THE SIGNIFICANCE OF SERUM C-REACTIVE PROTEIN ESTIMATION IN ACUTE MENINGITIS IN ADULTS
Konatham Rambabu1, M. K. M. Kathyayani2

HOW TO CITE THIS ARTICLE:
Konatham Rambabu, M. K. M. Kathyayani. “The Significance of Serum C-Reactive Protein Estimation in Acute Meningitis in Adults”. Journal of Evidence based Medicine and Healthcare; Volume 2, Issue 30, July 27, 2015; Page: 4468-4480, DOI: 10.18410/jebmh/2015/630

ABSTRACT: In the study of 50 cases of acute meningitis the following observations were made in sex incidence, age, clinical presentation, CSF analysis and serum C reactive protein levels and prognosis. Serum CRP level of less than 6 mg/l with signs of meningeal infection is a definitive indicative of viral meningitis and CRP levels more than 48 mg/l with clinical signs of meningeal infection is definite indication of bacterial meningitis. AIM OF THE STUDY: to evaluate the efficacy of serum C-reactive protein in differentiating bacterial meningitis from viral meningitis.

INTRODUCTION: The evolution of clinical signs and symptoms produced by meningitis or encephalitis varies greatly. Few conditions in medicine require as rapid and accurate therapeutic intervention as 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 aetiology, 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 aetiological 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. Deivanayagam. N et al (1993)(1) Clinical Epidemiology Unit, Madras Medical College, have declared that in developing countries, differentiating bacterial meningitis from viral meningitis and tuberculous meningitis is not easy. (2) 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 Immuno Electrophoresis (CIE) of the CSF for the immunoglobulins, lactic acid, creatine phosphokinase is enzyme and C-reactive protein. Brown et al (1978).(3) Because of easy availability of the kit andsimplicity 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.

MATERIALS AND METHODS: Fifty cases with definite clinical signs and symptoms of acute meningitis were taken up for the study. All the cases have shown the clinical signs and symptoms of meningeal infection. The following clinical signs and symptoms were given at most importance for the selection of cases.
1. Fever of acute onset.
2. Neck Stiffness: Passive flexion of the neck is difficult or impossible.
3. Kernig’s sign: With the patient on supine posture, when the hip is fully flexed the passive extension of the patient’s knee, causes pain and spasm of the hamstrings in meningeal irritation affecting the lower part of the spinal subarachnoid space.
4. Brudzinski’s Sign:
   (i) Contralateral reflex or Sign: On passive flexion of the leg on one side, a similar movement occurs in the opposite leg.\(^4\)
   (ii) Neck Sign: When the neck is passively flexed, flexion of the hip and knee occur.
5. Symptoms of increased intracranial pressure like Headache, Vomiting.
6. Altered Sensorium: All the selected cases 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. In one case lumbar puncture was not done because of bilateral papilledema.

CSF Analysis:
   a. The cerebrospinal fluid was tested for a. Colour: Clear, turbid, Opalescent, High coloured and/or blood stained.
   b. Tension: Normal or elevated
   c. Cell count: Cerebrospinal fluid was stained for cell count and examined under High power field for rapid results.
   d. Staining: A drop of centrifuged CSF was placed over the glass slide, dried and stained for AFB and Gram’s stain.\(^5\)
   e. Cob web: 2ml of CSF was collected in a test tube and mounted in a rack. Examined after 24 hours for the presence of cobweb. If present, the precipitate was again centrifuged and stained for AFB.
   f. Culture: CSF was sent for culture and sensitivity.
   g. Biochemical Analysis: CSF was sent for estimation of globulin, proteins, sugar and chloride. 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.

