

**CLINICO-BACTERIOLOGICAL STUDY OF PYOGENIC MENINGITIS WITH SPECIAL REFFERANCE TO C-REACTIVE PROTEIN IN CEREBRO SPINAL FLUID**

K. Koteswara Rao<sup>1</sup>, A. Krishna Prasad<sup>2</sup>, K. Adi Reddy<sup>3</sup>, Solomon Saawan P<sup>4</sup>, Krishna Kumari Agarwal<sup>5</sup>, S. Anusha<sup>6</sup>

**HOW TO CITE THIS ARTICLE:**

K. Koteswara Rao, A. Krishna Prasad, K. Adi Reddy, Solomon Saawan P, Krishna Kumari Agarwal, S. Anusha, "Clinico-Bacteriological Study of Pyogenic Meningitis with Special Refferance to C-Reactive Protein in Cerebro Spinal Fluid". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 77, September 24; Page: 13459-13469, DOI: 10.14260/jemds/2015/1928

**ABSTRACT:** Pyogenic meningitis is one of the most acute dramatic disease which can occur at all ages and is a potentially curable one. 80% of pyogenic meningitis cases occur in children.<sup>1</sup> it is 100% fatal if untreated and survivors are left with major intellectual, psychiatric and neurological handicap. The present study was undertaken in order to find out the age and sex distribution, incidence of presenting features, rapid and confirmatory diagnosis of pyogenic meningitis. We are frequently posed with problems in differentiating between tuberculous meningitis and partially treated pyogenic meningitis, because of the negative results of Gram's staining and culture.<sup>2</sup> The estimation of C-reactive protein in CSF, a rapid and highly sensitive tool, has been used to differentiate them.<sup>3</sup> The specificity of CRP test was found out by estimating CRP in CSF of twenty patients with various neurological disorders other than pyogenic meningitis.

**KEYWORDS:** Meningitis, CSF, CRP, CNS.

**INTRODUCTION:**

**Study Method:** The study includes children less than 12 years of age with suspected pyogenic meningitis, admitted to ICU and wards of department of Pediatrics, Government General Hospital, Kakinada, during the period from Sep. 2014 to Feb. 2015. This is a Prevalence study. The study includes 50 children.

**RESULTS:**

- Pyogenic meningitis occurred most frequently in the 1st year of life,<sup>4</sup> constituting 68% of cases in the present study. 12 cases were below 2 months of age (24%), 22 cases belonged to 2 months to 1 year.
- In the present study, slightly male predominance was seen.
- According to I.A.P classification of nutritional status, 44% patients were normal and remaining shows malnutrition.
- Fever was the most common accounting for 90% of the patients.<sup>5</sup> Convulsions were present in 70%, refusal of feeds in 54% and altered sensorium in 54% of the cases.
- 70% of the patients presented during the first 6 days of the disease. 38% within 72 hrs.
- 76% of patients had altered sensorium and 24% of patients were conscious and coherent. Altered sensorium was observed in 88% of the patients less than one year of age where as older age group (1-12yrs) showed an incidence of 50%.
- Majority of patients with pyogenic meningitis had polymorph cell count.<sup>6</sup> of 100-5000 mm<sup>3</sup> in CSF. Only 2 patients had less than 100 cells/mm<sup>3</sup>.

## ORIGINAL ARTICLE

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- Out of 50 cases, organisms were isolated from CSF in 22 cases (44%). Among them, with proven positive bacterial culture, 11 cases (50%) were due to pneumococcus, especially in older age group.
- Protein level in CSF was raised in all cases. Majority of the patients had protein content between 100 - 250 mg/dl in CSF. Pandy's test was positive in all cases.<sup>7</sup>
- Blood culture isolated the organisms in 14% (7 cases) of patients in which most common organism was Streptococcus.<sup>8</sup>
- Among the 50 cases of pyogenic meningitis studied in the present series, CRP was done in 44 cases, out of which 30 cases showed positive reaction to CRP.

