

A STUDY ON LEVELS OF SERUM C-REACTIVE PROTEIN ESTIMATION IN ACUTE MENINGITIS IN ADULTS AT A TERTIARY CARE HOSPITALPrashantakumar B. Jaikar¹, Shivaraj B. M², Shoukat A. R³**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: BACKGROUND AND OBJECTIVES: Few conditions in medicine require rapid and accurate therapeutic intervention as in acute pyogenic meningitis and viral meningitis. The present study helps to differentiate bacterial and viral meningitis or aseptic meningitis with help of serum C-reactive protein (CRP), however for diagnosis Cerebro Spinal Fluid (CSF) analysis is final.

MATERIALS AND METHODS: All patients who were admitted to Basaweshwara Teaching and General Hospital (BTGH) attached to M.R.M.C Gulbarga for approximately 2 years from September 2011 to April 2013 were considered with definite clinical signs and symptoms of acute meningitis were evaluated for serum CRP levels for the differentiation of pyogenic and aseptic meningitis.

RESULTS: In our study done in 50 cases of acute meningitis in adults admitted in BTGH Gulbarga were considered, out of 50 cases 16 cases in their CSF analysis showing predominant polymorphs with significant elevation in proteins and reduced sugar levels. Among 16 cases 8 cases show S-CRP >48mg/l and 8 cases showed 24-48mg/l. In remaining 34 cases CSF cell count with predominant lymphocyte among these 16 cases were having S-CRP 6mg/l normal sugar levels and mild elevation in proteins negative for Acid Fast Bacilli (AFB), Gram's stain, culture, CSF picture probably indicating viral or aseptic meningitis. 9 cases showed same CSF picture with S-CRP in range of 6-12mg/l. 8 cases showed S-CRP in range of 12-24mg/l were 2 cases are AFB POSITIVE, 1 case showed CSF picture of viral but S-CRP in range above 48mg/l. **INTERPRETATION AND CONCLUSION:** In our study we concluded that serum-CRP level less than 6mg/L, with clinical signs of Meningeal infection is definite indicator viral meningitis and patient with S-CRP more than 48mg/l indicate pyogenic meningitis.

KEYWORDS: Serum C Reactive Proteins, Bacterial Meningitis, Viral Meningitis.

INTRODUCTION: The evolution of clinical signs and symptoms produced by meningitis or encephalitis varies greatly. Few conditions in medicine require rapid and accurate therapeutic intervention as in acute pyogenic meningitis and viral meningitis, yet meningitis can also occur in chronic and recurrent forms. The major problem presented by patients with meningitis is rapid determination of its an etiology, the specific basis on which selection of potentially effective antimicrobial therapy is predicted. Thus, the clinician must sort out the form of clinical presentation, assess the rapidity of its evolution, and make a specific etiological diagnosis. The examination of cerebrospinal fluid is an essential and often critical tool in the evaluation and management of patients with meningitis. If interpreted carefully, the cerebrospinal fluid (CSF) analysis, can be very helpful in guiding the diagnostic evaluation and management of patients. Although examination of a Gram's stain of spinal fluid often defines the causative agent, this is not always the case. Cultures have the drawback of the time required, 24 to 48 hours or more to become positive, an unacceptable delay in initiating the treatment.¹ Clinical Epidemiology Unit, Madras Medical College, have declared that in developing countries, differentiating bacterial meningitis from viral meningitis and tubercular

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meningitis is not easy. Not all medical centers have viral diagnostic laboratories at their disposal. Moreover, serological confirmation of a viral infection is usually of academic interest, since by the time its result is available, the patients would have recovered or otherwise, it never determines specific therapy.

Not all medical centers have viral diagnostic laboratories at their disposal. Moreover, serological confirmation of a viral infection is usually of academic interest, since by the time its result is available, the patients would have recovered or otherwise, it never determines specific therapy. Further, the cost of antiviral therapy is very high when compared to antimicrobial therapy. So, in developing countries like India, we cannot institute empirical antiviral therapy to all patients of suspected viral meningitis. Therefore, several different techniques to discriminate rapidly between viral meningitis and bacterial meningitis have been evaluated.