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

1. Recent injury of any kind.
2. Recent surgery.\(^6\)
3. Patients in the immediate post-partum period,
4. Known case of Rheumatic Heart Disease (according to modified Jones Criteria).
5. Known case of Rheumatoid arthritis (according to ARA diagnostic Criteria).
6. Known case of acute or chronic glomerular nephritis and all cases of Genito- Urinary tract infection.
7. Focal infections like pneumonic consolidation, infections of skin etc.,

PRINCIPLE: Principle is based on a rapid agglutination procedure for the direct detection and semi-quantitation (on slide) of C-reactive protein (CRP). The reagent, a latex particle suspension coated with specific anti-human C-reactive protein antibodies, agglutinates in the presence of CRP in patient serum.

REAGENTS
a. CRP LATEX: 1 x 1.5 ml/ 1 x 2.5 ml Suspension of polystyrene particles coated with anti-human CRP goat antibodies.
b. CRP POSITIVE CONTROL 1 x 0.5 ml Human pooled serum.
c. CRP NEGATIVE CONTROL 1 x 0.5 ml Human pooled serum.\(^3\)
d. GLYCINE SALINE BUFFER CONCENTRATE 1 x 5 ml Dilute 1:10 with distilled water.
e. Accessories For 30 T For 50 T Reaction slide 1 1.
   Plastic Drophers 30 50.
   Applicators sticks 30 50.
   Rubber Teat (Blue) 1 1.

PRECAUTION: The reagents of human origin, used in the study have been tested and found to be negative for the presence of antibody to HIV I and II as well as for HBs Ag and HCV antibody. The reagent and controls contain less than 0.1 % of sodium aside.

STORAGE AND STABILITY:
1. Stored at 2-80C.
2. Protected from light.
3. Stability as per kit used.

PREPARATION OF GLYCINE SALINE BUFFER: Glycine saline buffer was prepared by adding 45ml of distilled water to 0.5ml of concentrate glycine saline buffer.\(^7\)

SENSITIVITY: The CRP sensitivity has been adjusted to detect a minimum of 0.6 mg/dL in the undiluted sample.

SAMPLE: Fresh serum sample (Free of haemolysis).
ORIGINAL ARTICLE

QUALITATIVE TEST: All reagents, as well as the sample were allowed to reach room temperature, and mixed well, before use.

1. One drop of serum sample was placed on to the slide with the help of disposable serum dropper.
2. One drop of CRP-Latex antigen was added to the above drop and mixed well with disposable applicator stick.
3. Slide was gently rocked to and fro for 2 minutes and examined under a good light source for agglutination within 2 minutes.
4. For positive and negative controls, the same procedure as mentioned above, was followed, by taking control serum from respective vials. (8)

RESULT AND INTERPRETATION:

POSITIVE RESULTS: The presence of agglutination indicates concentration of CRP in the sample equal to or greater than 0.6mg/dL.

NEGATIVE RESULTS: The lack of agglutination indicates a CRP concentration lower than 0.6 mg/dL. In the sample.

SEMI–QUANTITATIVE TEST–BY SERIAL DILUTION METHODOLOGY:

1. 50μL dilute Glycine saline Buffer was placed on to each of five circles of the slide.
2. Using a 50μL (0.05 mL) micropipette, 50μl (0.05ml) of the serum sample was added to the drop of Glycine – Saline Buffer in 1st circle.
3. Using the sample micro – pipette, the sample was mixed with saline by aspirating back and forth several times. 50μl (0.05ml) from 1st circle was aspirated and transferred to 2nd circle. The same operation was repeated up to the 5th circle. 0.05ml from 5th circle was aspirated and discarded. Following dilutions were obtained.
   Dilution: 1/2 1/4 1/8 1/16 1/32. (9)
4. One drop of CRP-latex Antigen was added, to each of the above circles and the slide was rocked gently to and fro for 2 minutes. Agglutination was observed under a good light source.

