

Diagnostic value of CSF C-reactive protein in meningitis: A prospective study

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Abstract

Objective: To establish diagnostic role of CSF C-reactive protein quantitatively in meningitis.

Method: It is a prospective observational study conducted at tertiary care centre in south Rajasthan. Total 100 patients were included and allocated into three groups based on clinical signs & symptoms; group-I Bacterial meningitis (n=50), group-II Tubercular meningitis (n=30) and group-III Control group (n=20). Along with other appropriate investigations, quantitative CSF C-reactive protein (CRP) was assayed and data were analysed to set a diagnostic level and sensitivity & specificity of CSF C-reactive protein (CRP) in meningitis

Result: In group-I patients CSF CRP value was 3.17 ± 2.68 µg/ml; in group-II CSF CRP value was 0.08 ± 0.12 µg/ml and in group-III CSF CRP value was 0.03 ± 0.02 µg/ml. The CSF CRP value in bacterial meningitis is significantly higher than tubercular meningitis and control (P value <0.001). The CSF CRP value >0.1 µg/ml has sensitivity 98.07%, specificity 96.00%, positive predictive value 96.22%, and negative predictive value 97.95%.

Conclusion: CSF CRP can easily differentiate bacterial meningitis from other meningitis with greater sensitivity and specificity.

Keywords: CSF C-reactive protein (CRP), meningitis.

1. Introduction

Meningitis is a significant cause of morbidity and mortality in children worldwide. Without treatment, the case-fatality rate can be as high as 70 percent, and one in five survivors of bacterial meningitis may be left with permanent sequelae including hearing loss, neurologic disability [1]. Neurological outcome and survival depends largely on damage to central nervous system prior to effective antimicrobial therapy. Quick diagnosis and effective management is key to success.

Diagnostic dilemma is due to large spectrum of signs and symptoms and majority of children who report to hospital have already been treated with inadequate doses of antibiotics and present with atypical features of CSF examination. The only reliable method is bacterial culture of CSF which is positive only in 30-60% and it requires at least 48-72 hrs to be positive [2]. Hence, a test that might help to diagnose and differentiate meningitis earliest is more useful.

CRP is the acute phase reactant which is synthesized by hepatocytes in response to infection or inflammation. CRP is normally present as a trace constituent of plasma (0.8 mg/dL) while it is negligible in cerebrospinal fluid. In acute infection, serum CRP concentration may reach up to 300 mg/dL within 24-48 hrs. The concentration of CSF CRP is

raised in patients with meningitis. Most of the studies have qualitative data of CRP in CSF [3,4,5,6] while only few studies have quantitative data of CRP in CSF [7,8,9,10,11] and most studies are from adult population. So we have planned this study to establish the diagnostic significance of CSF CRP in children with meningitis.

2. Materials & Methods

This prospective observational study was conducted in the department of pediatrics, RNT Medical College, Udaipur, Rajasthan from March 2015 to February 2016. Approval from institute ethical committee was obtained prior to the study. Written informed consent was taken from parents.

After exclusion of neonates and traumatic lumbar puncture, a total of 100 suspected cases of meningitis (fever, irritability, headache, vomiting, poor feeding, photophobia, altered sensorium, convulsion, bulging fontanelle and signs of meningeal irritation) were included in the study. All children were below 12 years. All the patients were gone through an initial work up including history and clinical examination as per proforma, relevant laboratory investigations including CBC, ESR, complete CSF analysis (Pressure, appearance, cell

count & differential, sugar, protein, gram stain, culture, Z&N stain and AFB culture if indicated and quantitative CSF (CRP), blood sugar, MT test in tubercular suspected, cranial CT. These 100 patients were divided into three groups based on the initial work up.

Group-I Bacterial meningitis suggested by history & examination, CSF analysis show CSF pleocytosis >500 cells/cmm with polymorphonuclear predominance, CSF protein >45 mg/dL, CSF sugar <40 mg/dL or < 60% of blood sugar, positive Gram smear or culture.

Group-II Tubercular meningitis suggested by history & examination, history of contact with case of tuberculosis, positive MT test, suggestive CXR, CSF pleocytosis in range

of 50-500 cells/cmm with lymphocytic predominance, CSF protein >45 mg/dL and low CSF sugar <40 mg/dL, positive AFB smear or culture, suggested cranial CT scan (basal exudates, hydrocephalus, tuberculoma, infarct etc).

