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Original Research Article

Prospective Observational Assessment of the Diagnostic Role of CSF C-Reactive Protein Quantitatively in Acute Meningitis and Differentiating Pyogenic Meningitis from Non-Pyogenic Meningitis

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Abstract

Aim: To assess the diagnostic role of CSF C-reactive protein quantitatively in acute meningitis and to evaluate the efficacy of CSF C-reactive protein in differentiating pyogenic meningitis from non-pyogenic meningitis.

Material and Methods: It is a prospective observational study of total 102 children with suspected meningitis allocated into three groups based on initial investigations; group- I Pyogenic meningitis, group-II Non-Pyogenic meningitis and group-III No meningitis (Control group). Quantitative CSF C-reactive protein was detected by the latex agglutination method. Data were analyzed to establish the diagnostic role of CSF-CRP and to evaluate the efficacy of CSF-CRP in differentiating pyogenic meningitis from non-pyogenic meningitis.

Results: The age distribution among pyogenic meningitis (79) shows the maximum of 31 cases (39.2%) in the age group 1 month to 1 year. The mean value of the total count of WBC/mm3 in CSF, in pyogenic meningitis was 921.28 + 829.01, in Non-Pyogenic meningitis was 166.2 + 146.8 and in the case of normal CSF was 2.71 + 1.8. CSF culture was positive only in 17% of patients and common bacteria were grown in CSF culture were Streptococcus pneumonia (7.59%), Staphylococcus aureus (5.06%) and H. influenza (2.53%) and E.Coli (1.27).

Conclusion: Detection of CSF-CRP provides a new dimension to establish the diagnosis of pyogenic meningitis. It is a rapid, reliable and sensitive diagnostic test. From this study it is concluded that CSF-CRP can be used to differentiate pyogenic from non-pyogenic meningitis. Early, accurate and appropriate therapy can ameliorate the morbidity and mortality rates in such cases.

Keywords: CSF-CRP, Meningitis, Brain Infections

Introduction

Meningitis is a neurological emergency with high mortality and morbidity. In the past few years, significant advances have been made in the process of diagnosis and management of meningitis. Various pathogens are involved in the etiology of meningitis. The most commonly responsible organisms for pyogenic meningitis are S. pnemoniae in 50%, N. meningitides in 25%, Grp B. streptococci

in 10%, L. Monocytogenes in 10% [1]. Tubercular meningitis is the most common cause of chronic meningitis and incidence in patients with tuberculosis varies from 7 to 12 % [2]. Enteroviruses (polio, coxsackie, Echo) are most common cause of viral meningitis in more than 75% cases.

However CSF protein, sugar and leukocyte count are performed routinely to diagnose meningitis but these are not absolutely reliable markers for differentiating various types of meningitis because these are overlapping in their values. In the best of laboratories in India, CSF culture was positive only in 25-40% cases in which CSF gram stains were positive only in 25-30% cases of meningitis [3].

Most patients without bacterial meningitis have a negative Gram's stain (specificity 99.9%) with a negative predictive value of 99.9% [4]. Detection of nuclear polymorph leukocytes in the CSF is a fairly reliable indicator of pyogenic meningitis. But CSF leukocyte count <250/mm3 may be present in as many as 20% of patients with bacterial meningitis. Pleocytosis may be absent in patients with severe overwhelming sepsis.

Pleocytosis with a lymphocytic predominance may be present during the early stage of acute bacterial meningitis; conversely, neutrophilic pleocytosis may be present in patients during the early stages of acute viral meningitis Use of antibiotics makes the gram's stain and culture-negative and may alter the CSF cytology from neutrophilic to lymphocytic predominance [5].

Because of these limitations, several rapid diagnostic tests have been developed to aid in the diagnosis& to discriminate rapidly between viral meningitis and bacterial meningitis [6]. These techniques include Counter Immuno Electrophoresis of the CSF for the immunoglobulins, lactic acid, creatine phosphokinase and C-reactive protein [7]. As CRP is the fastest reacting and most sensitive indicator of an acute inflammatory reaction, it is a useful aid in preliminary differentiation between acute bacterial and nonbacterial meningitis. Detection of CSF-CRP appears to provide a new dimension to the diagnosis of meningitis [8].

Hence, this study aims to assess the diagnostic role of CSF C-reactive protein quantitatively in acute meningitis and to evaluate the efficacy of CSF C-reactive protein in differentiating pyogenic meningitis from non-pyogenic meningitis.