CALCULATIONS: Whenever S-CRP is negative or positive in 1:2 or 1:4 serum it is taken as <5mg/L and 6mg/L respectively. If positive, in 1:8 dilution, it is 12-18 mg/L and in 1:6 dilution as 24 – 48 mg/L. The reading is taken as >48 mg/l whenever it is positive in 1:32 dilution.

| Sl. No. | Dilution | Qualitative | Quantitative |
|--------|----------|-------------|--------------|
| 1      | 1/2      | (-)         | <5mg/l       |
| 2      | 1/4      | (+)         | 6-12mg/l     |
| 3      | 1/8      | (++)        | 12-24mg/l    |
| 4      | 1/16     | (+++)       | 24-48mg/l    |
| 5      | 1/32     | (++++)      | >48 mg/l     |

The value of S-CRP in differentiating bacterial from non-bacterial meningitis was cross checked with CSF studies (Sugar, Protein, AFB, gram stain) and serum & CSF cultures. (10)
ORIGINAL ARTICLE

- CSF analysis observed for bacterial meningitis was CSF Proteins > 45 mg/dl.
- CSF Sugars <40 mg/dl.
- CSF Cell count Raised with predominant polymorphonuclear (PMN) cells (Harrison 16th edn)

OBSERVATION AND RESULTS: In the study of fifty cases of acute meningitis admitted in Govt. Stanley Hospital, Chennai, the following observations were made in sex incidence, age, clinical presentations, CSF analysis, serum C-reactive protein level and prognosis of the illness as follows:

Sex Incidence: Fifty cases of acute meningitis infection have been observed. The study showed a male predominance of 56% while the female was 44%. (Table –1)

| Sl. No | Sex | Number of patients | Percentage |
|-------|-----|-------------------|------------|
| 1.    | Male | 28                | 56%        |
| 2.    | Female | 22               | 44%        |

Table 1: Sex Incidence in the Study

P value is <0.007.

Age Incidence: It is observed in the study that, 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. (Table – 2)

| Sl. No | Age in Year | Number of patients | Percentage |
|--------|-------------|--------------------|------------|
| 1.     | 13-20       | 16                 | 32%        |
| 2.     | 21-40       | 14                 | 28%        |
| 3.     | 41-60       | 16                 | 32%        |
| 4.     | >60         | 4                  | 8%         |

Table 2: Age incidence in the study

P value is <0.007.

Symptoms: The sequence of symptoms observed from the study was as follows. 98% (11) of cases presented with fever while 48% (12) presented with vomiting. (Table-3).

| Sl. No | Symptoms & Sign | Number of Patients | Percentage |
|--------|-----------------|--------------------|------------|
| 1.     | Fever           | 49                 | 98%        |
| 2.     | Altered Sensorium | 41               | 82%        |
| 3.     | Head ache       | 30                 | 60%        |
| 4.     | Vomiting        | 24                 | 48%        |
| 5.     | Neck rigidity   | 50                 | 100%       |
| 6.     | Seizures        | 21                 | 42%        |
| 7.     | Neurological deficits | 20                | 40%        |
| 8.     | Abdominal pain & Diarrhoea | 5             | 10%        |

Table 3: Symptoms Table

J of Evidence Based Med & Hlthcare, pISSN- 2349-2562, eISSN- 2349-2570/ Vol. 2/Issue 30/July 27, 2015  Page 4472
The incidence of seizure were observed in 42%\(^{(1)}\) of cases, 40%\(^{(1)}\) had neurological deficits and 10%\(^{(5)}\) had abdominal pain and diarrhea.\(^{(18)}\)

**Meningeal Signs:** Neck stiffness was seen in all the fifty cases, as it was considered as the prime sign for the selection of cases. Thirty eight cases (76%) were found to have positive Kernig’s sign whereas Brudzinski’s sign was positive in thirty cases (60%).