Group-III Control (included cases of febrile seizure, cerebral malaria).

Immuno Turbidimetric Assay was used for quantitative analysis of CSF CRP.

Statistical analysis: Unpaired t-test was used for comparing mean difference between groups. SPSS version 16.6 (SPSS Inc, Chicago, IL, USA) was used for all Statistical analysis and a P value of <0.05 was taken as significant.

3. Result

Table I: Demographic data

Age	Bacterial meningitis			Tubercular meningitis			Control		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
1mo-1yr	19 (38%)	6 (12%)	25 (50%)	2 (6.6%)	5 (16.8%)	7 (23.4%)	2 (10%)	2 (10%)	4 (20%)
>1yr-5yr	7 (14%)	5 (10%)	12 (24%)	9 (30%)	5 (16.6%)	14 (46.6%)	4 (20%)	1 (5%)	5 (25%)
>5yr-12yr	9 (18%)	4 (8%)	13 (26%)	3 (10%)	6 (20%)	9 (30%)	6 (30%)	5 (25%)	11 (55%)
Total	35 (70%)	15 (30%)	50 (100%)	14 (46.6%)	16 (53.4%)	30 (100%)	12 (60%)	18 (40%)	20 (100%)

Table I shows that the study population contains total 100 cases and includes 50 cases of Bacterial meningitis, 30 cases of Tubercular meningitis and 20 control. Bacterial meningitis is more common in below 12 months (50%) and

most children were below the age of 5 years (74%) and more common in male patients (M:E=2.3:1). Tubercular meningitis is more common in above 12 months and almost equal incidence in both sex (M:E=0.9:1).

Table II: Bacteriology in Bacterial meningitis

Bacteriology	No. of cases (n=50)
Staphylococcus aureus	6 (12%)
Pneumococcus	2 (4%)
H. influenza	2 (4%)
Meningococcus	1 (2%)
E. coli	1 (2%)
Streptococci	1 (2%)
Culture positive	13(26%)

Table II shows that in Bacterial meningitis group, CSF culture was positive only in 26% patients and common bacteria grown in CSF culture were Staphylococcus aureus (12%), Pneumococcus (4%) and H. influenza (4%). Among

the 6 cases of Staphylococcus aureus meningitis, 4 cases were below 12 months and 2 cases were more than 12 months (14 mo & 84 mo).

Table III: CSF parameters in different groups

CSF Parameters	Bacterial meningitis (Group-I)	Tubercular meningitis (Group-II)	Control (Group-III)
Cell count (cells/cmm)	2892±2176.8	139.8±103.8	0.89±0.2
Cell type	83.04±16.12 (Polymorphs)	92.8±9.8 (Lymphocytes)	0.89±0.2 (Lymphocytes)
CSF sugar (mg/dL)	31.3±20.39	46.37±25.43	74±23.84
CSF protein (mg/dL)	72.48±53.14	123±56.3	48.2±14.69
CSF CRP (µg/ml) (Range)	3.17 ±2.68 (0.06-12.8)*	0.08 ±0.12 (0.03-0.7)**	0.03 ±0.02 (0.001-0.06)***

Mean ±SD

*Group-I&III- P value 0.001; 95% CI 1.93-4.34; **Group-I&II- P value 0.001; 95% CI 2.11-4.06

*** Group-II&III- P value 0.072; 95% CI (-) 0.0046-0.1046

Table III shows that CSF CRP value in Bacterial meningitis group was $3.17 \pm 2.68 \mu\text{g/ml}$, in Tubercular meningitis group it was $0.08 \pm 0.12 \mu\text{g/ml}$ and in control

group it was $0.03 \pm 0.02 \mu\text{g/ml}$. CSF CRP value was significantly higher in Bacterial meningitis group than Tubercular meningitis and control groups (P value <0.05).