Material & Methods:

Cross-Sectional, Descriptive study was carried out in the Department of Pediatrics, Darbhanga Medical College and Hospital, Darbhanga, Bihar, India. Patients with suspected cases of meningitis with clinical signs and symptoms of acute meningitis, aged 1 month to 12 years, admitted to Department of Pediatrics, Darbhanga Medical College and Hospital, Darbhanga, Bihar, India.

Inclusion criteria:

- Age 1 month to 12 years.
- Clinical features are suggestive of meningitis.
- Patients with high body temperature.
- Feeding problems.
- Vomiting.
- Irritability
- Seizures or sluggishness.
- High pitched crying

Exclusion criteria:

- Patients in whom lumbar puncture is contraindicated i.e.
- Sepsis at the local site
- Papilloedema or other signs of raised intracranial pressure
- Marked spinal deformity
- Bleeding diathesis or on anticoagulant therapy

- Patients on steroid
- Traumatic lumbar puncture
- Refusal to consent
- Patients having congenital CNS abnormality and who is known case of neurodegenerative disorder of the brain.

Methodology

Total 150 patients were included after the protocol was approved by an ethical review committee. Informed written consent was taken.A detailed history has been taken. A general physical and systemic examination was done. Investigations including Complete Blood Count with CSF analysis (appearance, cell count & differential, sugar, protein, gram's stain, culture), quantitative CSF ,CRP, blood sugar, Mantoux Test (MT) in tubercular suspected, cranial CT scan and MRI brain if indicated was done.

Patients investigated as above were divided into three groups as mentioned below:

Group-I: Pyogenic meningitis

Group-II: Non-Pyogenic meningitis (Tubercular meningitis, Aseptic meningitis, etc.)

Group-III: No Meningitis (Normal CSF: cerebral malaria, febrile convulsion, dyselectrolytemia etc.)

Statistical Analysis:

We assessed the role of CSF C-reactive protein quantitatively in acute meningitis by using computer based program statistical package for social science (SPSS) version 20.0 programs. Statistical test used was ANOVA and unpaired t-test.

Results:

Total 150 clinically suspected meningitis children were enrolled for this cross-sectional observational study. Among 150 cases, 79 (52.7%) were diagnosed as Pyogenic meningitis (Group I), 37 (24.6%) as Non- Pyogenic meningitis (Group II) and 34 (22.6%) as No meningitis (Group III, normal CSF). [Figure 1, 2]

In most of the cases of the study population were in the age group of 1 month to 5 years. The age distribution among Pyogenic meningitis (79) shows the maximum of 31 cases (39.2%) in the age group 1 month to 1 year followed by 22 (27.8%) in the age of >1 year to 5 years [Table 1].

Sex distribution of study population where male patients were 82 (54.6%) and female 68 (45.3%). However, the difference between males and females was not statistically significant [Table2].

Clinical findings of acute meningitis in the study population where all of the study population (150) were suffering from fever (100%), Headache was present in Pyogenic meningitis 18 (22.7%) and Non-Pyogenic meningitis 8 (21.6%) respectively. Other clinical findings of enrolled children were described in Table 3.

The mean value of the total count of WBC/mm3 in CSF, in pyogenic meningitis was 921.28 + 829.01, in Non-Pyogenic meningitis was 166.2 + 146.8 and in the case of normal CSF was 2.71 + 1.8. All 79 cases (100%) of pyogenic meningitis had more than 50%Polymorphs in CSF. In Non-Pyogenic meningitis 37 cases (100%) cell type of Lymphocytes was > 50%. The mean value of Polymorphs in CSF, in pyogenic meningitis was 77.20 + 11.2, in Non-Pyogenic meningitis was 80.1 + 10.5 and in the case of normal CSF was 73.1 + 53.5. The mean value of Glucose level (mg/dl) in CSF, in pyogenic meningitis was 42.8 + 17.81, in Non-Pyogenic meningitis was 68.1 + 20.8 and in the case of normal CSF was 61.2 + 6.8. All 79 (100.0%) cases of Pyogenic meningitis had elevated protein levels>45 mg/dl of CSF. The mean value of protein level (mg/dl) in CSF, in

Pyogenic meningitis was 132.91 + 59.8, in Non-Pyogenic meningitis was 87.8 + 62.8and in the case of normal CSF was 62.1 + 6.7 [Table 4].

In 78 cases (98.7%) of Pyogenic meningitis CSF-CRP level was >1.1µg/ml and in 1 case (1.2%) was in the range of 0.05-0.10 µg/ml. In the case of Non-Pyogenic meningitis 36 (97.3%) The mean value of CSF CRP level in pyogenic meningitis was 6.51 ± 2.31µg/ml, in Non-Pyogenic meningitis was 0.10±0.066and in case of normal CSF was 0.01±0.010 [Table 5, 6].