**Papilledema:** Papilledema was present in seven out of fifty cases. Among them five belong to bacterial meningitis group, of which three expired. The other two who belong to non-bacterial group have recovered and are alive.

| Sl. No. | Fundus          | Number of patients | Percentage % |
|--------|-----------------|--------------------|--------------|
| 1.     | Normal          | 43                 | 86%          |
| 2.     | Papilledema     | 7                  | 14%          |

**Table 4: Fundus Examination**

**Neurological Deficit:**

**Abducent Nerve Palsy:** Of the fifty cases, five cases developed VI cranial nerve palsy. Among the five, the VI Cranial nerve palsy was unilateral in four and bilateral in one who has papilledema also. Three cases belonged to the bacterial meningitis group, of which two were having papilledema. One case belonged to the viral meningitis group, and one belonged to tuberculosis meningitis group. Of the five, two expired (Table 5).

| Sl. No. | Neurological Deficits       | Number of patients | Percentage % |
|--------|-----------------------------|--------------------|--------------|
| 1.     | Abducent nerve palsy        | 5 (3B, 1V,TB)     | 10%          |
| 2.     | Facial Nerve Palsy          | 4(1B,3V)          | 8%           |
| 3.     | Other Cranial Nerve Palsy   | 0                  | 0            |
| 4.     | Aphasia                     | 4(1B,2V, 1TB)     | 8%           |
| 5.     | Hemiparesis                 | 6(1B,5V)          | 12%          |
| 6.     | Quadriparesis               | 1(V)              | 2%           |

**Table 5: Neurological deficits**

B – Bacterial, V-Viral, TB – Tubercular.

**Facial Nerve Palsy:** Four cases were found to have unilateral VII cranial nerve palsy of which three belonged to the viral meningitis group, two of them presented with papilledema, hemiparesis and aphasia. All of them survived. (Table 5).

**Hemiparesis:** Hemiparesis was observed in six cases. (Table - V). One belonged to the bacterial meningitis group, who had papilledema and VI cranial palsy expired. Five cases belonged to the viral meningitis group. Two had associated papilledema, VII cranial nerve palsy and aphasia.

**Aphasia:** Four cases developed aphasia during the course of illness. Two had associated papilledema, VII cranial nerve palsy and hemiparesis. Of these, one was bacterial, one tubercular and two of viral origin. (Table 5).
Quadriparesis: One case belonged to the viral meningitis group, developed spasticity in all the four limbs, (Table 5) soon became unconscious and expired. No other neurological abnormalities were observed.

S-CRP and Mortality: 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 (18%) expired. Nine cases (18%) were having S-CRP of 6 mg/L level, of which 2 cases (4%) expired. Eight cases (16%) had S-CRP levels 12-18 mg/L level of which there was no mortality. Nine cases (18%) had S-CRP levels 24-48 mg/L, of which one died (2%) and eight cases (16%) were having strongly positive levels of > 48 mgms/ L indicating a definite bacterial infection, of which two cases (4%) expired. (Table 5).

| Sl. No | s-CRP (mg/l) | s-CRP Qualitative | Number of Patients | Death | Percentage |
|-------|-------------|------------------|--------------------|-------|------------|
| 1.    | <6          | -                | 16                 | 9     | 18%        |
| 2.    | 6-12        | +                | 9                  | 2     | 4%         |
| 3.    | 12-24       | ++               | 8                  | 0     | 0%         |
| 4.    | 24-48       | +++              | 9                  | 1     | 2%         |
| 5.    | >48         | ++++             | 8                  | 2     | 4%         |

Table 6: Serum – CRP and mortality(1)

In 25 cases, S-CRP levels were less that 12 mg/l. of these, 16 cases had SCRP <6 mg/l and 9 cases had SCRP 6-12 mg/l. All these 25 cases were having clinical signs in favour of meningitis or meningoencephalitis and CSF formula in favour of viral infection. The CSF glucose level in all the 25 cases was near normal limit and protein is normal or slightly elevated, indicating the possibility of viral infection.

S-CRP and Prognosis: In all fifty cases, S-CRP was done first, at admission, second after three days of hospitalization and the third one before discharge, so as to assess the prognosis of the patient.

