

## Original Article

### Role of CSF-CRP in Diagnosis of Meningitis

Savita Chaudhary<sup>1</sup>, Amit Chaudhary<sup>2</sup>

<sup>1</sup>Associate Professor, Dept. Of Dermatology, ELMCH, Lucknow , <sup>2</sup>Consultant Pediatrician, Lucknow, U.P., India


#### ABSTRACT:

**Background:** Meningitis is an acute inflammation of the membranes covering brain and spinal cord. Meningitis may be caused by infection with virus, bacteria, fungus etc. Diagnosis of meningitis and differentiating between various types of meningitis remains a challenge for the physician. **Aim:** The aim of this study is to examine the role of CSF-CRP in diagnosis of meningitis. **Material and method:** A total of 60 children with meningitis and suspected meningitis were included in the study. Detailed history was taken and clinical examination was done. Routine CSF examination included cell count, protein, sugar, gram stain, culture, ADA and chloride levels estimation. The Level of C Reactive Protein in CSF of all meningitis groups was recorded. **Result:** Out of 60 cases, clinically and by CSF examination, tuberculous meningitis was diagnosed in 25 cases (42 %), followed by bacterial meningitis, 20 cases (33 %). 8 (13 %) cases were diagnosed viral meningitis and 7 children (12 %) were normal. A statistically significant association between CSF CRP positivity and Pyogenic meningitis was seen. **Conclusion:** CSF-CRP levels can be used as a nearly diagnostic tool or confirmatory test in meningitis. It helps in differentiating various types of meningitis.

**Key words:** Tuberculous, pyogenic, viral meningitis, cerebrospinal fluid, C – reactive protein,

**Correspondence Address:** Dr Savita Chaudhary, Associate Professor, Dept. Of Dermatology, ELMCH, Lucknow , U.P., India

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#### INTRODUCTION:

Meningitis and especially bacterial meningitis is a serious problem faced worldwide. Severity of the infection depends on the damage caused to central nervous system. According to W.H.O., fatality rate of 4% to 27% is predicted for meningitis in developing countries.<sup>1</sup> Incidence rate of 12.8 and 6.6 cases per 100,000 populations for men and women was found for all children suffering from meningitis under the age of 15 years, in Tehran metropolis.<sup>2</sup> The diagnosis of meningitis remains a serious problem due to the complex nature of disease overlapping each other. However, early diagnosis is the key to success. Over many years different diagnostic aids like DNA probe, ADA level in CSF, radiographical, laboratory methods etc. have been used. However, a gold standard diagnostic aid is still lacking. Use of C reactive protein in diagnosis of different types of meningitis has been advocated.<sup>3</sup> Tillett et al. discovered C-reactive protein (CRP) and the acute phase inflammatory response in 1930.<sup>4</sup> CSF-CRP is found to be elevated in many other diseases like Rheumatoid Arthritis, Ankylosing Spondylitis, Reiters Syndrome etc. John, et al.

found that detection of CRP in CSF is a useful test for the diagnosis of bacterial meningitis with high sensitivity.<sup>5</sup> Routine diagnostic use of CSF-CRP is reported in fewer studies.<sup>6,7</sup> The present study was designed to study the role of CSF-CRP in diagnosis of meningitis.

#### MATERIALS AND METHOD:

The present study was conducted in the Department of Pediatrics, with the help of Department of Pathology of Vivekananda Polyclinic & Institute of Medical Sciences, Lucknow for a period of 1 year. A total of 60 patients were evaluated for the study. Age group selected for the study was 1 month to 14 years. Duration of the study was one year. Ethical committee clearance was obtained. Patients/Guardians were explained about the study. A written informed consent was obtained from patient's guardian. All the patients were examined; a detailed case history was obtained regarding age, sex, past history of tuberculosis, history of contact with tuberculosis patients etc. Inclusion and exclusion criteria were as follows:

**Inclusion Criteria**

1. Children admitted in Pediatric ward / Pediatric ICU of Vivekananda Polyclinic & Institute of Medical Sciences with meningitis and suspected meningitis.
2. Patients between the age group of one month to fourteen years.

**Exclusion Criteria**

1. Patients not fulfilling the age criteria i.e. less than one month and more than fourteen years
2. Patients with history of previous CNS illness.

Cases were divided into four groups (Table 1),

Group 1-Tuberculous Meningitis

Group 2-Pyogenic Meningitis

Group 3-Viral Meningitis

Group 4-Normal (Febrile seizures)

Patients were subjected to routine blood investigations, Mantoux test, CSF Examination – Routine, CRP etc. Immunoturbidimetric method was used to determine CSF-CRP.

**DATA ANALYSIS:**

Data was collected, tabulated and subjected to analysis using Statistical Package for Social Sciences (SPSS) Version 15.0. Non parametric data has been represented as frequencies and percentages.

**RESULTS:**

60 patients were included in the study. Out of 60 cases, based on clinical and CSF examination, 25/60 (42%) cases were diagnosed as tuberculous meningitis, followed by pyogenic/bacterial meningitis, 20/60 (33%) cases. 8(13%) cases were diagnosed as viral meningitis and 7(12%) cases were normal (Table 1). 72 % of cases of TBM were under the age of 5 years and most were in the age group of 2-5 year accounting for 52 %. Viral meningitis was more common in children above five years of age (Table 2). 16/60 patients were aged between 1month and 2 years. Among the study subjects, majority (61.67%) were males while around two-fifth (38.33%) were females (Graph 1). The male to female ratio of study subjects was 1.61:1. The proportion of males was highest in viral meningitis group (75%) while it was minimum in TBM Group (56%). However, statistical comparison of the data did not reveal a significant difference among the groups (p=0.778).CSF CRP was measured in all the 60 cases. Out of 20 cases of pyogenic meningitis, raised and positive CRP (more than 5 mg/dl) was found in 10 cases (Table 3).CRP positivity was seen in 50% cases of pyogenic meningitis. A statistically significant association between CRP positivity and pyogenic meningitis was seen. No association between CRP positivity and TBM was seen.Sensitivity of CRP was 50 % and specificity was 100 %.