Table 7 shows that in the pyogenic meningitis group, CSF culture was positive only in 17% of patients and common bacteria were grown in CSF culture were Streptococcus pneumonia (7.59%), Staphylococcus aureus (5.06%) and H. influenza (2.53%) and E.coli (1.27). [Table 7]

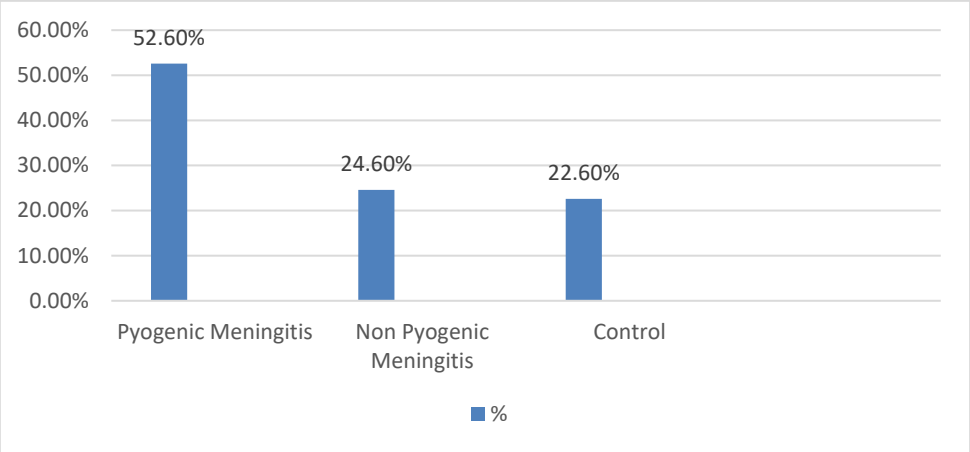

Figure 1: Categories of the study population based on CSF findings

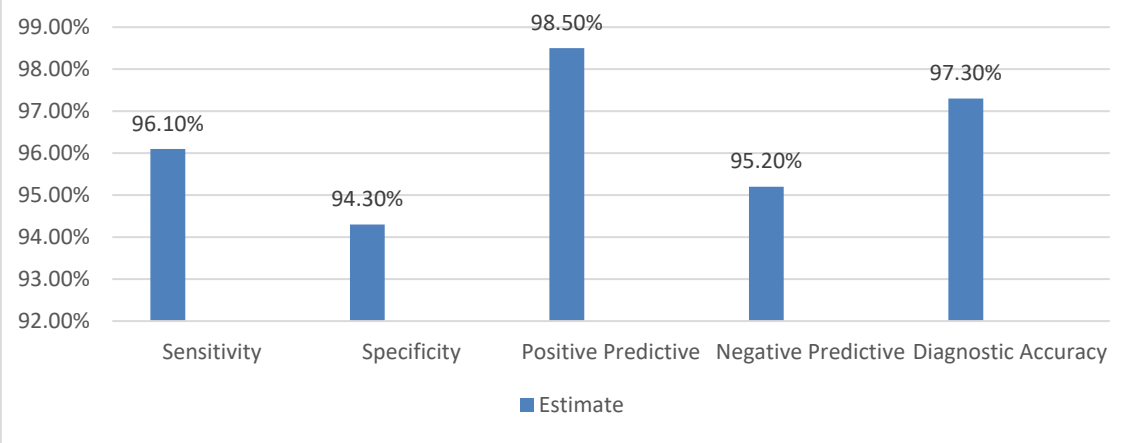

Figure 2: Categories of the study population based on CSF findings

Table 1: Age distribution of the study population (N=150)

Age group	Pyogenic meningitis	%	Non-Pyogenic meningitis	%	Normal CSF (Controls)	%	Total	%
1 month to 1 year	31	39.24	7	18.92	8	23.53	46	30.67
>1year to	22	27.85	19	51.35	18	52.94	59	39.33

5 years								
>5 years to 10 year	18	22.78	4	10.81	7	20.59	29	19.33
>10 years to 12 years	8	10.13	7	18.92	1	2.941	16	10.67
Total	79	100	37	100	34	100	150	100

Table 2: Sex distribution of the study population (N=150)

Sex	Pyogenic meningitis	%	Non-Pyogenic meningitis	%	Normal CSF (Controls)	%	Total	%
Male	44	55.7	20	54.05	18	52.94	82	54.67
Female	35	44.3	17	45.95	16	47.06	68	45.33
Total	79	100	37	100	34	100	150	100