Of these, sixteen had shown a rapid fall in S-CRP levels and a very good prognosis. The S-CRP indicated good prognosis earlier than other investigations. One case was having sustained high S-CRP levels and expired despite treatment.

In another eight cases that were positive for S-CRP levels subsequent tests revealed negativity and this again indicated a good prognosis. In the remaining twenty five cases, the S-CRP levels were negative, subsequently tested again to rule out false negativity but it revealed the same results.(19)

Level of Consciousness and Mortality: It is observed from the study that 4 cases were unconscious at the time of admission. Of them, two between 21-40 years, had history of unconsciousness for 6 hrs. One of them had a S-CRP level of >48 mg/L and the CSF picture in favour of bacterial infection, showed a very good improvement from treatment with antibiotics.
Table 7: Level of consciousness at admission

| Sl. No. | Level of conscious | Number of patients | Percentage % |
|---------|-------------------|--------------------|--------------|
| 1.      | Conscious         | 9                  | 18%          |
| 2.      | Semiconscious     | 37                 | 74%          |
| 3.      | Unconscious       | 4                  | 8%           |
| 4.      | Semiconscious later became unconscious | 12 | 24% |

The other one, of the 13-20 age group and a S-CRP level of <6mg/L and a CSF picture in favour of viral infection, was treated with antibiotics and other supportive measures showed a good prognosis. The remaining two cases between 21-40 years who were admitted in unconscious state, developed unconsciousness 48 hrs before admission which showed a delay in admission. One of them had a S-CRP level of <6mg/L and CSF picture in favour of viral infection and not improved with adequate supportive measures, had only two days of hospitalization and expired. (Table 7).

The other one was having Cheyne-Stoke breathing with papilledema and other clinical signs in favour of CNS infection. The C.T. scan was normal, but the serum C-reactive protein was found to be very high > 48 mg/L. Thirty seven cases were found to be semiconscious on admission. The symptom duration before admission varied from few hours to three weeks. Twenty five cases were showing improvement with antibiotic treatment. Twelve cases became unconscious soon after the admission and expired despite all possible supportive measures. Of the twelve cases, eight cases were of adolescent (13-20 years) age group, three cases were between 20-40 years and one between 40-60 years.

Table 8: Level of consciousness and mortality

| Sl. No. | Level of conscious | No. of patients | Death | Percentage % |
|---------|-------------------|-----------------|-------|--------------|
| 1.      | Conscious         | 9               | 0     | 0            |
| 2.      | Semiconscious     | 13              | 2     | 4            |
|         | a. Disoriented    | 13              | 3     | 6            |
|         | b. Not obeying commands | 11 | 9 | 18 |
|         | c. Became unconscious not responding to painful stimuli. | |
| 3.      | Unconscious       | 4               | 2     | 4            |

Among the three adults, one was a known case of pulmonary tuberculosis (by sputum examination). His CSF picture was in favour of a definite tuberculous meningitis positive for cobweb AFB stain and S-CRP levels of 24-48 mgs/L. He was not showing any improvement with adequate antibiotics, antituberculous drugs and steroid therapy. Patient developed hydrocephalus, confirmed by C.T. scan and expired. The other two adult cases were having a CSF picture in favour of viral infection and this is supported by low S-CRP levels of <6 mg/L. They did not improve with antibiotic treatment and expired. (Table 8).
Cerebrospinal Fluid: Lumbar puncture was done in all fifty cases. In seven cases, guarded lumbar puncture was done due to papilledema and bad clinical condition. In two cases the AFB staining was positive (4%).

Ten cases had Gram positivity and seven had Gram negativity. All the seventeen were observed to have low CSF sugar value and with empirical treatment all the patients had good prognosis. Also all the 8 persons with S-CRP of 12-24 mg/l were Gram negative.