**CONCLUSION:** Pyogenic meningitis is still one of the commonest central nervous system infection. Incidence of pyogenic meningitis is more common in early age group and children belonging to low socioeconomic groups.<sup>9</sup> Fever, convulsions, altered sensorium, refusal of feeds and vomiting's were common modes of presentation. Mortality from pyogenic meningitis in the present study was 28.88% excluding the cases which had been discharged against medical advice. It is unfortunate that Gram's staining and CSF culture which are the definitive evidence of pyogenic meningitis are frequently negative in significant no of cases. Estimation of CRP in CSF was positive in 86% of clinical pyogenic meningitis and negative in all cases of various neurological disorders other than pyogenic meningitis indicating its sensitivity of 68% and specificity of 100%. It does not stand superior to the routine laboratory parameters in diagnosing a frank case of pyogenic meningitis but having an immense value if positive in differentiating between partially treated pyogenic meningitis and tuberculous meningitis because of its high specificity.

### **MATERIALS AND METHODS:**

**Source of Data:** All children less than 12 years of age with suspected pyogenic meningitis, admitted to ICU and wards of department of Pediatrics, Government General Hospital, Kakinada during the period from Sep. 2014 to Feb. 2015. The study includes 50 children.

**Sampling Method:** Random Sampling.

**Inclusion Criteria:** Presentation with complaints and features of persisting vomiting and fever, irritability and insomnia, fever or hypothermia, neurological deficits, umbilical infection, pyoderma or septicemia, bulging of anterior fontanelle, photophobia, petechiae over skin and mucosae, tremors and convulsions, history of prior lumbar punctures, sucking difficulties/refusal of feeds.<sup>10</sup>

**Exclusion Criteria:** Cases of Congenital CNS malformations, history of head trauma, intracranial space occupying lesions, convulsive disorders, and Drug withdrawal seizures are excluded from the study

**Method of collection of data:** Data was collected with detailed case taking and examination in all children (50) included in the study. Diagnosis was made based on the following criteria - Clinical examination and physical examination.

CSF analysis - included Colour, pressure, Pandy' s test, sugar (Benedict's), Protein and Sugar levels (Blood sugar was also obtained at the time of lumbar puncture for comparison), Cytology,

## ORIGINAL ARTICLE

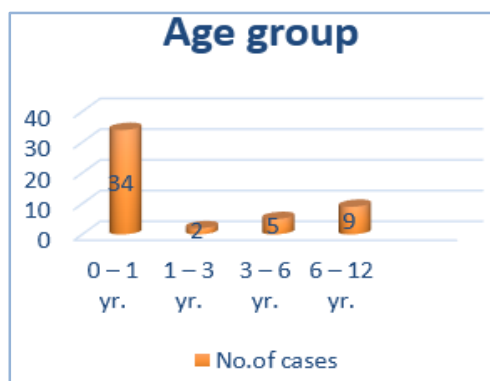
Gram's staining, Culture and C-reactive protein, Total WBC count, Blood culture, culture of any infective foci.

All cases of pyogenic meningitis diagnosed by the above criteria were clubbed in group I. A control group II was selected for estimation of CRP in the CSF from patients of neurological disorders other than pyogenic meningitis.

Detection of CRP in CSF. Kits used - Monozyme India limited. India.

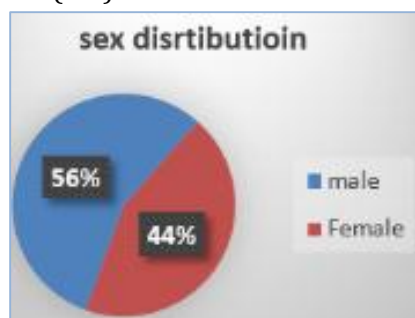
**RESULTS:** Clinical bacteriological study of pyogenic meningitis with special reference to CRP in CSF was done in 50 patients admitted in hospital. The results as follows.

- Age distribution:** Pyogenic meningitis occurred most frequently in the 1st year of life, constituting 68% of cases in the present study. 12 cases were below 2 months of age (24%), 22 cases belonged to 2 months to 1 year, 2 cases in the age group between 1 -3yrs. of life (4%), 5 cases in the age group between 3 -6yrs. of life (10%), 9 cases belonged to age group of 6 - 12 years (18%).