Table IV: Comparative Sensitivity, Specificity, Positive predictive value and Negative predictive value in differentiating Bacterial meningitis from non- Bacterial meningitis

Parameter	CSF CRP ($>0.1 \mu\text{g/ml}$)
Sensitivity	98.07%
Specificity	96.00%
Positive predictive value	96.22%
Negative predictive value	97.95%

Table IV shows that CSF CRP $>0.1 \mu\text{g/ml}$ has a good sensitivity (98.07%), specificity (96.00%), good positive predictive value (96.22%), and good negative predictive value (97.95%) to differentiate Bacterial meningitis from Tubercular meningitis and control groups.

4. Discussion

Meningitis is an important cause of morbidity and mortality. There is diagnostic dilemma in diagnosing and differentiating bacterial meningitis from tubercular meningitis and to start specific treatment. There is always a need of a reliable, cost effective, rapid screening tests which can be performed in any standard laboratory and differentiate various types of meningitis.

In our study, bacterial meningitis is more common in below 12 months (50%) and most children were below the age of 5 years (74%) and more common in male patients (M:E=2.3:1). Tubercular meningitis is more common in above 12 months and almost equal incidence in both sex (M:E=0.9:1). These results are accordance to Bhat *et al* [12], Bhandari *et al* [13], Kabra *et al* [14].

In our study we found Staphylococcus aureus(12%), Pneumococcus(4%), H. influenza(4%) are most common bacteria. In bacterial meningitis CSF culture was positive only in 26% cases. Singh *et al* in their study (25 cases) found that the organisms isolated in CSF culture were; *Klebsiella* species in 8%, *H. influenzae* in 4% and *Streptococcus pneumoniae* in 4%. CSF culture was positive in 16% cases [3]. The higher culture yield in our study is supported by other studies [2]. Among the 6(12%) cases of Staphylococcus aureus meningitis, 4 cases were below 12 months and 2 cases were more than 12 months (14 mo & 84 mo).

In our study we found that the CSF CRP value is significantly higher in bacterial meningitis ($3.17 \pm 2.68 \mu\text{g/ml}$) compared to Tubercular meningitis ($0.08 \pm 0.12 \mu\text{g/ml}$) and controls ($0.03 \pm 0.02 \mu\text{g/ml}$). Gray *et al* found that CSF CRP level in bacterial meningitis was $1.46 \mu\text{g/ml}$ and in aseptic meningitis $0.017 \mu\text{g/ml}$ [10]. Donald *et al* found CSF CRP level in bacterial meningitis was $9.6 \mu\text{g/ml}$, in tubercular meningitis $0.29 \mu\text{g/ml}$, viral meningitis $0.01 \mu\text{g/ml}$ and in no meningitis group it was $0.08 \mu\text{g/ml}$ [11]. The results of these studies are consistent with our study. Singh N *et al* in children found higher CSF CRP positivity in bacterial meningitis

compared to aseptic meningitis [3]. Amulya C Belagavi *et al* [7], Anil Kumar T *et al* [8] also found significantly higher CSF CRP value in adult patients with bacterial meningitis compared to non- bacterial meningitis cases.

In our study the CSF CRP value of $>0.1 \mu\text{g/ml}$ has a good sensitivity (98.07%), specificity (96.00%), good positive predictive value (96.22%), and good negative predictive value (97.95%) for bacterial meningitis. Gray *et al* found that the CSF pleocytosis $>10 \text{ WBC}/\mu\text{L}$ CRP $>0.1 \mu\text{L/ml}$ was 95% accurate in identifying bacterial meningitis [10]. Amulya C Belagavi *et al* in their study in adult patients observed that the sensitivity and specificity of the test was 83.3% and 100% respectively with an accuracy of 98% [8]. Patel N *et al* found that CSF CRP has a sensitivity of 83.3%, specificity of 87.5%, and positive predictive value of 75% and negative predictive value of 92% in cases of bacterial meningitis [5]. They both have qualitative CSF CRP data.

In conclusion we found that CSF CRP level is significantly higher in bacterial meningitis patients compared to non-bacterial meningitis patients and CSF CRP value of $>0.1 \mu\text{g/ml}$ has a good sensitivity, specificity, good positive predictive value, and good negative predictive value and can be set as cut of value to diagnose bacterial meningitis. We can easily differentiate bacterial meningitis from non-bacterial meningitis by CSF CRP level.

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