Seven cases were observed to have positive cob-web of which two were AFB positive. All the seven cases were found to have elevated proteins, normal or low sugar values in the CSF. The CSF culture was positive in twenty five of the fifty cases.(20)

CSF Cell Count: There was significant pleocytosis in thirty six cases (of which seventeen cases were having elevation of polymorphonuclear cells which are usually absent in normal CSF, and nineteen cases had lymphocyte predominance. Ten cases were found to give positive results for Gram’s staining as already stated. Eight cases were having S-CRP levels of more than 48 mg/L, 9 cases were having S-CRP level between 24 to 48 mg/L, 12 to 18 mg/L in 8 cases, 6mg/l in one case and <5mg/L in four cases. One of the four cases with CRP levels <5mg/l, three cases had a poor prognosis and expired. All the seventeen cases showed a marked fall in CSF sugar levels and elevated protein levels.

The other cases with S-CRP between – to ++, were having elevated CSF lymphocytes. In these groups, two cases were positive for AFB staining and seven for cob web suggestive of tuberculosis meningitis. Five cases had levels of 24-48mg/L of which, one case had a bad prognosis, developed hydrocephalus and expired. In five cases the S-CRP levels were between 12 to 18 mg/L and 6 to 12mg/L in six cases of which one case expired who had elevated protein and normal sugar in CSF. Seven cases had S-CRP levels of <5mg/L of which three cases expired, all of them showed a near normal protein and sugar levels in CSF.(21)

Positive Predictive Value Estimation: Twenty five cases had S-CRP of >12 mg/l. Of these, seventeen cases were diagnosed to have bacterial meningitis and eight cases of tuberculous meningitis.

\[ PPV = \frac{TP}{TP+FP} \]
\[ = \frac{17}{17+8} \]
\[ = 17/25 \]
\[ = 68\%. \]

PPV - Positive predictive value TP – True positive FP – False Positive.

Sex and Mortality: The total mortality rate of the study was 28% (14 cases). Of which 18% (9 cases) were males and 10% (5 cases) were females. (Table 9).

| Sl. No | Prognosis | Sex | Number | Percentage % |
|-------|-----------|-----|--------|--------------|
| 1     | Survived  | M   | 19     | 38%          |
|       |           | F   | 17     | 34%          |
| 2.    | Dead      | M   | 9      | 18%          |
|       |           | F   | 5      | 10%          |

Table 9: Sex and Mortality
Of the 72% cases who survived, 38% (19 cases) were males and 34% (17 cases) were females. It shows a male predominance in mortality rate also.\(^{22}\)

| Sl. No. | Age in years | Number of Patients | Death | Percentage % |
|---------|--------------|--------------------|-------|--------------|
| 1.      | 13-20        | 16                 | 8     | 16%          |
| 2.      | 21-40        | 14                 | 2     | 4%           |
| 3.      | 41-60        | 16                 | 2     | 4%           |
| 4.      | >60          | 4                  | 2     | 4%           |

Table 10: Age group and mortality

As shown in the Table – X, 8 cases of 13-20 years of age group expired, constituting a mortality rate of 16% and 4% each in all other age groups.

**DISCUSSION:** 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.

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.

**Sex Incidence:** 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, 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. 1991 26 in his study on viral meningitis.

**Age Incidence:** 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,

**Symptoms:** It is observed in the study that, fever is the most common presenting feature (98%) of meningeal infection compared to the 85%.