These include counter immune Electrophoresis (CIE) of the CSF for the immunoglobulin's, lactic acid, creatine phosphokinase isoenzyme and c-reactive protein.² Because of easy availability of the kit and simplicity of the procedure, serum C-reactive protein (CRP) was selected to differentiate viral meningitis and bacterial meningitis, which is elevated in the latter, were observed in the selection of cases. Further, CRP was used only to differentiate bacterial meningitis from other meningitis, but not for the diagnosis of meningitis which was done only by routine clinical methods. CRP is the fastest reacting and most sensitive indicator of an acute inflammatory reaction. It is an useful aid in preliminary differentiation between acute bacterial and viral infections with sensitivity and specificity rates of 100% and 98% respectively.³

AIMS AND OBJECTIVES: To study serum C-reactive protein levels in differentiating bacterial meningitis from viral meningitis.

MATERIALS AND METHODS: Fifty cases with definite clinical signs and symptoms of acute meningitis of both sex admitted in Basaveshwar Teaching and General Hospital, Gulbarga attached to Mahadevappa Rampure Medical College, Gulbarga during November 2011-April 2013 were taken up for the study. All the cases who had shown the clinical signs and symptoms of meningeal infection were investigated for serum C-reactive protein levels which were done by Rapid latex test. CSF study was done in all cases, to confirm the S-CRP findings. The results were correlated with the results of S-CRP levels and the cases were differentiated into bacterial meningitis or meningitis due to other causes. It was a cross sectional study which was done at in-patient setting of Department of internal medicine Basaveshwara Teaching and General Hospital, Gulbarga.

Inclusion Criteria:

1. Above 12 years of age.
2. History suggestive of meningitis.
3. Neck Rigidity.

Exclusion Criteria Observed for Serum CRP Testing: All cases which had the following history were excluded from the study in order to avoid false positive S-CRP results.

Recent injury of any kind, Recent surgery, Patients in the immediate post-partum period, Known case of Rheumatic Heart Disease (According to modified Jones Criteria), Known case of Rheumatoid arthritis (According to ARA diagnostic Criteria), 6. Known case of acute or chronic

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glomerular nephritis and all cases of Genito-Urinary tract infection, Focal infections like pneumonic consolidation, infections of skin etc.

OBSERVATION AND RESULTS: Out of 50 study subjects 28 were males and 22 were females. 16 cases belong to the age group of 13-20 years (32%), another 14 cases (28%) in 21-40 years group, 16 cases (32%) were from 41-60 years group and 4 cases (8%) were above 60 years of age. Mean and standard deviation of age in male is 35.57 ± 15.64 ; females is 35.50 ± 17.90 .

| Age | Gender | | | | Total Number of Patients | Percentage |
|--------------|-----------|-----------------|-----------|-----------------|--------------------------|------------|
| | Male | Percentage | Female | Percentage | | |
| 13-20 | 8 | 28.6 | 8 | 36.4 | 16 | 32 |
| 21-40 | 8 | 28.6 | 5 | 22.7 | 13 | 26 |
| 41-60 | 10 | 35.7 | 7 | 31.8 | 17 | 34 |
| >60 | 2 | 7.1 | 2 | 9.1 | 4 | 8 |
| TOTAL | 28 | 100(56%) | 22 | 100(44%) | 50 | 100 |

Table.1: Age and Gender Wise Distribution of Subjects

| S-CRP | S-CRP Qualitative | Number of patients | Percentage | Death | Percentage |
|--------------|-------------------|--------------------|------------|-----------|------------|
| <6 | - | 16 | 32 | 9 | 56.2 |
| 6-12 | + | 9 | 18 | 2 | 22.2 |
| 12-24 | ++ | 8 | 16 | 0 | 0 |
| 24-48 | +++ | 9 | 18 | 1 | 11.1 |
| >48 | ++++ | 8 | 16 | 2 | 25 |
| TOTAL | | 50 | 100 | 14 | |

Table 2: Serum - CRP and mortality

Chi square test= 6.12, $P=0.0482$ ($p < 0.05$) p value is significant lower the serum CRP deaths are more.

S-CRP levels were analyzed in all the fifty cases. Sixteen cases (32%) showed negative results for S-CRP indicating a possibility of viral infection. Of these nine cases (56.2%) expired. Nine cases (18%) were having S-CRP of 6 mg/L level, of which 2 cases (22.22%) expired. Eight cases (16%) had S-CRP levels 12-18mg/L level of which there was no mortality. Nine cases (18%) had S-CRP levels 24-48mg/L, of which one died (11.11%) and eight cases (16%) were having strongly positive levels of >48mg/L indicating a definite bacterial infection, of which two cases (25.0%) expired. In 25 cases, S-CRP <6 mg/L and 9 cases had SCRP 6 signs in favour of meningitis or meningoencephalitis and CSF formula in favour of viral infection. The CSF glucose protein is normal or slightly elevated, indicating the possibility of CRP levels were less than 12mg/L of these, 16 cases had SCRP 6-12mg/L. All these 25 cases were having clinical levels in all the 25 cases were near normal limit and viral infection.