**Table 1:** The diagnosis in the study population

Group	Diagnosis	No. of cases	Percentage
I	Tuberculous Meningitis	25	42
II	Pyogenic Meningitis	20	33
III	Viral Meningitis	8	13
IV	Normal (Febrile seizures)	7	12

**Table 2:** Age distribution of the study population

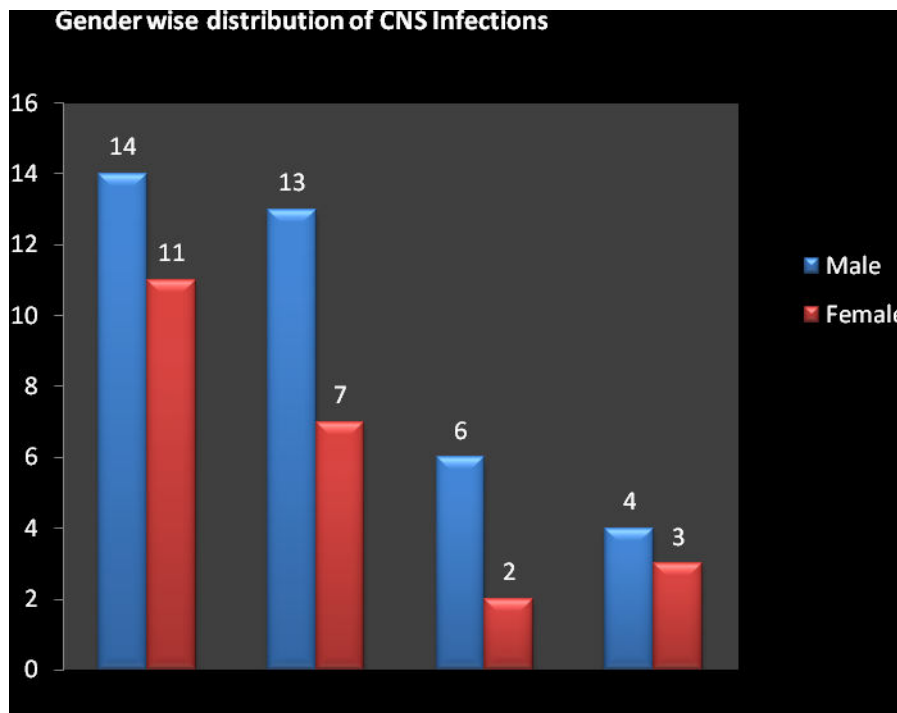
Group	No. of cases	>1 mt-2 yr	>1 mt-2 yr %	>2-5 yr	>2-5 yr %	>5-14 yr	>5-14 yr %
I	25	5	20	13	52	7	28
II	20	5	25	4	20	11	55
III	8	1	12.5	1	12.5	6	75
IV	7	5	71	2	29	0	0

**Table 3:** CRP Positivity

Groups		CRP		Total
		Negative	Positive	
TBM		25	0	25
	Pyogenic	10	10 (50%)	20
	Viral	8	0	8
	Other	7	0	7
<b>Total</b>		50	10	60

$\chi^2=24.00$  (df=3); p<0.001

**Graph 1:** Gender distribution



$\chi^2=1.096$  (df=3); p=0.778

**DISCUSSION:**

The diagnosis of meningitis remains a controversial issue in spite of availability of various diagnostic measures. Initial treatment by the physicians involves antibiotic therapy. Antibiotic therapy sometimes makes it impossible to isolate the organisms from blood or CSF. As recommended by Pepys MB, due to more sensitive and precise assays for the measurement of CRP levels there has been a recent resurgence of interest in its biological applications.<sup>8</sup>In our study CRP positivity was seen in 50% cases of pyogenic meningitis. A statistically significant association between CRP positivity and pyogenic meningitis was seen in our study. Kumar et al. reported that the CSF cultures for pyogenic organisms were positive in only 30–60% of cases.<sup>9</sup>Our study is in agreement with those reported by Kumar et al.

Various authors suggested that children younger than 3 years of age have a poorer prognosis for survival than do older children, a fact that might relate to the easier recognition of the disorder in older children. In current study, most common age group found was 2-5 years.<sup>10</sup> Denis R et al. suggested that CSF C-reactive protein is too insensitive to be useful, while serum CRP is too nonspecific for routine application, however this does not correlate with our study.<sup>11</sup> In present study Sensitivity of CRP was 50 % and specificity was found to be 100 %. Phillip and Baker studied CSF from neonates with pyogenic meningitis and

tested for CRP by using a sensitive Laser Nephelometry technique, they found elevated CRP levels in only two of 11 patients with culture proved pyogenic meningitis<sup>12</sup>. In our study CRP was positive for 10 cases in pyogenic meningitis i.e. 50% cases. CRP was negative for all other groups. Our study is in agreement with results reported by John et al, which suggest that CRP can be used to distinguish bacterial from viral, tubercular or other central nervous system disorders.<sup>5</sup>

**CONCLUSION:**

Although much data is not available on role of CSF-CRP as a diagnostic aid in meningitis, based on the results of our study, we recommend use of CSF-CRP levels as a diagnostic aid in differentiating bacterial meningitis from other forms of meningitis. The procedure is easy to perform and can be used for evaluating patients of suspected meningitis.

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