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Original research article

CRP level in various neuro-infections and its correlation in determining bacterial meningitis from non-bacterial meningitis in relation to CSF-CRP

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Abstract

C-reactive protein (C-RP), an acute phase reactant detected in the CSF by Latex agglutination method is a helpful tool to differentiate between bacterial and non-bacterial meningitis at bed side. Many studies doubt efficacy of the test. Absence of C-RP rather than its presence is more important for the diagnosis of tubercular meningitis. This prospective study was being performed on children between age group of 2 month to 18 years of age with symptoms and signs suggestive of meningitis with CSF showing pleocytosis admitted in hospital. In the present study positive qualitative blood CRP (>0.6 mg/dl) is seen 100% positive in BM, 46% positive in TBM and 100% negative in viral memingitis. However taking quantitative blood CRP level of more than 4.8mg/dl has senisitvity, specificity, positive predictive value and negative predictive value of 100% in diagnosing BM.

Keywords: CRP, CSF, meningitis

Introduction

Acute infection of Central Nervous System (CNS) is the most common cause of fever associated with signs and symptoms of CNS disease in children. Most common infections of CNS are meningitis and encephalitis. Meningitis implies primary involvement of meninges whereas encephalitis indicates brain parenchymal involvement. Because these anatomic boundaries are often not distinct, many patients have evidence of both meningeal and parenchymal involvement and should be considered to have meningoencephalitis [1].

In a multi centric survey in India, Bacterial Meningitis (BM) constituted 1.5 % of admission in Pediatric ward and mean case fatality was 16% [2].

Diagnosis of CNS infections depends on careful examination of Cerebrospinal fluid (CSF). Other investigations are Latex agglutination test for bacterial antigens, Counter Immuno Electrophoresis (CIE), Enzyme Linked Immunno Sorbent Assay (ELISA) [2], Lactate dehydrogenase, Radioimmuno assay [3], Polymerase Chain Reaction (PCR), serological test for virus, viral culture, imaging studies [4]. These investigations are expensive, time consuming and not available at all centers.

C-reactive protein (C-RP), an acute phase reactant detected in the CSF by Latex agglutination method is a helpful tool to differentiate between bacterial and non-bacterial meningitis at bed side [5]. Many studies doubt efficacy of the test [6, 7]. Absence of C-RP rather than its presence is more important for the diagnosis of tubercular meningitis [8].

Detection of CSF C-RP by Latex agglutination test is cost effective and rapid test compared to culture which can be useful in early institution of proper therapy and ensure better prognosis [9].

Methodology

This prospective study was being performed on children between age group of 2 month to 18 years of age with symptoms and signs suggestive of meningitis with CSF showing pleocytosis admitted in hospital.

Method of collection of data

Relevant epidemiological data is obtained in a self-administered pretested proforma.

1) Investigations:

a. Hb estimation

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b. Blood count.
c. Blood CRP level by latex slide agglutination test (Semi-Quantitative Test).
d. Blood sugar estimation by using electronic glucometer.
e. Chest X-ray and Mantoux test.
f. CSF examination was done after obtaining sample by lumbar puncture under strict aseptic methods.
- CSF-cell type and cell count.
- CSF-Protein by pyrogallol red method.
- CSF-Sugar by glucose oxidase method.
- CSF-Chloride.
- Gram stain, ZN stain.
- CSF culture on choclate agar.
- CSF CRP by latex slide agglutination test (Qualitative Test).
g. CT scan.

CRP latex agglutination test
Slide latex agglutination for determination of C-reactive protein.

Qualitative test
Kit used
Agappe diagnostics Pvt. Ltd.

Principle
It is a rapid agglutination procedure for the direct detection and semi-quantitation of C-reactive protein. The reagent, a latex particles suspension coated with specific antihuman C-reactive protein antibodies, agglutinates in the presence of CRP in the patient CSF.

Sensitivity
0.6 mg/dl of CRP can be detected by this kit.

Procedure of test
Allow all reagents as well as the sample to reach room temperature, mix well before use. The manufactures instruction were followed during the test, using a pipette one drop of CSF, positive and negative controls were put on a slide. One drop of latex reagent was added and slide rotated and mixed and observed for any agglutination.

Interpretation of test
The presence of agglutination within 2 minutes indicates concentration of CRP in the CSF equal or greater than 0.6 mg/dl and test is taken as positive. Absence of agglutination is taken as negative result.

Results

Table 1: Mean Blood CRP Levels in Variuous CNS Infection

	RANGE(mg/dl)	MEAN(mg/dl)
BM	4.8-76.8	32.06
TBM	0.6-2.4	0.55
VM	Negative	Negative

Mean blood CRP level in BM was 32.06mg/dl and 0.55mg/dl in TBM. Blood CRP was negative in all cases of viral meningitis.