Table 3: Clinical Presentation

Clinical findings	Pyogenic meningitis (Group I)	%	Non-Pyogenic meningitis (Group II)	%	Normal CSF (Controls) (Group III)	%	Total (N=150)	%
Fever	79	100	37	100	34	100	150	100
Headache	18	22.78	8	21.62	4	11.76	25	16.67
Nausea/ Vomiting	44	55.7	22	59.46	15	44.12	67	44.67
Altered Sensorium	51	64.56	36	97.3	17	50	83	55.33
Convulsion	37	61.67	16	43.24	36	105.9	64	42.67
Neck Rigidity	31	51.67	18	48.65	0	0	44	29.33
Kerning' Sign	29	48.33	9	24.32	0	0	29	19.33
Brudzinski' Sign	13	21.67	11	29.73	0	0	26	17.33

Table 4: Comparison of cytological and biochemical examination of CSF of the study population (N=150)

Parameters	Pyogenic meningitis (n=79)	Non-Pyogenic meningitis (n=37)	Normal CSF (Controls) (n=34)	P value*
Cell Count (cells/cmm)	921.28 + 829.01	166.2 + 146.8	2.71 + 1.8	0.0001
Cell_type	77.20 + 11.2 (Polymorphs)	80.1 + 10.5 (Lymphocytes)	73.1 + 53.5 (Lymphocytes)	0.0001

CSF Sugar (mg/dl)	42.8 + 17.81	68.1 + 20.8	61.2 + 6.8	0.0001
CSF Protein (mg/dl)	132.91 + 59.8	87.8 + 62.8	62.1 + 6.7	0.0001
CSF CRP (µg/ml)	6.7 + 2.6	0.11 + 0.068	0.01+0.012	0.0001

Table 5: CSF-CRP level among the study population (N=150)

CSF CRP (µg/ml)	Pyogenic meningitis (n=79)	Mean ±SD	Non-Pyogenic meningitis (n=37)	Mean ±SD	Normal CSF (Controls) (n=34)	Mean ±SD
0.001-0.04	0 (0.0%)	6.51 ± 2.31	0 (0.0%)	0.10±0.066	34 (100%)	0.01±0.010
0.05-0.10	1 (1.2%)		26 (97.3%)		0 (0.0%)	
0.11-1	0 (0.0%)		1 (2.7%)		0 (0.0%)	
1.1-15	78 (98.7%)		0 (0.0%)		0 (0.0%)	

Table 6: CSF-CRP Test Evaluation

CSF CRP (µg/ml)	Pyogenic meningitis (n=79)	Non-Pyogenic meningitis (n=37)	Normal CSF (Controls) (n=34)	Total
more than 0.1ug/ml	77	1	0	53
less than 0.1ug/ml	2	36	34	49
Total	79	37	34	150

Table 7: Bacteriology in Pyogenic meningitis

Bacteriology	No. of cases (n=79)	%
Streptococci	6	7.59
H. influenza	2	2.53
Staphylococcus aureus	4	5.06
E. coli	1	1.27
Culture positive	10	12.7

Discussion:

Singh N et al [9] who reported CSF CRP test had sensitivity of 84% in PM group. Similar sensitivity in PM group was found in study by Kishore R et al [10] (85.7%),

Mishra O.P. et al [11] (75%),However Finley F.O. et al [12], Przyjalkowski W. et al[13], Kaldor J. et al[14], Benjamin D.R. et al[15] found less sensitivity of CSF CRP test in PM group as 58%,62.5%,62.26% and 66% respectively.

Levels of CRP in serum and CSF increase as a result of invasive central nervous system infection. [16]Increased CRP production is an early and sensitive response to most forms of microbial infections and the value of its measurement in the diagnosis of various

infective conditions was established in previous studies. [17]

Additionally, blood CRP was positive in 29/32 cases of PM, giving a sensitivity of 90.62%. Similar findings have been reported by other researchers. [18]

According to Corral et al., this was a more sensitive test for differentiating bacterial from non-bacterial meningitis than any other laboratory test for CSF. Their study demonstrated that CSF CRP levels are also useful in diagnosing partially treated cases of meningitis. [19]

CSF-CRP has been reported to be one of the most reliable and early indices to differentiate bacterial from non-bacterial meningitis [3]. CRP estimation can help in diagnosing cases of acute bacterial meningitis more effectively than culture. It is also useful in monitoring the clinical course of meningitis [20]. This study aids to evaluate the diagnostic significance of CSF-CRP and as an indicator in the differentiation of bacterial from non-bacterial meningitis. [21]