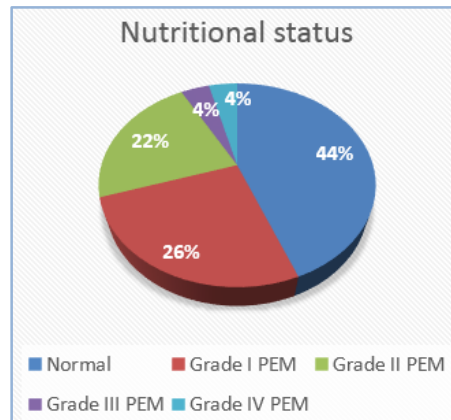
Age group	No. of cases	%
0 - 1 yr.	34	68
1 - 3 yr.	2	4
3 - 6 yr.	5	10
6 - 12 yr.	9	18
<b>Total</b>	<b>50</b>	<b>100</b>

- Sex distribution:** In the present study, slightly male predominance was seen. I.e. 28 cases were male and 22 were female. (4:3).<sup>12</sup>



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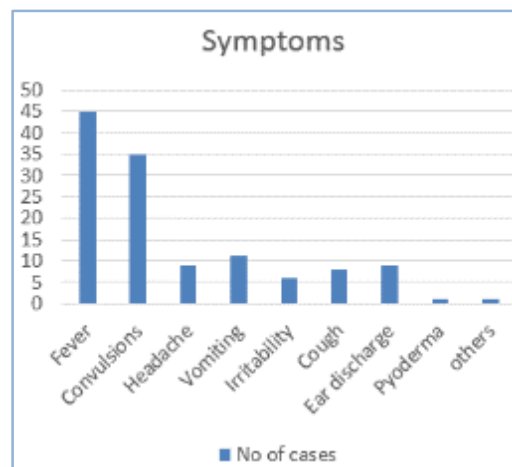
3. **Nutritional Status:** According to I.A.P classification of nutritional status, 44% patients were normal and remaining shows malnutrition.



Nutritional status	No. of cases	%
Normal	22	44
Grade I PEM	13	26
Grade II PEM	11	22
Grade III PEM	2	4
Grade IV PEM	2	4
<b>Total</b>	<b>50</b>	<b>100</b>

4. **Presenting symptom:** The major presenting symptoms were fever, convulsions, refusal of feeds and altered sensorium. Fever was the most common accounting for 90% of the patients. Convulsions were present in 70%, refusal of feeds in 54% and altered sensorium in 54% of the cases.

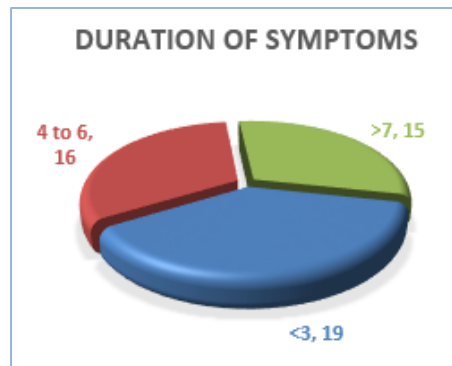
Fever and convulsions were observed in 90% and 70% respectively. But fever was observed in only 60% cases in age group less than 1 year. Refusal of feeds and altered sensorium were more common in the age group of less than 1 year. On the other hand, ear discharge, headache, vomiting and fever were significantly more in the age group of more than 1 year.



## ORIGINAL ARTICLE

Symptom	No. of cases	%
Fever	45	90
Convulsions	35	70
Headache	9	18
Vomiting	11	22
Irritability	6	12
Cough	8	16
Ear discharge	9	18
Pyoderma	1	2
others	1	2

5. **Duration of Symptoms:** 70% of the patients presented during the first 6 days of the disease. 38% within 72 hrs.



Duration(Days)	No. of cases	%
<3	19	38
4-6	16	32
>7	15	30
<b>Total</b>	<b>50</b>	<b>100</b>

6. **Physical signs:** The following physical signs were observed.