**Meningeal Signs:** Neck stiffness was present in all cases as it was considered as the prime sign for the selection of cases. The Kernig’s sign was present in 76% cases and the Brudzinski’s sign in 60% of cases

**Neurological Deficits:** It is observed in the study that, hemiplegia with facial nerve involvement, was the commonest neurological deficit with an incidence of 12 percent isolated abducent nerve palsy unilateral or bilateral having an incidence of 10% tops the cranial nerve deficits whereas isolated facial nerve palsy and isolated aphasia were found in 8% of cases each and Quadriparesis in one case. The overall neurological deficits in the study was 40 percent
Serum C-Reactive Protein: 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, 17 cases were diagnosed as bacterial meningitis, another 33 cases as meningitis due to non-bacterial causes. In patients with bacterial meningitis eight cases were having the S-CRP levels of more than 48 mg/L. The S-CRP levels of 24-48 mg/l, were found in 9 cases. In eight cases, S-CRP was 12-24 mg/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 <5 mg/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 that 35 mg/dl. was taken as evidence of bacterial aetiology.

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 48 mg/l indicates a definite bacterial aetiology.

S-CRP and Prognosis: On serial monitoring, it is observed that a fall in the S-CRP concentration is a sensitive indicator of recovery from meningeal infections long before other signs. Of the eight cases who had S-CRP level of more than 48 mg/L, 6 patients had a good prognosis which has been demonstrated by repeated S-CRP and by repeated lumbar puncture. 2 cases expired within 2 days of hospitalization despite adequate antibiotic therapy, they were unconscious at admission and had poor general condition. To assess the prognostic value of S-CRP, the test was done first at admission, the second, 3 days after hospitalization and the third one before discharge. Six cases showed a rapid fall of more than 10 mg/L in S-CRP levels had a very good prognosis. In one case the S-CRP levels showed a sustained high level. The repeated CSF examination showed near normal values in favour of a good prognosis. But the patient developed hydrocephalus and expired despite all possible supportive measures. This shows that S-CRP is a better prognostic indicator than repeated CSF examination, thereby reducing the repeated invasive techniques.

Mortality: It is observed from the study that, the overall case fatality rate was 28% (14 cases). All these cases were found to have altered sensorium at the time of admission. This indicates an increase in case fatality rate in patients who had a altered level of consciousness at the time of admission.

CONCLUSIONS:
1. Estimation of C-reactive protein in serum is the cheapest, sensitive and specific test to differentiate bacterial from viral infections.
2. It is a simple qualitative as well as quantitative test and can be done as a bed side investigation.
3. With serum C-reactive protein, a definite aetiological diagnosis can be made rapidly at the time of admission itself.
4. A serum CRP level of less than 6 mg/l with clinical signs of meningeal infection is a definite indicator of viral meningitis.

5. A serum CRP level of more than 48 mg/l with clinical signs of meningeal infection is a definite indication of bacterial meningitis.

6. Preadmission treatment with steroids causes a fall in CRP levels in bacterial meningitis.

7. Serum CRP has 68% predictive value in adults.

8. 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.(23)

9. Serum CRP can be used as the best and most sensitive bedside prognostic indicator of bacterial infections.

10. Meningeal infections have a definite male predominance.

11. Altered level of consciousness at the time of admission is associated with bad prognosis and high case fatality rate (28%).

12. Fever is the commonest presenting feature followed by altered sensorium, symptoms of increased intracranial tension and seizure. Among neurological deficits, hemiparesis, 6th cranial nerve palsy and 7th cranial nerve palsy were found to be common.

13. The earlier the recognition of bacterial meningitis and more rapid the institution of antimicrobial therapy the better the chance of a favourable outcome.

14. 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 centres.(24)

REFERENCES:

1. Deivanayagam, N., et al; Clinical Epidemiology Unit, Madras Medical College, India. Evaluation of CSF variables as a diagnostic test for bacterial meningitis. J Trop Pediatr 1993 Oct: 39 (5); 284-7.

2. Aehar, S.T. RamaRao G et al; Meningitis in Infancy and childhood other than tuberculous meningitis, Indian J. Pediatr 2953; 20; 55-59.

3. Brown, R.L. Zinner, S.H. Meglio, F.D. et al: Counter-current immunoelectrophoresis in the diagnosis of viral infections of the central nervous system J. Infect Dis., 138; 911-9, 1978.