Conclusion:

CSF CRP estimation was highly sensitive to diagnose and differentiate pyogenic meningitis

from tubercular and viral meningitis, while serum CRP was highly sensitive to diagnose and differentiate pyogenic and tubercular meningitis from viral meningitis. Detection of CSF-CRP provides a new dimension to establish the diagnosis of pyogenic meningitis. It is a rapid, reliable and sensitive diagnostic test. From this study it is concluded that CSF-CRP can be used to differentiate pyogenic from non-pyogenic meningitis. Early, accurate and appropriate therapy can ameliorate the morbidity and mortality rates in such cases.

References:

1. Roos K.L., Tyler K.L. Bacterial meningitis and other suppurative infection. Harrison's principles of internal medicine. 15th edition. P. 2462-2472.
2. Venkatraman VSM, Gorthi S.P., Dhamija R.M. Infection of the central nervous system. J. Postgrad. Med. 2000, Vol., 14:459-482.
3. Vaidya A.K., Wagle N.M. Use of CSF CRP in differentiating bacterial and nonbacterial meningitis. J. Postgrad. Med. 1987;33:58-60.
4. Neuman MI, Tolford S, Harper MB. Test characteristics and interpretation of cerebrospinal fluid gram stain in children. Pediatr Infect Dis J. 2008 Apr;27(4)309-13.
5. Whittle HC, Tugwell P, Egler LJ, Greenwood BM. Rapid bacteriological diagnosis of pyogenic meningitis by latex agglutination. Lancet. 1974 Sep 14;2(7881)619-21.
6. Chowdhury MZU, Rahman KM, Miah RA, SattarH, Hussain T. Bacterial Meningitis in children. Bangladesh Medical Journal. 1991;3–7.
7. Brown RL, Zinner SH, Meglio FD, Garrity FL. Countercurrent immunoelectrophoresis in the diagnosis of viral infections of the central nervous system. J Infect Dis. 1978 Dec;138(6)911-5.
8. Pemde HK, Harish K, Thawrani YP, Shrivastava S, Belapurkar KM. C-reactive protein in childhood meningitides. Indian J Pediatr. 1996 Jan- Feb;63(1)73-7.
9. Singh U.K. Cerebrospinal fluid C-reactive protein in the diagnosis of meningitis in children. Indian Pediatr 1994; 31:939-42.
10. Kishore R, Dwevedi R.N., Chandra R. Study of C-reactive protein level in CSF as a diagnostic marker in meningitis. JAPI Jan. 1999; Vol. 47:100.
11. Mishra O.P. Loiwal V, Aliz. CSF-ADA activity and CRP in tuburculous

and partially treated bacterial meningitis. Indian Pediatr Aug. 1995; 32(8):886-889.
12. Finlay F.O., Witherow H., Rudd PT: Latex agglutination testing in bacterial meningitis. Arch. Dis. Child 73:160;1995.
13. Przyjalkowski W., Lipowski D. CRP and its significance in purulent meningitis. Neurol Neurochir Pol. 1996. Jan- Feb. 30(1):177.
14. Kaldor J., Asznowicz R., Buist DGP. Latex agglutination in diagnosis of bacterial infections with special reference to patient with meningitis and septicemia. Am. J. Clin. Pathol 1977;68:284-289.
15. Benjamin D.R. Olpheim K.E., Brewer L. is C-reactive protein useful in the management of children with suspected bacterial meningitis. Am. J. Clin. Pathol, 1984;81:779-782.
16. Peltora HO. C-reactive protein for rapid monitoring of infections of the central nervous system. Lancet 1982; 1:980–2.
17. Debeer FC, Kirsten GF, Gie RP, Beyers N, Strachan AF. Value of C-reactive protein measurement in tuberculous, bacterial and viral meningitis. Arch Dis Child 1984; 59:653–6.
18. McCarthy PL, Frank AL, Ablow RC, Masters SJ, Dolan TF Jr. Value of the C-reactive protein test in the differentiation of bacterial and viral pneumonia. J Pediatr 1978; 92:454–6.
19. Corral CJ, Pepple JM, Moxon R, Hughes WT. C-reactive protein in cerebrospinal fluid in children with meningitis. J Pediatr 1981; 99:365–9.
20. Singh N, Arora S, Kahlon PS. Cerebrospinal fluid C-reactive protein in meningitis. Indian Pediatr. 1995 Jun;32(6):687-8.