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| S-CRP in mg/l | S-CRP | Number of viral meningitis | Number of bacterial meningitis | Chi square test and p value |
|---------------|-------|----------------------------|--------------------------------|---------------------------------|
| <6 | - | 16 | 0 | Chi square Test =45.6, p<0.0001 |
| 6-12 | + | 9 | 0 | |
| 12-24 | ++ | 8 | 0 | |
| 24-48 | +++ | 1 | 8 | |
| >48 | ++++ | 0 | 8 | |
| TOTAL | - | 34 | 16 | |

Table 3: Comparison of S-CRP with viral and bacterial meningitis

| Variables | | Viral Meningitis | Bacterial Meningitis | Chi square Test and p-Value |
|--------------|---------|------------------|----------------------|------------------------------|
| GENDER | MALES | 19 | 09 | Chi square =0.00029, P=0.732 |
| | FEMALES | 15 | 07 | |
| TOTAL | | 34 | 16 | |
| DEATHS | | 10 | 04 | Chi square =0.0043, P=0.63 |
| CULTURE | | | | Chi square =03.94, P=0.048 |
| POSITIVE | | 07 | 16 | |
| NEGATIVE | | 27 | 00 | |
| AFB | | | | Chi square =0.98, P=0.43 |
| POSITIVE | | 02 | 00 | |
| NEGATIVE | | 32 | 16 | |
| GM STAIN | | | | Chi square =26.56, P=0.001 |
| POSITIVE | | 02 | 10 | |
| NEGATIVE | | 32 | 06 | |
| CSF GLUCOSE | | 33.41±4.48 SD | 21.0±2.37SD | t=12.79 p=0.00021 |
| CSF PROTEIN | | 47.14±5.23 | 58.5±3.10 | t=9.48 P=0.00053 |
| AGE | | 36.61±15.96 | 33.25±16.7 | t=0.67 p=0.0326 |

Table 4: Comparison of variables with viral and bacterial meningitis

Meningeal infection still remains a significant health problem, although the overall incidence had decreased. The diagnosis and treatment of acute meningitis is a challenge for the primary care physician. The earlier the recognition of bacterial meningitis and the more rapid the institution of antimicrobial. Therapy, the better the chance of a favorable outcome. Since the modality of treatment for bacterial and viral meningitis are totally different, it is very important to differentiate the meningitis on aetiological basis from bacterial and viral origin.

It is generally held that the confirmation of viral meningitis by means of a positive culture is of academic interest, since no specific antiviral therapy exists to change the clinical outcome. The CSF examination is most critical in distinguishing bacterial from viral meningitis.

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When a definite diagnosis of viral meningitis is made, anti-microbial therapy could be discontinued and the hospital stay might be significantly shortened.

Not all medical centers have viral diagnostic laboratories at their disposal. Moreover, the serologic confirmation of a viral infection is usually of academic interest, since by the time its result is available, the patient has recovered and it never determines specific therapy. Therefore, several different techniques to discriminate rapidly between viral and bacterial meningitis have been evaluated. These include counter immune electrophoresis (CIE) of the cerebrospinal fluid (CSF) for the detection of viral antigens and examination of the CSF for immunoglobulin's, Lactic acid dehydrogenase, creatine phosphokinase isoenzyme and C-reactive protein (CRP).

The sine quo none of establishing viral meningitis on the basis of culture is very expensive and moreover it is not available in most of the places in our country and unfortunately no simple and easily performed procedure to distinguish viral from bacterial meningitis is available which has 100 percent predictive positive and negative values. For this reason the C reactive protein (CRP) was chosen to differentiate bacterial from viral infections of the central nervous system. Abramson J.S. Hamton K. D. et al⁴ studied the use of C-reactive protein for differentiating meningitis and have pointed out that the C-reactive protein may be the single best nonspecific indicator of bacterial infection with sensitivity and specificity rates of 100 and 98 percent, respectively. Further the serum C-reactive protein measured by rapid latex test can be done as a bedside procedure which cost only fifty rupees and two minutes time. If the result is viral, unnecessary antibiotics administration for prolonged period can be avoided, and only supportive measures are sufficient for all cases of viral meningitis. Even if the virus is isolated, at present no specific antiviral drug therapy is available. Therefore, the serum C-reactive protein estimation is most useful in differentiating bacterial from viral infection of the central nervous system, especially for developing countries like ours, even in peripheral medical centers.

