
	Absent	5.1 ± 3.8		
CSF LDH	Present	211.1 ± 49.0	0.000	HS
	Absent	23.71 ± 10.29		

The table shows the t-test results of the variables in the cases (meningitis) and controls; p-value <0.05 is significant and <0.001 is considered highly significant (HS), NS: Nonsignificant; SD: Standard deviation

Table 3: Comparison of the variable in the serum samples

	Cases (mean ± SD)	Controls (mean ± SD)	Significance
Serum protein, gm/dL	6.82 ± 1.05	7.02 ± 0.69	0.446, NS
Serum CRP	69.29 ± 7.99	9.1 ± 5.79	0.343, NS
Serum sodium	134.22 ± 5.4	128.5 ± 2.12	0.190, NS
Serum chloride	94.8 ± 8.7	86.8 ± 5.2	0.334, NS
Serum potassium	4.08 ± 0.77	4.37 ± 1.38	0.677, NS

Student's t-test was used to compare the mean of the variables in cases and controls in serum sample. p<0.05 is significant; NS: Nonsignificant

for biochemical parameters, cell counts, and culture. Normal CSF values were less than 50 mg/dL of protein, a CSF-to-serum glucose ratio greater than 0.6, less than 5 white blood cells (WBCs)/ μ L, and a lactate concentration less than 3.5 mEq/L. In patients with bacterial meningitis, the observations were: WBC count of 1000 to 5000/ μ L (range of <100 to >10,000) with a percentage of neutrophils usually greater than 80%, protein of 100 to 500 mg/dL, and glucose <40 mg/dL (with a CSF:serum glucose ratio of \leq 0.4), with 80% culture as positive for the causative organism. However, in viral meningitis, the observations include a WBC count that is generally less than 250 cells/ μ L, a modest elevation in CSF protein concentration (generally less than 150 mg/dL), and a normal glucose concentration, and culture-negative for Gram stain.⁶

Meningitis being aggressive in type and treatment required to be initiated at the earliest, the differentiation of meningitis is essential. The current study aimed to assess the utility of the CRP, enzymes and electrolyte to aid in establishing the meningitis and differentiating from the negative for meningitis.⁷ The CRP, AST, and electrolytes in the CSF sample were analyzed along with

Table 4: Correlation of the CSF variables for the assessment of strength of association

<i>Pearson association (r value)</i>	<i>CSF protein</i>	<i>CSF glucose</i>	<i>CSF CRP</i>	<i>CSF AST</i>	<i>CSF LDH</i>	<i>CSF sodium</i>	<i>CSF chloride</i>	<i>CSF potassium</i>
CSF protein		-0.150	0.350*	0.362*	0.209	-0.027	-0.460	0.155
CSF glucose	-0.150		-0.347*	-0.227	-0.328	0.741**	-0.274	0.676*
CSF CRP	0.350*	-0.347*		0.581**	0.374	0.279	0.279	0.461
CSF AST	0.362*	-0.227	0.581**		-0.126	0.152	-0.412	0.343
CSF LDH	0.209	-0.328	0.374	-0.126		-0.232	0.243	0.025
CSF sodium	-0.027	0.741**	0.279	0.152	-0.232		-0.150	0.942**
CSF chloride	-0.460	-0.274	-0.242	-0.412	0.243	-0.150		-0.152
CSF potassium	0.155	0.676*	0.461	0.343	0.025	0.942**	-0.152	

The table shows the strength of association among the variable in CSF sample. *p-value < 0.05 is significant; **p-value < 0.001 highly significant

the serum sample. The CRP was found to be increased in the meningitis patient, showing the increased leakiness of the membrane in the meningitis, and even increased levels of the albumin in CSF, demonstrating the damage to the membrane caused due to the inflammatory reactions and events occurring.⁸ The study conducted by Rekha et al⁹ also showed the statistical difference in the analyzed variables in the meningitis, aiding for early diagnosis and initiation of the treatment. The CRP has a good strength of association with the changes in CSF protein and even activity of enzymes like AST in CSF. Electrolytes did not show much significant difference to decide the meningitis or negative for it. But CRP and AST, LDH enzymes can be added to the routine CSF glucose and protein to diagnose a case of meningitis.

CONCLUSION

From the current study, the parameters have shown a good relation with the protein and glucose levels in CSF sample of meningitis cases. The CRP, LDH, and enzymes like AST can be used in conjunction with the current panel of the CSF analysis in biochemistry for differentiating the different types of the meningitis. As in case of bacterial meningitis, the level of CSF CRP, and LDH was significantly increased with the good strength of association with the change in the levels of CSF glucose and protein.

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