Physical signs	No. of cases	%
Altered sensorium	38	76
Bulging anterior frontonelle	19	38
Cranial Nerve Palsy Occulomotor	1	2
Abducent	1	2
Facial	6	12
Motor system Hemiplegia	4	8
Neck rigidity	26	52
Kernig's sign	18	36
Brudzinski's sign	11	22
Fundal changes papilledema	7	14
Subdural effusion	2	4

## ORIGINAL ARTICLE

76% of patients had altered sensorium and 24% of patients were conscious and coherent. Altered sensorium was observed in 88% of the patients less than one year of age where as older age group (1-12yrs) showed an incidence of 50%.

Bulging anterior frontonelle was seen in 38% of patients.

Cranial nerve palsy.<sup>13</sup> was seen in 14% of cases, one with Abducent palsy, one with Occulomotor and facial palsies and five with isolated facial palsy. Hemiplegia was noted in 8% of the cases.

**Spinal/Nuchal signs:** Neck stiffness was observed in 52% of all cases. 94% of more than one year age group showed this sign, in contrast to only 29.5% in less than one year age group Kernig's sign was observed in 36% of all patients. 87.5% of more than one year age group showed this sign, in contrast to only 12% in less than one year age group.

Brudzinski's sign was noted in 22% of total cases. 3% of less than one year age group showed this sign, in contrast to 62.5% of more than one year age group.

Papilledema was seen in 7 patients only Subdural effusion was noted in a seven month old child and a 12 years old child.

### 7. CSF analysis:

**Pressure:** It was observed that CSF pressure was raised in 62%of patients.

**Colour:** CSF was clear in 12% cases and remaining 88%showed an opalescent or turbid CSF.

**Cytology:** Cell count per mm<sup>3</sup> in the present series of patients were as follows.

Polymorph cell count	No. of cases	%
5-100	2	4
100-500	21	42
500-1000	22	44
1000-5000	5	10
<b>Total</b>	<b>50</b>	<b>100</b>

Majority of patients with pyogenic meningitis had polymorph cell count of 100-5000 mm<sup>3</sup> in CSF. Only 2 patients had less than 100 cells/mm<sup>3</sup>.

**Bacteriology:** Organisms isolated from CSF of cases of pyogenic meningitis as follows.

Age	Pneumococci	Menigococci	Streptococci	H.influenzae	E.coli	K. pneumoniae
< 2 months	-	-	2	-	2	-
2-12 months	3	-	-	4	-	1
1-3yrs	1	-	-	1	-	-
3-6yrs	2	-	-	1	-	-
6-12yrs	5	-	-	-	-	-
Total No	11	-	2	6	2	1
<b>Total%</b>	<b>50</b>	-	<b>9.09</b>	<b>27.27</b>	<b>9.09</b>	<b>4.54</b>

## ORIGINAL ARTICLE

Out of 50 cases, organisms were isolated from CSF in 22 cases (44%). Among them, with proven positive bacterial culture, 11 cases (50%) were due to pneumococcus, especially in older age group. Next common organism isolated was H. influenzae 6 cases (27.27%). H. influenzae meningitis occurred in the age between 2 months and 6 years. In less than 2 months age group, only in 4 cases organisms were isolated - Streptococcus and E. coli. Neisseria meningitis was isolated in a 7 years old child.

Gram's staining of CSF smear was positive in 36% (18 cases). 11 were Gram positive diplococci, 2 were Gram positive streptococci and 5 were Gram negative bacilli.

### 8. Biochemical analysis of CSF:

#### Proteins:

Protein level in CSF was raised in all cases. Majority of the patients had protein content between 100 - 250 mg/dl in CSF. There was less rise of protein in cases of early and partially treated pyogenic meningitis. Pandy's test was positive in all cases.

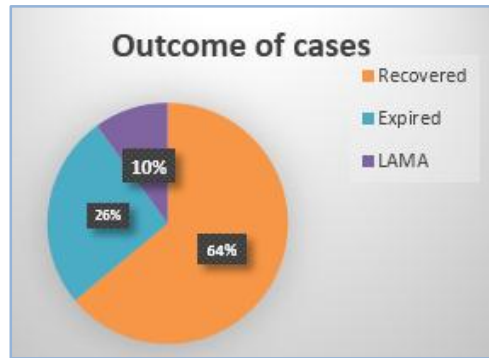
Protein content of CSF(mg/dl)	No. of cases	%
50-100	8	16
100-250	32	64
250-500	10	20
<b>Total</b>	<b>50</b>	<b>100</b>

**Sugar:** CSF sugar levels (Blood sugar levels was also obtained at the time of lumbar puncture for the comparison) was less than 20 mg/dl in 74% (37 cases) of patients. Partially treated cases had less fall in CSF sugar.