Meningeal infection both bacterial and viral has got a male predominance as observed in the study correlations well with the study of National Institute of Communicable Diseases 68, Directorate General of Health, India, during the epidemics of bacterial meningitis in the year 1966, 1985 and 1987. The male predominance of 69 percent was shown Etter C.G. 1991⁵ in his study on viral meningitis. 32% were in 13-20 years age group whereas 28% were in 21-40 years age group and 32% were in 41-60 age group, which correlates well with Choi, C 1992,⁶ who has pointed out that meningitis remains a significant health problem for the older adults. The ability of serum C-reactive protein (S-SRP) to differentiate between acute bacterial and non-bacterial meningitis was evaluated in fifty cases, of adult population. The patients underwent lumbar puncture for suspected central nervous system (CNS) infections. Of the fifty cases, 16 cases were diagnosed as bacterial meningitis, another 34 cases as meningitis due to non-bacterial causes. Ill patients with bacterial meningitis eight cases were having the S-CRP levels of more than 48mg/L. The S-CRP levels of 24-48mg/L were found in 8 cases. In eight cases, S-CRP was 12-24mg/L and were diagnosed as tubercular meningitis. There was no case of fungal or atypical meningitis in the study. In nine cases the S-CRP levels were 6-12 mg/L. In sixteen cases the S-CRP was <5mg/L. All the 25 cases were diagnosed as cases of viral meningitis. Therefore, a significant positive S-CRP supported by:

1. Cerebrospinal fluid pleocytosis.
2. Elevated protein and low CSF sugar.
3. A CSF sugar value of less than 35 mg/dl was taken as evidence of bacterial aetiology.

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From the study, in adults, a S-CRP level of less than 6 mg/L with clinical signs of meningitis, is a definite indicator of viral meningitis. Whereas, a S-CRP level of more than 48mg/L indicates a definite bacterial aetiology; this is supported by Hensen. L., Kamin, W 1992 and Riberio, M.A. Kimura, R.T.⁷ As the patients who have shown S-CRP level of 24-48mg/L and 12-24mg/L were having the history of preadmission treatment with antibiotics and steroids. These patients may have partially responded to the treatment, further the steroids might have reduced the S-CRP level. This view is supported by Smith et al (1990)⁸ and H. Gevold, H.E. et al in 1992⁹ as per their studies, the steroids inhibit macrophage secretion and synthesis of interleukin 1 the messenger and modulator for CRP stimulation from hepatocytes. In all these patients, the CSF analysis showed a definite possibility of bacterial meningitis.

DISCUSSION AND CONCLUSION: Estimation of C-reactive protein in serum is the cheapest, sensitive and specific test to differentiate bacterial from viral infections. It is a simple qualitative as well as quantitative test and can be done as a bed side investigation. With serum C-reactive protein, a definite aetiological diagnosis can be made rapidly at the time of admission itself. A serum CRP level of less than 6mg/l with clinical signs of meningeal infection is a definite indicator of viral meningitis. A serum CRP level of more than 48mg/l with clinical signs of meningeal infection is a definite indication of bacterial meningitis. Serum CRP has 68% predictive value in adults. The rapid differentiation facilitates an early, accurate and appropriate therapy thereby reducing the mortality and morbidity rates, the overall cost of the treatment and the duration of hospitalization. Serum CRP can be used as the best and most sensitive bedside prognostic indicator of bacterial infections. Meningeal infections have a definite male predominance. Altered level of consciousness at the time of admission is associated with bad.

Prognosis and high case fatality rate (28%). Fever is the commonest presenting feature followed by altered sensorium, symptoms of increased intracranial tension and seizure among neurological deficits, hemi paresis, VIth cranial nerve palsy and VIIth cranial nerve palsy were found to be common. The earlier the recognition of bacterial meningitis and more rapid the institution of antimicrobial therapy the better the chance of a favourable outcome. Therefore, the serum C-reactive protein estimation is most useful in differentiating bacterial meningitis from viral meningitis, especially for developing countries like India, even in peripheral health centers.

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