4. Benjamin. D.R. Opheim, K.E: is CRP useful in the management of children with suspected bacterial meningitis-Am J Clin Pathol 1984; 81; 779-782.

5. Bohr, V., et al; Diagnostic procedures and the impact of preadmission antibiotic therapy J. Infect 1983; 7; 193-202.

6. Briem M-H., et al; Creatine Kinase isoenzyme BB in CSF from patients with meningitis and encephalitis. J infect Dis 148; 180, 1983.

7. Brown, K G E; Meningitis in Queen Elizabeth Central Hospital Balantyre, Malawi. East Afr. Med J 1975; 52: 376-3, 9.

8. Carl-Bortil Laurell-Acute phase proteins a group of protective proteins – Recent advances in Clinical Biochemistry-1985., 118., J. Infectr. Dis 151: 854, 1 1985.

9. Choi, C.; Bacterial Meningitis in St. Mary’s Medical Center, Long beach, California, Clin Geriatr Med 1992 Nov; 8(4): 889-902, 1992. 54.
10. Chakarvarthu, A.K., Chakravarthu, S.K. Charkaravarthy, M.S., Japanese Encephalitis in Assam, Indian Journal of Public Health 1980 XXX 1:1.
11. Indian council of medical Research; Bulletin March 1975.
12. Diculencu D, Miftode E, Turcu T, Buiac D. The value of C-reactive protein for the differentiation of bacterial meningitis from viral meningitis, Rev Med chiv soc Med Nat Iasi, 1995 j-an-june, 99 (1-2): 144-50.
13. Feigin, R d., et al; Diagnosis and management of meningitis. pediatr Infect Dis. J 11:785, 1992.
14. Defour, J F., et al; Meningitis in adults in Geneva. Schweiz Med Wochenschr Suppl. 1991; 35; 1-37.
15. Pomeroy, L S., et al; Seizures and other neurological sequelae of bacterial meningitis in children N Engl J med 323; 1651, 1990.
16. swartz, M N., Dodge, P R., et al., Bacterial meningitis review of selected aspects; N. Enmgl J Med 1965,272:725-730.
17. Dastur, D.K. Lalitha, V.S., et al: The many facts of neurotuberculous and pathology, prognosis., Neuropathol, 2:351-408. 1973.
18. Deivanayagam, N. et al; Bacterial meningitis diagnosis with Latex agglutination tests and Clinical features, Prognosis, Indian Pediatr 1993 Apr; 30(4) 495-500.
19. Gevold.H, H E., Kierulf, P., et al., Acute phase reactants and interleukin 6 and effects of high dose corticosteroids. Eur J. Surg 1992 Jun-Jul; 158 (6-7); 339-45.
20. Gopal, V., Bisno, AL., et al; Fluminant pneumococcal infections in normal. Aspleenic hosts. Archives of internal medicine 137:1526-1530., 1997.
21. Government of India, Ministry of Health and Family Welfare 1993.
22. Gupta, D., The role of CRP measurements in serum and CSF in meningitis. Thesis submitted for M.D (paed) AIIMS, New Delhi 1987.
23. Japanese encephalitis; world organization for animal health (OIE) June 3, 2003; 1-3.
24. Jaye DL, Waites KB-Clinical application fo C-R-P in pediatr. Infect. Dis J 1997; 16: 735-44.

AUTHORS:
1. Konatham Rambabu
2. M. K. M. Kathyayani

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of General Medicine, Andhra Medical College, Visakhapatnam.
2. Assistant Professor, Department of General Medicine, Andhra Medical College, Visakhapatnam.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Konatham Rambabu,
Associate Professor,
Department of General Medicine,
Andhra Medical College,
Visakhapatnam.
E-mail: rambabu.konatham@gmail.com

Date of Submission: 23/07/2015.
Date of Peer Review: 24/07/2015.
Date of Acceptance: 26/07/2015.
Date of Publishing: 27/07/2015.