Sugar content (mg/dl)	No. of cases	%
0-10	23	46
11-20	14	28
21-40	11	22
41-60	2	4
<b>Total</b>	<b>50</b>	<b>100</b>

**Chlorides:** There was no significant change in chloride levels of CSF.

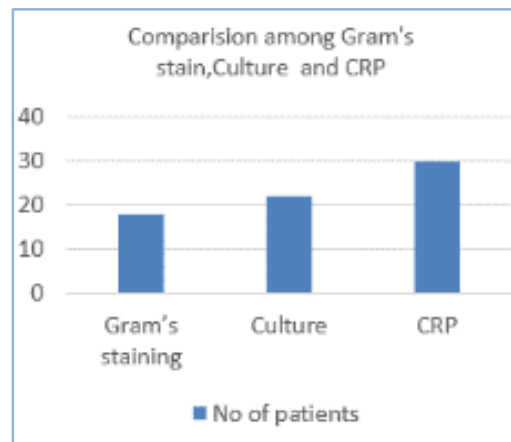
**9. Blood culture:** Blood culture isolated the organisms in 14% (7cases) of patients. Among the patients of age 0 - 2 months, who also had septicemia, streptococcus was isolated in three patients and E.coli was isolated in two. Pneumococcus was isolated in two patients in the older age group. The pus from the infective foci which could have been the likely source of pyogenic meningitis like ear discharge (9 cases), and pyoderma (1 case) were sent for culture. Organisms were isolated in three patients with otitis media and the same organism (pneumococcus) was isolated in CSF in two of them. In the third patient organism isolated was H.influenzae, however CSF was sterile.

**10. Outcome of Patients:**

Outcome	No. of cases	%
Recovered	32	64
Expired	13	26
Leaving against medical advice(LAMA)	5	10
<b>Total</b>	<b>50</b>	<b>100</b>

**11. C-Reactive protein in Cerebrospinal fluid:** Among the 50 cases of pyogenic meningitis studied in the present series, CRP was done in 44 cases, out of which 30 cases showed positive reaction to CRP.<sup>14</sup>

Among these 44 patients, a comparison was done between gram staining, positive CSF culture and positive CRP in CSF. Gram staining was positive in 36% and CSF culture isolated organism in 44% cases. In contrast to these, 68% of cases showed positive CRP in CSF.<sup>15</sup>

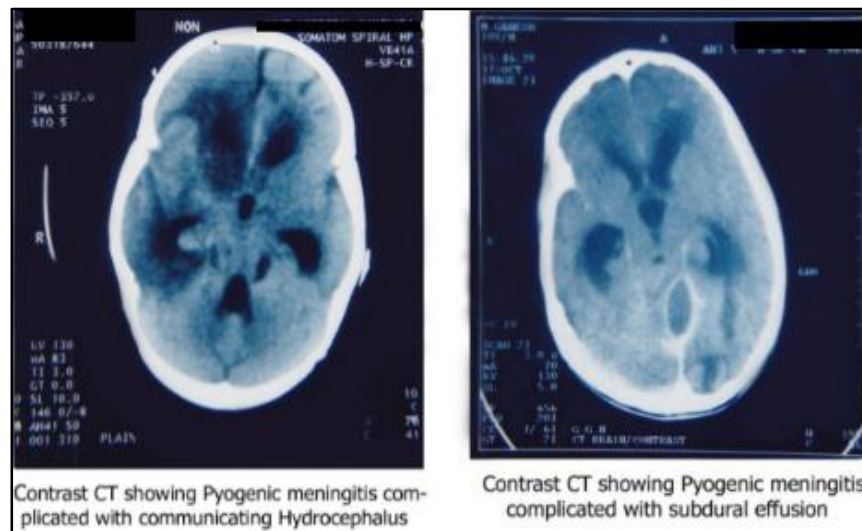


Parameter	No. of cases	%
Gram's staining	18	36
Culture	22	44
CRP	30	68



## ORIGINAL ARTICLE

Twenty patients with various neurological disorders other than pyogenic meningitis, as confirmed by clinical and laboratory parameters, were taken as control and their CSF was tested for CRP. All were negative.<sup>16</sup>