Table 2: Blood CRP Level in Variuous CNS Infections

Blood CRP (mg/dl)	BM	TBM	VM
<0.6	00	07 (54%)	18 (100%)
0.6-2.4	00	06 (46%)	00
>4.8	25(100%)	00	00

Blood CRP was positive (>0.6mg/dl) in all cases 25(100%) of BM and 6(46%) cases of TBM and it was negative in all cases of VM.

Positive Qualitative blood CRP (>0.6mg/dl) has
Sensitivity - 100%.
Specificity - 83.87%.
Positive predictive value - 83.33%.

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Negative predictive value -100%for diagnosing bacterial meningitis.

Taking quantitative blood CRP level of more than 4.8mg/dl has
Sensitivity - 100%.
Specificity - 100%.
Positive predictive value - 100%.
Negative predictive value - 100% for diagnosing bacterial meningitis.

Table 3: CSF CRP in BM, TBM and VM

		CSF-CRP	
	No	**Positive**	**Negative**
BM	25	21(84%)	04(16%)
TBM	13	00	13(100%)
VM	18	00	18(100%)

In the present study CSF CRP was positive in 21 out of 25 cases (84 %) in bacterial meningitis while it was negative in all cases of tubercular and viral meningitis.
Positive qualitative CSF-CRP by latex agglutination method in diagnosing bacterial meningitis has
Sensitivity - 84%.
Specificity - 100%.
Positive predictive value - 100%.
Negative predictive value - 88.57%.

Table 4: Co-relation of Blood & CSF CRP in BM

Blood CRP (mg/dl) Level	Total Cases	CSF-CRP	
		Positive	**Negative**
4.8	01	00	01(100%)
9.6	05	03(60%)	02 (40%)
19.2	07	06 (86%)	01(14%)
38.4	08	08(100%)	00
76.8	04	04(100%)	00

As the blood CRP level increases the positivity of Qualitative CSF-CRP increases.

Discussion
In the present study positive qualitative blood CRP (>0.6 mg/dl) is seen 100% positive in BM, 46% positive in TBM and 100% negative in viral memingitis.
However taking quantitative blood CRP level of more than 4.8mg/dl has senisitvity, specificity, positive predictive value and negative predictive value of 100% in diagnosing BM.

Table 5: CSF CRP in Bacterial meningitis

	Cases studied	CSF CRP	
		Positive	**Negative**
Pemde *et al.* [10]	30	30(100%)	0
Chinchankar *et al.* [11]	54	22(41%)	32(59%)
Present study	25	21(84%)	04(16%)

While positive qualitative CSF-CRP in diagnosing BM has shown senisitvity (84%), specificity (100%), positive predictive value (100%) and negative predictive value of 88.5%. However study by Pemde *et al.* showed sensitivity of 100%. Chinchankar *et al.* showed sensitivity of 41%.
When we correlated the quantitative blood CRP level with qualitative CSF-CRP, we found that as blood CRP level increases positivity of CSF-CRP increases which also explains the theory of passive diffusion of CRP from blood to CSF across highly inflammed meninges. In present study children with blood CRP level more than 38.4mg/dl had 100% positive CSF-CRP

Table 6: CSF CRP in TBM

	Cases studied	CSF CRP	
		Positive	**Negative**
John *et al.* [12]	18	00	18(100%)
Ajay gaur *et al.* [7]	40	06(15%)	34(85%)
Present Study	13	00	13 (100%)

In the present study CSF CRP was negative in all (100%) cases of TBM which is consistent with the study done by John *et al.*, however it was poitive in 15% of cases as reported by Ajay gaur *et al.*

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Table 7: CSF CRP in VM

	Cases studied	CSF CRP	
		Positive	Negative
Prasad *et al*. [8]	04	00	04(100%)
U.K Singh [9]	70	00	70(100%)
Present study	18	00	18(100%)

CSF CRP was consistently negative in all the 18 cases of VM in the present study and it correlates with the study done by Prasad *et al*. and U.K. Singh.

Conclusion

Measurement of CSF-CRP is the best method that could be utilized to distinguish between BM and non BM. Considering the need for rapid, accurate and inexpensive diagnostic tools for distinguishing between bacterial and non-bacterial meningitis and consequently initiating treatment of BM patients and also to limit the unnecessary use of anti-microbrial agents in patient with VM, we recommend the combined application of blood CRP and CSF-CRP tests can be used as adjunct with other tests in the diagnosis of bacterial meningitis.

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