**DISCUSSION:** Pyogenic meningitis is one of the commonest type of neurological infections in the children in our country. Most of pyogenic meningitis cases were observed in less than one year age group. Male to female ratio in the present study was 4:3. Majority of them showed no evidence of malnutrition. Major symptoms are fever, convulsions, refusal of feeds, altered sensorium. Most of the patients presented within 6 days and 38% of them within 72 hours of onset of symptoms. Altered sensorium was seen more frequently, probably because this hospital is mainly a referral center and patients were being examined in the periphery hospitals and referred late in the course of the disease. Polymorph nuclear cells found in CSF analysis of all patients. Gram staining of CSF, CSF culture and blood culture are useful investigations in pyogenic meningitis. Mortality rate was 28.88%

## ORIGINAL ARTICLE

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in this study. When CRP positivity in CSF was compared with positive Gram staining and positive culture in CSF, it was found that CRP has higher sensitivity than both of them.<sup>17</sup> CRP was estimated in various neurological disorders other than pyogenic meningitis, where it was negative in all (specificity 100%).

### CONCLUSION:

- 50 cases of pyogenic meningitis in children were studied with special reference to estimation of CRP in CSF.
- Pyogenic meningitis is still one of the commonest central nervous system infection. Because of the absence of spinal/nuchal signs and high incidence of sequelae and mortality especially in infants, high index of suspicion is a must to make the diagnosis.
- Incidence of pyogenic meningitis is more common in early age group and children belonging to low socioeconomic groups.
- Fever, convulsions, altered sensorium, refusal of feeds and vomiting's were common modes of presentation.
- Mortality from pyogenic meningitis in the present study was 28.88% excluding the cases which had been discharged against medical advice.
- Detailed history, clinical examination when supported with the CSF analysis will establish the diagnosis in most of the cases. It is unfortunate that Gram's staining and CSF culture which are the definitive evidence of pyogenic meningitis are frequently negative in significant no of cases.
- Estimation of CRP in CSF was positive in 86% of clinical pyogenic meningitis and negative in all cases of various neurological disorders other than pyogenic meningitis indicating its sensitivity of 68% and specificity of 100%.
- It does not stand superior to the routine laboratory parameters in diagnosing a frank case of pyogenic meningitis but having an immense value if positive in differentiating between partially treated pyogenic meningitis and tuberculous meningitis because of its high specificity.

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### AUTHORS:

1. K. Koteswara Rao
2. A. Krishna Prasad
3. K. Adi Reddy
4. Solomon Saawan P.
5. Krishna Kumari Agarwal
6. S. Anusha

### PARTICULARS OF CONTRIBUTORS:

1. In charge Professor, Department of Pediatrics, Rangaraya Medical College, Kakinada.
2. Associate Professor, Department of Pediatrics, Rangaraya Medical College, Kakinada.
3. Junior Resident, Department of Pediatrics, Rangaraya Medical College, Kakinada.
4. Junior Resident, Department of ENT, Rangaraya Medical College, Kakinada.

### FINANCIAL OR OTHER

**COMPETING INTERESTS:** None

5. Junior Resident, Department of Pediatrics, Rangaraya Medical College, Kakinada.
6. Junior Resident, Department of Pediatrics, Rangaraya Medical College, Kakinada.

### NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. K. Adi Reddy,  
Junior Resident,  
Department of Pediatrics,  
Rangaraya Medical College,  
Kakinada.  
E-mail: adi9949844121@gmail.com

Date of Submission: 15/09/2015.  
Date of Peer Review: 18/09/2015.  
Date of Acceptance: 19/09/2015.  
Date of Publishing: 22/09/2015.